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Effectiveness and implementation of enhanced recovery after surgery programmes: a rapid evidence synthesis

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Abstract

Objectives

To assess the evidence on the impact of enhanced recovery programmes for patients undergoing elective surgery in acute hospital settings.

Design

Rapid evidence synthesis. Eight databases were searched from 1990 to March 2013 without language restrictions. Relevant reports and guidelines, websites, and reference lists of retrieved articles were scanned to identify additional studies. Systematic reviews, RCTs not included in the systematic reviews, economic evaluations and UK NHS cost analysis, implementation case studies and surveys of patient experience in a UK setting were eligible for inclusion.

Primary and secondary outcome measures

We assessed the impact of enhanced recovery programmes on health or cost-related outcomes, and assessed implementation case studies and patient experience. Studies were quality assessed where appropriate. using the CRD DARE critical appraisal process.

Results

Seventeen systematic reviews and 12 additional RCTs were included. Ten relevant economic evaluations were included. No cost analysis studies were identified. Most of the evidence focused on colorectal surgery. Fourteen innovation case studies and 15 implementation case studies undertaken in NHS settings described factors critical to the success of an enhanced recovery programme.

Evidence for colorectal surgery suggests that enhanced recovery programmes may reduce hospital stays by 0.5 to 3.5 days compared with conventional care. There were no significant differences in reported readmission rates. Other surgical specialties showed greater variation in reductions in length of stay reflecting the limited evidence identified.

Findings relating to other outcomes were hampered by a lack of robust evidence and poor reporting.

Conclusions

There is consistent, albeit limited, evidence that enhanced recovery programmes can reduce length of patient hospital stay without increasing readmission rates. The extent to which

managers and clinicians considering implementing enhanced recovery programmes can realise savings will depend on length of stay achieved under their existing care pathway.

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Strengths and limitations of the study

- Enhanced recovery programmes have been adopted with enthusiasm by the NHS as a means to achieving productivity gains and cost-savings. This evolution makes combining studies over different periods and interpreting results of earlier studies in relation to the current context more difficult.
- The evidence base to support such widespread implementation suggests possible benefits in terms of reduced length of hospital stay, fewer postoperative complications, reduced readmissions and improved patient outcomes.
- Althouth there is a reasonable volume of evidence evaluating enhanced recovery programmes in colorectal surgery, robust evidence is sparse. Optimal care is certainly the right thing to do, but the evidence does not identify which enhanced recovery programme elements and combinations of elements are most effective.
- Findings relating to other outcomes, costs of enhanced recovery programmes, experience in using the programmes, and patient experience were limited by generally poor quality evidence and poor reporting. As such, conclusions on which combinations provide greatest gains and how best to implement them cannot be made.

Introduction

The National Health Service (NHS) faces severe funding constraints now and in the medium term. The forecast reduction in resources provides an enormous challenge to NHS organisations and staff. Service redesign can save money and improve quality but much depends on how care is co-ordinated and the way services are implemented in a local setting.[1, 2] NHS decision makers need to consider not only the effectiveness and cost effectiveness of any initiative but also efficient implementation. Enhanced recovery programmes (also known as ERAS, fast track, multimodal, rapid or accelerated recovery programmes) seek to deliver an optimal pathway (covering the preoperative, intraoperative and postoperative periods) that is focused on optimal recovery and discharge for patients. The approach was pioneered in Denmark in the late 1990s for patients undergoing colorectal surgery[3] and is now spreading to other surgical pathways such as orthopaedic, urology and gynaecology.

Enhanced recovery programmes have been delivered in the UK NHS since the early 2000s. Implementation has to date been variable despite the support of the Department of Health and more recently the Royal Colleges. In 2011, 14 innovation sites were established as part of the Enhanced Recovery Partnership Programme. These sites acted as pathfinders for implementation; some sites were self-selecting and others were encouraged to join. The aim was to raise the profile, promote the benefits and inform the uptake of enhanced recovery for elective surgical care across the NHS. These sites had little or no experience in enhanced recovery pathways. It is likely that this variation seen across these sites reflects both the complexity of enhanced recovery programmes themselves and issues around implementing change in established surgical pathways . Differences in programme implementation may also reflect differences between surgical specialities. Set against the benefits of enhanced recovery programmes are concerns that discharging patients too soon after surgery could increase complications and readmissions, thereby worsening patient experience and potentially health outcomes, and increasing pressure on primary and/or secondary healthcare services.

Before embarking on adoption of an enhanced recovery programme, NHS managers and clinicians need to be fully aware of the strength of the underlying evidence. They need to have a clear understanding of how best to implement such programmes and the likely implications for service delivery within finite budgets and considering the need for equity of access. The aim of this project was to conduct a rapid synthesis of the evidence on the clinical and cost effectiveness, implementation, delivery and impact of enhanced recovery programmes in secondary care.

Methods

Eight databases, including DARE, NHS EED and MEDLINE were searched to from 1990 to March 2013 without language restrictions. The PROSPERO database was searched to identify ongoing systematic reviews. Relevant reports and guidelines were screened for further studies. Reference lists of retrieved articles, reviews and evaluations were scanned, and relevant individuals contacted for additional evidence.

Systematic reviews, RCTs not included in the systematic reviews, economic evaluations, and UK NHS cost analysis studies were included if they evaluated the impact of enhanced recovery programmes (encompassing more than one of the following elements: preoperative, intraoperative, and postoperative) on health or cost-related outcomes. Eligible studies included patients undergoing elective surgery in an acute hospital in the UK NHS or a comparable healthcare system. Comparators were only relevant to clinical and cost-effectiveness evaluations, and included conventional (usual/standard) care without a structured multimodal enhanced recovery patient pathway (as defined in the included studies). Case studies, impact assessments and surveys of patient experience that documented the experience of implementing enhanced recovery in a UK setting were also eligible.

Quality assessment of systematic reviews, RCTs and economic evaluations was based on existing CRD critical appraisal methods (http://www.crd.york.ac.uk/crdweb/HomePage.asp; CRD, 2009). Cost analysis studies, studies of patient experience, and case studies of implementation were not formally quality assessed.

All stages of the review process were performed by one researcher and checked by a second. Disagreements between reviewers were resolved by discussion or by recourse to a third reviewer where necessary.

The type and range of evidence precluded meta-analysis and we therefore performed a narrative synthesis, differentiating clinical outcomes (eg. mobilisation, mortality and morbidity, and length of hospital stay), patient-reported outcomes (eg. patient experience and satisfaction), resource use in secondary care (eg. workforce utilisation and costs), and implementation case studies.

Results

Seventeen systematic reviews[4-20] and 12 additional RCTs[21-33] were included in the evidence on clinical effectiveness (see Figure 1: flow diagram). The quality of the systematic reviews varied and the additional RCTs were considered to be at high risk of bias (see tables 1 and 2). One RCT was a four arm trial; this was the only multicentre trial, the remaining trials were small, single centre trials.[34] We included 15 case studies of implementation of ERAS in NHS settings, and evaluations of the 14 Enhanced Recovery Partnership Programme innovation sites. In addition, 10 relevant economic evaluations were also included (summary evidence tables are available on request from the review authors). Most of the evidence focussed on colorectal surgery.

Where reviews reported the number of included patients, sample sizes ranged between 99 and 5,747 patients in the ERAS group and between 99 and 1,062 in comparator groups. Most individual RCTs analysed fewer than 100 patients (range 44 to 597 patients). Where indications for surgery were reported in systematic reviews and individual RCTs, most trials were in patients with cancer. Where reported, patients were adults within similar age ranges.

The number and combination of ERAS elements varied considerably across all types of evidence; ranging from four to 14 elements across systematic reviews and from 10 to 14 elements across individual RCTs (see full report for details; in press). Follow-up was generally up to 30 days post discharge.

Despite the large number of studies, robust evidence was sparse (see tables 3 and 4; full outcome details are available in the full review; in press). Seven reviews in colorectal surgery performed meta-analyses and showed a significant mean reduction in primary or total length of stay that ranged from 1.56 days (95% CI 0.50 to 2.61 days)(18) to 3.75 days (95% CI 5.11 to 2.40 days).(Walter 2009) Evidence from individual RCTs in colorectal surgery also suggest reduced length of hostpital stay following an ERAS programme (mean length of stay 4.15 days to 6.43 days) compared to conventional care (mean length of stay 6.6 days to 11.7 days). There were no significant differences in reported readmission rates, but it was unclear how readmissions were defined and measured in the reviews and RCTs.

Other surgical specialties showed greater variation in reported reductions in length of stay, but this is likely to reflect the greater uncertainty due to the more limited evidence base for these specialties. Statistical heterogeneity varied between reviews and was often not formally explored, but may have reflected differences in ERAS protocols and surgical populations.

Deaths were rare and no significant differences between treatment groups were found in the systematic reviews and additional RCTs, regardless of surgical speciality. Morbidity was defined differently across systematic reviews and RCTs; rates between treatment groups were sometimes inconsistent, but generally indicated no statistically significant differences.

Mobilisation rates were inconsistent across systematic reviews, but most reported no significant differences in time to mobilisation between treatment groups. Mobilisation was rarely reported as an outcome in the additional RCTs.

Where systematic reviews and additional RCTs assessed quality of life and patient experience/satisfaction, equivocal findings were reported. Evidence on reintervention rates, pain and resource use was lacking in both systematic reviews and RCTs.

Other Reviews

A systematic review in colorectal surgery, identified after the last literature search, showed similar findings to the systematic reviews discussed above.[35] Mean length of primary hospital stay was statistically significantly reduced in ERAS patients; mean difference (MD) -2.44 (95% CI -3.06 to -1.83; 11 RCTs) but with significant statistical heterogeneity (I^2=88%). There was no evidence to suggest increased rates of readmissions, complications and mortality. Some of the individual RCT results for primary length of stay did not appear to be consistent with results reported in other systematic reviews, and this may have impacted on the estimated reduction in length of primary hospital stay.[35]

Two reviews[36, 37] focusing on individual ERAS elements were found and details can be found in the full review (in press).

Case studies

Ten of 14 UK NHS innovation sites provided adequate data for inclusion in this section.[38-40] Fifteen case studies of implementation of ERAS in NHS settings, and 11 NHS trusts (mostly in colorectal surgery) provided evidence relating to the implementation of an ERAS programme within their Trust.

There were variations in practice in terms of numbers and combinations of ERAS elements implemented; the most frequently implemented programme elements in the case studies were pre-admission information/counselling and early postoperative mobilisation. Available evidence did not address which enhanced recovery elements and combinations of elements were most effective. Substantial variation in what constitutes an enhanced recovery programme within and between different surgical specialities, and difficulties in implementing

certain ERAS components, suggest that the enhanced recovery pathway may be used as a framework and adapted to suit local situations. Evidence on compliance/adherence to enhanced recovery programmes was lacking.

Case studies identified the factors believed to act as barriers or facilitators to implementing an ERAS programme. Barriers to implementation included resistance to change from patients and staff, lack of funding or support from management,[38, 41-43] staff turnover, problems arising from poor documentation, the time required to complete documentation, and other practical issues.

Facilitators included the presence of a dedicated ERAS project lead/nurse to coordinate and sustain multidisciplinary working and continuity of the pathway, a multidisciplinary team approach, and continual education for staff and patients/patient representatives. One innovation site mentioned that it did not offer a seven day service for enhanced recovery due to staff resources. Patients operated on towards the end of the week may have to wait until after the weekend to be discharged if they need to be seen by any health care professionals or social services. The need to sustain multidisciplinary working means that, in the absence of 24/7 working for elective procedures, enhanced recovery programmes will tend to be front loaded into the start of the working week (typically Monday to Thursday). Recent evidence suggests a higher risk of death for patients who have elective surgical procedures carried out later in the working week and at the weekend,[44] the capcity to implement ERAS throughout the working week might ensure continuity of best care and help mitigate against such variation.

We included two published studies of patient experience of ERAS.[45, 46] Each study used qualitative research methods to analyse audiotaped material. The two studies provided limited evidence suggesting that patients who were willing to provide feedback took a positive view of their experience of treatment in an ERAS programme. The studies suggested that patients were willing to comment on their experience in a way that can help healthcare providers to identify areas for improvement.

Cost-effectiveness

Ten economic evaluations in adult populations undergoing various surgical procedures evaluated costs and outcomes over short time horizons (see Table 5).[47-56] All of the evaluations suggested that programmes that achieve a reduction in length of stay are cost saving, and are not to the detriment of patients in terms of complication rates, readmission and health-related quality-of-life. The quality of the clinical studies on which these evaluations were based was variable, but generally poor. The generalisability of the results of

these evaluations was limited by a lack of transparency in reporting, and the disparity in standard protocols and what had been evaluated across the settings made it unfeasible to select a cost-effective programme.

Discussion

Statement of Principal Findings

Overall, the systematic reviews and additional RCTs suggest that length of hospital stay is reduced in ERAS patients compared to patients receiving conventional care. The evidence was based mainly on colorectal surgery and the applicability of findings to other surgical specialities remains less clear. Evidence for colorectal surgery suggests that enhanced recovery programmes may reduce hospital stays by 0.5 to 3.5 days compared with conventional care.

There were marked differences in length of stay across reviews and individual studies regardless of speciality. These differences may reflect differences in ERAS protocols and health care systems and/or outcome definitions. This raises questions regarding the magnitude of effect of the ERAS protocols on length of stay, which may be overstated in some reviews.

The evidence suggests that ERAS programmes do not compromise patient morbidity, mortality and readmission rates but outcome definitions varied across reviews and individual studies. Such differences make it difficult to determine the reliability and generalisability of the findings.

Equivocal findings were reported for quality of life and patient experience/satisfaction but the evidence was based on few studies, which utilised various methods to measure these outcomes. The limited evidence precludes conclusions on the effects of ERAS protocols on pain, mobilisation and reintervention.

The implementation evidence included resource use in terms of the professionals involved in delivery of enhanced recovery programmes, but details were very limited and did not add to the evidence synthesis. Most case studies were uncontrolled and represent experiences of a sample of centres that chose to report their data; their outcomes may not be representative of those achieved elsewhere in the UK NHS. Their main value as evidence is the light they shed on NHS clinicians' perceptions of requirements for successful implementation and barriers to implementation of ERAS.

The impact of surgical experience and surgical volume on clinical outcomes was not explored and any implications of differences in these areas remain unknown. As enhanced recovery invariably targets the fitter, more mobile patient, frailer patients may not receive parity of access to what may be considered optimal treatment and management. Managers and clinicians considering implementing such programmes should think about the likely implication on equity of access. Whether inequity is an unintended outcome of enhanced recovery, merits further investigation.

Our review of the cost effectiveness literature suggests that enhanced recovery programmes that achieve a reduction in length of stay may save costs without detrimental effects on complication rates, readmission and health-related quality of life. However, generalisability of the results of the economic evaluations is limited by a lack of transparency in reporting, use of different settings and populations and variable methodology in analyses. Data were lacking for resource use associated with the programmes evaluated and could not usefully inform the review of economic evaluations. In addition, the clinical effectiveness of some of the programmes considered in economic evaluations was not based on robust evidence.

Strengths and weaknesses

The main strength of this study was our use of multiple approaches to acquire and synthesise evidence. The main limitations were poor methodological quality and poor reporting of the included studies, and the inherent difficulty of reviewing a complex intervention in different healthcare systems and surgical specialities. Current methods for synthesising such complex interventions are limited. The methodological limitations and are not discussed here as this was outside the scope of this project, but have been addressed in previous publications (eg. Noyes et al, 2013).[57] Another complication is that elements of early enhanced recovery programmes have become accepted practice within conventional care. This evolution makes combining studies over different periods and interpreting results of earlier studies in relation to the current context more difficult.

We found a large number of systematic reviews but there was substantial overlap in the included studies and evidence was not as abundant as the existence of multiple systematic reviews suggested. Most of the RCTs were small and not high quality. With the exception of one RCT, the remainder were single centre trials and therefore appear to have been undertaken to support implementation of an enhanced recovery programme in a specific setting rather than being planned as research studies. There were significant clinical and methodological differences between individual trials, and we therefore presented a narrative

synthesis. Relatively few trials were conducted in the UK and this may limit the generalisability of evidence to UK NHS settings.

Lack of evidence on important outcomes including pain and quality of life is also an issue for research in this field. Trials tended not to report on adherence to the planned enhanced recovery programme. Assessing adherence to interventions and the impact this has on health outcomes is an important issue which is often overlooked in studies, and is a limitation in the evidence base in this review.

An important feature of our review is the inclusion of evidence on the implementation of enhanced recovery programmes in the UK NHS. This evidence has not been synthesised previously and the original programme webistes are archived, so future access is not assured. By summarising this evidence, we have ensured that the main findings continue to be publicly available. We sought evidence on the experience of health professionals and patients of a broad range of sources and study types. Important themes emerged from this evidence that may be of value for implementing and sustaining enhanced recovery programmes in UK NHS settings. Due to the rapid nature of the evidence synthesis, the list of sources searched to identify data on implementation and delivery of enhanced recovery programmes was not exhaustive and we acknowledge that relevant evidence may have been missed. Indeed, evidence from Scotland has been noted and eligible case studies have been identified from the NHS Scotland Quality Improvement Hub website. It should be noted that these are as limited as those included in the review.

However, case studies are susceptible to risk of bias. Use of a standard reporting format was a potential strength of the case studies but variation in what each site actually reported (particularly in terms of evidence of benefit from the introduction of enhanced recovery programmes) reduced the usefulness of the evidence.

We sought to incorporate published and unpublished evidence on patient experiences and views of enhanced recovery programmes. Evaluation of patient experience of care is increasingly important for the NHS, especially in view of unacceptable failures of care such as those highlighted in the Francis Report.[58] Though the evidence was generally positive for enhanced recovery, it was limited by a shortage of studies that used validated measures of patient experience and by study designs that could bias results in favour of enhanced recovery.

A further strength of this study was the consideration of cost-effectiveness evidence, but the nature of the evidence did not permit any analyses. There is a clear need to capture better

evaluated data on costs and benefits of enhanced recovery programmes from a clearly stated perspective.

Implications for healthcare

Overall, there is consistent, albeit limited, evidence that enhanced recovery programmes can reduce length of patient hospital stay without increasing readmission rates. Data on re-intervention rates and patient-reported outcomes did not suggest significant differences between enhanced recovery and conventional care, but the evidence was very limited and based on small numbers of patients. The lack of evidence on patient outcomes, resource use and costs precludes firm conclusions on the overall value of enhanced recovery programmes.

ERAS does not appear to reduce complication or readmission rates; the only cost benefit may lie in a reduction in post-operative bed days. Optimal care is certainly the right thing to do, but the evidence does not identify which enhanced recovery programme elements and combinations of elements are most effective. As such, conclusions on which combinations provide greatest gains and how best to implement them cannot be made.

The extent to which managers and clinicians considering implementing enhanced recovery programmes can realise reductions and cost savings will therefore depend on length of stays achieved under their existing care pathway. Important themes emerged from the relevant evidence identified on implementation, including the role of ERAS facilitators and the need for full support from management. It appears that these components are essential for the successful implementation and sustained delivery of enhanced recovery programmes in NHS settings. Consideration of potential benefit also needs to take account of the costs of service redesign, the resource use associated with programmes of this nature, the potential for improvement in patient outcomes and the impact on equity of access.

Implications for research

RCTs comparing an enhanced recovery programme with conventional care continue to be conducted and published, although mostly not in the UK. Given the available evidence, further single centre RCTs of this kind are not a priority. Rather, what is needed is improved collection and reporting of how enhanced recovery programmes are implemented, resourced and experienced in NHS settings. Also, exploration into the effect that varying levels of surgical volume and surgical experience, and different discharge protocols might have on the

success of an enhanced recovery pathway and subsequent outcomes.This will enhance our existing knowledge and understanding and provide evidence to support local decision-making about whether to adopt and how best to implement.

The two groups of implementation case studies included in our synthesis, although all were conducted in the UK, provide very limited information on how enhanced recovery programmes have actually been implemented in UK NHS settings. The standard reporting format originally proposed by The Enhanced Recovery Partnership Programme would enhance the value of future case studies if adhered to. Knowledge of how well the intervention has been implemented (fidelity) is essential for understanding how and why the intervention works and hence how outcomes can be further improved. Assessing fidelity may involve considering not only adherence to the requirements of the programme but also potential moderating factors, such as strategies used to assist delivery of the intervention, quality of delivery and participant responsiveness to new practices.[59] It would be helpful if future innovation programmes used standardised reporting. For multi-site programmes, a formal synthesis of findings from all participating sites should be undertaken as part of the evaluative process. This would ensure that the insights and contextual information which can inform the wider spread and adoption (or indeed discontinuation) would be systematically captured in a generalisable format.

Adherence/compliance to elements by staff and patients also requires further investigation. Rigorous data on patients' experiences of enhanced recovery programmes are lacking. Validated tools should be used and administered independently of those providing the service. Efforts should be made to obtain data from representative samples of patients receiving conventional care as well as those treated with enhanced recovery protocols, along with evidence on the experiences of their families/carers.

Evidence relating to the cost-effectiveness of enhanced recovery programmes in UK NHS settings is lacking. Whist enhanced recovery programmes have the potential to deliver cost savings, improved measurement of costs and benefits is crucial to help decision-makers decide how best to make optimal use of limited resources.

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41. Enhanced Recovery Partnership Programme Case Studies 2011: Colorectal, Gynaecology, Urology, MSK: Medway NHS Foundation Trust, Contract No.: Document Number|.

42. Enhanced Recovery Partnership Programme Case Studies 2011: Colorectal surgery (all elective procedures) and most major emergencies from decision to treat surgically; Urology: radical Prostatectomy, Cystectomy, Nephrectomy; MSK: 1 Hip and knee replacement; Gynaecology: Hysterectomy (vaginal, abdominal and laparoscopic) moving to all majors: Royal Berkshire Hospital, Contract No.: Document Number|.

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Figure 1: Study flow diagram

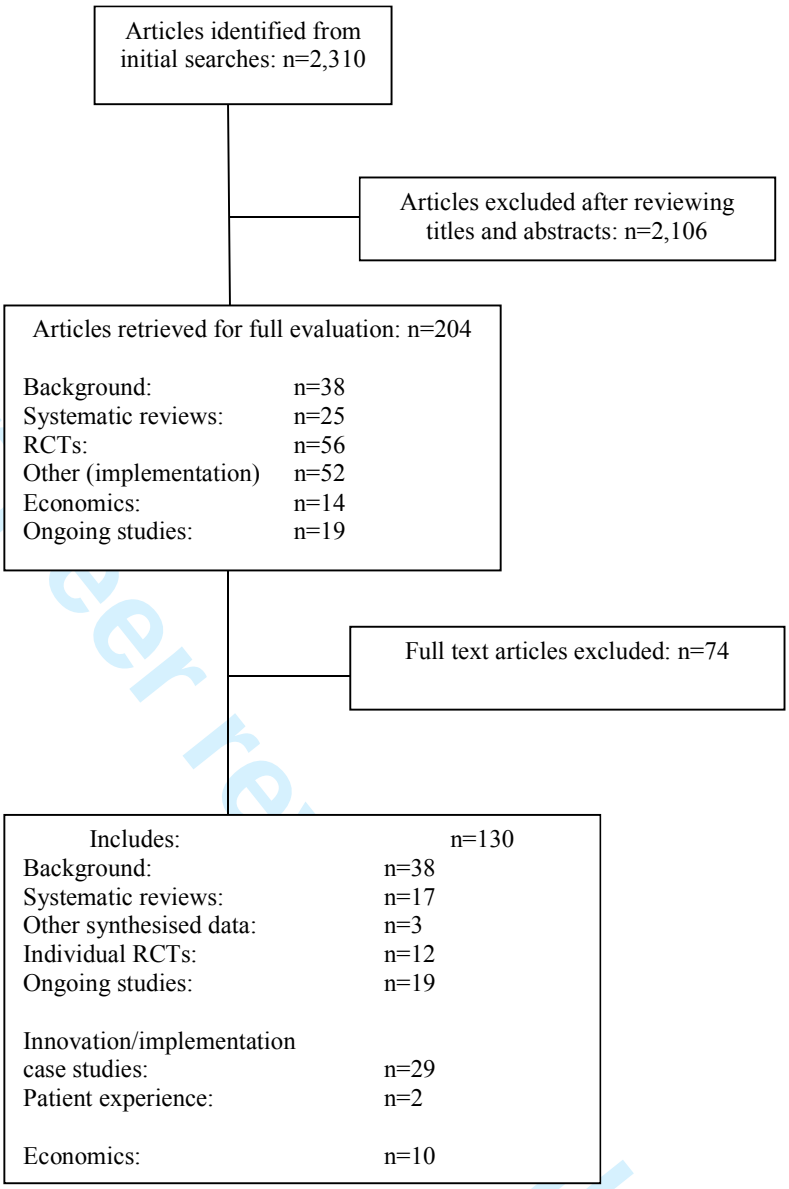

Table 1: Systematic review risk of bias assessment

Author	Adequate search	Risk of bias assessed	Quality score accounted for in analysis	Study details reported and differences accounted for	Statistical heterogeneity investigated	Gaps in research identified	Conclusions justified
Colorectal/Colon surgery							
Adamina (2011)[5]	✓	✓	UC	✓	UC	✓	✓
Ahmed (2012)[6]	✓	X	X	X	X	X	✓
Eskicioglu (2009)[9]	✓	✓	X	✓	✓	✓	✓
Gouvas (2009)[10]	✓	✓	X	✓	✓	✓	✓
Khan (2010)[12]	✓	✓	X	✓	X	✓	✓
Lv (2012a)[20]	✓	✓	X	X	✓	✓	✓
Rawlinson (2011)[14]	✓	X	X	✓	UC	X	UC
Spanjersberg (2011)[15]	✓	✓	✓	✓	✓	✓	✓
Varadhan (2010)[16]	✓	✓	X	✓	✓	✓	✓
Walter (2009)[17]	✓	✓	✓	✓	✓	✓	✓
Wind (2006)[18]	✓	✓	✓	✓	✓	✓	✓
Gynaecological surgery							
Lv (2012b)[19]	✓	X	X	X	X	✓	✓
Liver/pancreatic surgery							
Coolsen (2012)[7]	✓	✓	X	✓	X	✓	✓
Coolsen (2013)[8] Link to [60]	✓	✓	✓	✓	✓	✓	✓
Hall (2012)[11]	X	X	X	✓	X	✓	✓
Various surgical specialities							
Lemmens (2009)[13]	✓	X	X	✓	X	✓	✓
Sturm (2009)[4]	✓	X	X	✓	UC	✓	✓

UC=unclear reporting

Table 2: RCT quality assessment

Author	Adequate random allocation	Adequate allocation concealment	Blinding of healthcare professional	Blinding of participants	Blinding of outcome assessor	Unexpected imbalances in drop-outs between groups	Imbalances accounted/adjusted for	Intention to treat analysis	ITT appropriate and appropriate methods used to account for missing data
Bariatric surgery									
Lemanu (2013)[26]	✓	✓	X	X	X	X	NA	UC	UC
Colorectal/colon surgery									
Garcia-Botello (2011)[23]	UC	X	UC	X	UC	X	NA	UC	✓
Ionescu (2009)[24]	✓	✓	X	X	UC	X	NA	UC	UC
Lee (2011)[25]	✓	✓	UC	X	UC	X	NA	UC	UC
Ren (2012)[28]	✓	✓	X	X	✓	X	NA	UC	UC
Wang (2011)[30]	UC	UC	UC	X	UC	X	NA	✓	✓
Wang (2012)[31]	UC	UC	X	X	✓	UC	UC	UC	UC
Yang (2012)[32, 33]	✓	UC	X	X	UC	X	NA	X	X
Gastric surgery									
Chen (2012)[21]	UC	UC	X	✓	✓	X	NA	UC	UC
Kim (2012)[22]	UC	UC	X	X	X	X	NA	UC	UC
Liu (2010)[27]	UC	X	X	X	X	X	NA	UC	UC
Wang (2010)[29]	UC	UC	X	X	UC	X	NA	X	X

UC: unclear reporting; NA: not applicable

Table 3: Systematic reviews – main clinical outcomes

Author & no. included studies	Length of hospital stay (days)	Readmission rates (N/%)
Colorectal/colon surgery		
Adamina (2011)[5] *6 RCTs*	Primary length of stay: ERAS reduced stay by 2.5 days (95 CrI -3.92 to -1.11)	ERAS did not increase readmission rates (RR 0.59, 95% CrI 0.14 to 1.43)
Ahmed (2012)[6] *11 studies; study designs not reported*	2 to 11 days (10 studies)	0 to 22% (8 studies) Shortest length of stay (2 days) associated with highest readmission rate (22%)
Eskicioglu (2009)[9] *4 RCTs*	Three out of four trials reported a significantly shorter length of primary hospital stay in the ERAS group. Two trials reported overall hospital stay, both of which found a significantly reduced length of stay in the ERAS group.	7/99 ERAS, 11/99 control; no significant difference between groups (RR 0.67, 95% CI 0.20 to 2.19, 4 trials; I^2= 24%)
Gouvas (2009)[10] *11 studies; 4 RCTs,* *7 non-randomised case control studies*	Significantly reduced primary hospital stay with fast track: 3.3 to 6.7/5.8 to 10 days (WMD -2.35, 95% CI -3.24 to -1.46; I^2=75% , 9 studies). Similar results in subgroup analysis. Significantly reduced total hospital stay with fast track: 4 to 5.5 days/6.5 to 13 days (WMD -2.46, 95% CI -3.43 to -1.48; I^2= 0%, 5 studies). Similar results for subgroup analysis.	0 to 24%/0 to 20%: NS (RR 1.37, 95% 0.97 to 1.92; I^2=0%, 10 studies). Subgroup analysis showed that non-RCTs had significantly lower readmission rates in the control group.
Khan (2010)[12] *10 studies; 4 RCTS, 6 non-randomised comparative studies*	Not applicable	Not applicable
Lv (2012a)[20] *7 RCTs (one multi-arm RCT analysed as 2 separate comparisons)*	Total length of stay significantly shorter for ERAS treated patients (MD -1.88 days, 95% CI -2.91 to -0.86; 7 RCTs/8 comparisons, I^2=75%). Sensitivity analysis did not significantly alter the results.	No statistically significant differences between groups (RR 0.90, 95% CI 0.52 to 1.53; 7 RCTS/8 comparisons, I^2=0%).
Rawlinson (2011)[14] *13 studies; 6 RCTs and 7 non-randomised clinical trials*	Eleven studies reported on primary hospital stay, of which 10 reported a significantly shorter stay in the ERAS group.	Readmissions ranged from 0 to 24% with ERAS and from 0 to 20% with traditional care; 12 studies; no significant difference between groups.
Spanjersberg (2011)[15] *6 RCTs (2 did not meet inclusion criteria and were not included in primary analyses)*	Statistically significantly reduced in ERAS patients (MD -2.94 days, 95% CI -3.69 to -2.19 days; I^2=0%, 4 RCTs) Subgroup analyses including the 2 RCTs involving limited number of ERAS elements did not significantly alter the findings.	ERAS 4 (3.3%); control 5 (4.2%) No significant difference between groups (I^2=59%, 4 RCTs) Subgroup analyses including the 2 RCTs involving limited number of ERAS elements did not significantly alter the findings.
Varadhan (2010)[16] *6 RCTs*	Primary hospital stay was significantly shorter in the ERAS group (WMD -2.51 days, 95% CI -3.54 to -1.47, 6 trials; I^2 = 55%).	10/226 ERAS, 13/226 control; no significant difference between groups (RR 0.80, 95% CI 0.32 to 1.98, 4 trials with events; I^2 = 9%
Walter (2009)[17] *4 studies; 2 RCTs, one quasi-randomised trial, 1 cohort*	Total length of stay (mean (SD) days) Statistically significant reduction in ERAS compared to control groups WMD -3.75 days (95% CI -5.11 to -2.40 days; I^2=0%, 2 RCTs) Primary length of stay (mean (SD) days) Statistically significant reduction in ERAS compared to control groups WMD -3.64 days (95% CI -4.98 to -2.29 days; I^2=0%, 2 RCTs)	No statistically significant difference between groups (RR 0.26, 95% CI 0.03 to 2.25; one RCT) and (RR 1.73, 95% CI 1.00 to 3.01; I^2=0%, 2 CCTs). (p=0.05 which the authors consider significant).

Author & no. included studies	Length of hospital stay (days)	Readmission rates (N/%)
Wind (2006)[18] *6 studies; 3 RCTs, 3 CCTs*	Primary hospital stay (mean) Primary hospital stay statistically significantly lower in the ERAS group (WMD -1.56, 95% CI -2.61 to -0.50; I^2=52.9%, 3 RCTs, 3 CCTs). Subgroup analyses showed similar results for RCTs and CCTs. Overall hospital stay (mean) All three trials showed statistically significantly shorter overall hospital stay in ERAS patients (p<0.05)	No statistically significant differences between groups (RR 1.17, 95 %CI 0.73 to 1.86; I^2=23.6%, 2 RCTs, 3 CCTs). Subgroup analyses showed similar results in favour of ERAS in RCTs, but in favour of traditional care in CCTs.
Gynaecological surgery		
Lv (2012b)[19] *0 studies*	Not applicable	Not applicable
Liver/pancreatic surgery		
Coolsen (2012)[7] *6 studies; 3 case-control, 2 RCTs (both arms ERAS elements; equivalent to prospective case series), one retrospective case series.*	3 comparative studies: ERAS 5 to 7 days; control 7 to 11 days: difference (NS one study, p<0.001 2 studies) Non-comparative studies: 4 to 7 days	3 comparative studies: ERAS 0 to 13%; control 0 to 10%: difference (NS 3 studies) 3 non-comparative studies: 0 to 5%
Coolsen (2013)[8] **Link to** [60] *8 studies; 5 case-control (historical controls receiving traditional care); 2 retrospective case series; 1 prospective case series.*	It was unclear whether results were mean or median number of days. Comparative studies ERAS 6.7 to 13.5 days; control 8 to 16.4 days (4 of 5 studies reported statistically significant differences in favour of ERAS) Non-comparative studies 10 days (range 4 to 115), three studies	No significant differences (RD 0.8%, 95% CI -2.6% to 4.1%; I^2=0%, 4 studies)
Hall (2012)[11] *10 studies; Two studies with a single intervention in one parameter of peri-operative care but within an ERAS programme (including one RCT); 6 prospective case series comparing ERAS programmes versus historical controls, one retrospective case study, and one multicentre study.*	Reduced with ERAS programme: Pancreatic 10 to 13 days (range 4 to 115 days; 4 studies); liver 4 to 7.2 days (range 2 to 82 days; 5 studies).	Pancreatic 3.5 to14.6% (4 studies); liver 0 to 13 % (5 studies)
Various surgical specialities		
Lemmens (2009)[13] *13 studies; One RCT, 3 controlled clinical trials, 2 case-control, one retrospective case series, 6 pre- post-pathway studies*	Statistically significant decrease in clinical pathway group in 11 studies; mean number of days decreased from between 5.9 and 21.7 days to between 3.3 and 18.5 days (9 studies). Median number of days decreased from between 5 and 13 days to between 2 and 7 days (4 studies). 2 studies reported no significant difference between groups.	One study reported statistically significant reduction (13% to 6%); 2 studies not reported; 10 studies NS
Sturm (2009)[4] *11 RCTs plus one systematic review*	Length of stay was clearly significantly shorter in the ERAS group in 6 trials (3 colorectal, 3 other). There was no significant difference in 1 trial (lung surgery). In the remaining trials, significance was unclear or was not reported.	Eight trials reported on readmission rates. Rates ranged from 0 to 9.7% in the ERAS groups and 0 to 20% in the control groups. Only one trial reported a statistically significant difference and this favoured the ERAS group (p = 0.022).

Table 4: RCTs – main clinical outcomes

Author	Length of hospital stay (days)	Readmission rates (N/%)
Bariatric surgery		
Lemanu (2013)[26]	Median days (interquartile range) Length of index admission: ERAS 1 (1 to 2); control 2 (o), p<0.001 Total hospital stay (including admission plus subsequent readmissions): ERAS 1 (1 to 3); control 2 (2 to 3), p<0.001	Defined as presentation to hospital within 30 days of surgery after the day of discharge; subsequent hospital stay had to be more than 24 hours. ERAS 8/40 (20%); control 8/38 (21%) Median length of readmission was 6 days with no difference between groups.
Colorectal/colon surgery		
Ionescu (2009)[24]	Mean (SD) ERAS 4.15 (2.2); control 9.23 (7), p<0.001	ERAS 3 (5%); control 2 (3%), p=0.51
Lee (2011)[25]	ERAS 6.43 (3.41); control 9.16 (2.67), p=0.001	ERAS 0 (0); control 0 (0)
Ren (2012)[28]	Post-operative: Rehabilitation 7 (6 to 8); control 8 (7 to 9), p=0.065 Total: Rehabilitation 9 (8 to 10); control 10 (9 to 11), p=0.054	30-day: rehabilitation 0; control 0
Wang (2011)[30]	*Mean (SD) ERAS 5.7 (1.6); control 6.6 (2.4), p<0.001*	*Not reported*
Wang (2012)[31]	*Median (range) post-operative hospital stay ERAS 5 (2 to 41); control 7 (3 to 55), p<0.01*	*No statistically significant differences between groups within 30 days after resection. ERAS 4 (4%) patients re-admitted for wound infection; control 9 (9%) readmitted due to bowel obstruction, vomiting, and wound infection.*
Yang (2012)[32, 33]	*Median days: ERAS 5.5 (5 to 6); control 7.0 (6 to 8), p<0.001*	*Not reported*
Ionescu (2009)[24]	*Mean (SD) ERAS 6.0 (1.0); control 11.7 (3.8), p<0.05*	*No hospital readmissions due to complications.*
Gastric surgery		
Chen (2012)[21]	Median days (range) Compared with ODG, the remaining three groups had shorter post-operative hospital stay (p<0.05) FTS + LADG 7 (5.5 to 10); LADG 7.5 (6 to 11); FTS + ODG 7.5 (6 to 11); ODG 8.75 (7 to 14)	Not reported
Kim (2012)[22]	Possible post-operative hospital stay (mean days, SD) ERAS 4.68 (0.65) (range 4 to 6); control 7.05 (0.65) (range 6 to 9), p<0.001 Post-operative hospital stay (mean days, SD) ERAS 5.36 (1.46) (range 4 to 11); control 7.95 (1.98) (range 6 to 15), p<0.001	ERAS 1/22 (4.5%); control 0/22 (0%)
Liu (2010)[27]	*Primary length of stay (mean (SD)): ERAS 6.2 (1.9); control 9.8 (2.8), p<0.001*	*Readmitted within 30 days after surgery ERAS 1/33 (3%); control 0/30 (0%)*
Wang (2010)[29]	*Median (quartile range) ERAS 6 days (6 to 7); control 8 (7 to 8), p<0.001. Primary clinical endpoint of the trial.*	*ERAS 1/45 (2.2%); control 1/47 (2.1%), no significant difference between groups*

Table 5: Economic evaluations meeting the inclusion criteria

Study Details	Study Comparators	Main Analytical Approaches, primary outcomes, and costs	Incremental cost-effectiveness (ICER) estimates and Decision Uncertainty
Salihiyyah *et al* (2011)[55] UK Hospital setting Study Population Cardiac surgery Inpatients Time horizon 6 months	Intervention Fast-track transfer post-surgery to an independent theatre recovery unit 1-2-1 nursing (n=84) Comparator Transfer post-surgery to hospital intensive care unit (n=52)	Economic evaluation based on a single study Perspective Hospital Primary outcomes Length of stay; Duration of intubation Direct Costs Total expenditure of unit divided by number of patients Productivity Costs n/a	Results The costs and benefits were not synthesised mean cost FT: £4182 (SD:2284) mean cost C: £4553 (SD:1355) (p<0.001) total LOS NSD 8 patients failed FT & were transferred to ICU 5 patients (4 FT & 1 C) required readmission Uncertainty One-way & multi-way sensitivity analysis demonstrated robustness in result that FT costs less than C
Lin *et al* (2011)[52] China Hospital setting Study Population Liver resection Inpatients Time horizon Not reported	Intervention Multidisciplinary team, streamlining of preoperative evaluation, education of patients and families, earlier oral feeding, earlier discontinuation of IV, no drains or naso-gastric tubes, early ambulation, urinary catheter <24 hours, planned discharge 6 days post-surgery (n=56) Comparator Conventional pathway (limited reporting) (n=61)	Economic evaluation based on a single study Perspective Hospital Primary outcomes Length of stay; Complications; Mortality; Readmission Direct Costs Hospital charges: operation and anaesthesia; pharmacy; auxiliary examination; other Productivity Costs n/a	Results The costs and benefits were not synthesised mean charge pre-pathway RMB 26,626 mean charge post-pathway RMB 21,004 (p<0.05) LOS reduced from 11 days to 7 days (p<0.005) Complications, mortality & readmissions NSD Uncertainty n/a
Kariv *et al* (2006)[54] USA Hospital setting Study Population Patients undergoing open ileoanal pouch surgery Time horizon	Intervention Presurgery patients provided with FT protocol and documentation of post-surgery milestones. Epidural or analgesia were not used; early food and mobilisation (day of surgery/anaesthesia), patients who lived 100 to 150 miles from hospital discharged to hotel for 1 to 3 days. Success defined as discharge within 5 days (n=97)	Economic evaluation based on a single study Perspective Hospital Primary outcomes Length of stay; Readmission; Reoperation Direct Costs Total costs for each of the categories were presented: per case of hospitalisation; operating room; radiology;	Results The costs and benefits were not synthesised total per case cost FT US$ 5,692 total per case cost C US$ 6672 diff US$980 (p=0.001) median postoperative los FT = 4 days C= 5 days (p=0.012) NSD in readmission outcomes Uncertainty

Study Details	Study Comparators	Main Analytical Approaches, primary outcomes, and costs	Incremental cost-effectiveness (ICER) estimates and Decision Uncertainty
30 days	 Comparator Based on professional preferences of surgeon; no supporting documentation; sat out of bed on POD 1, walked POD 2; food withheld until stool or flatus (n=97)	anaesthesia; pharmacy; laboratory; ICU; and nursing care Productivity Costs n/a	n/a
Yanatori *et al* (2007)[56] Japan Hospital setting Study Population Cardiovascular surgery (cardiac arrest requiring cardiopulmonary bypass) Time horizon 2 years	Intervention Admitted 4 days prior to surgery, preoperative education by nurses, surgeons and rehab staff; discharge at day 7 post surgery Comparator Conventional protocol – details not reported	Economic evaluation based on a single study Perspective Healthcare provider/hospital Primary outcomes Length of stay; Complications Direct Costs Only total costs were presented Productivity Costs n/a	Results The costs and benefits were not synthesised Total mean cost for FT YEN 712,545 Total mean cost for C YEN 383,268 (p=0.038) Mean post-op LOS FT=15(12.4) C=36.7(6) (p=0.01) Uncertainty n/a
Larsen *et al* (2009)[53] Denmark Hospital setting Study Population All patients for elective primary total hip/knee arthroplasty or unicompartmental knee arthroplasty Time horizon One year	Intervention Patients receive info pre-hospitalisation; separate ward; one nurse in charge of multidisciplinary nurses, occupational therapists, and physiotherapists; nutrition screening and special focus on daily consumption of 1.5L fluid (including 2 protein beverages); mobilisation and exercise started on day of surgery; intensive mobilisation of patients in teams; eight hours of mobilisation daily (n=45: 28 total hip; 15 total knee; 2 unicompartmental knee) Comparator Patients receive info on day of admission; patients randomly among wards, various nurses in charge of care; and various occupational and physio-therapists responsible for mobilisation; mobilisation and exercise started on first postoperative day; individual and gradual mobilisation according to patient tolerance; four hours mobilisation daily (n=42: 28 total hip; 12 total knee; 2 unicompartmental knee)	Economic evaluation based on a single study Perspective Societal Primary outcomes Length of stay; Adverse events (first 3months) Health-related quality-of-life QALYS (EQ-5D) (baseline to 3 months) Direct Costs Patients followed over one-year. Resource use: based on patient level mix of activity based costing and step down methods. Discharge to 3 months cost diary Productivity Costs Average wage rate for age-specific groups	Results Accelerated intervention was both more effective and less costly than the comparator Average total cost for I DKK90,227 (+/- 47,475) Average total cost for C DKK71,344 (+/- 39,958) Average QALYs was 0.83 for the intervention and 0.78 in the comparator. Average QALY gain for hip patients I v C = 0.08 (CI: 0.02 to 0.05) (p=0.006) Average QALY gain for knee patients was NS Uncertainty Bootstrapping, uni and multivariate
Sammour *et al* (2010)[49]	Intervention	Economic evaluation based on a single study	Results

Study Details	Study Comparators	Main Analytical Approaches, primary outcomes, and costs	Incremental cost-effectiveness (ICER) estimates and Decision Uncertainty
New Zealand Hospital setting Study Population Elective colonic resection patients >15 years old Time horizon Unclear	Emphasised structured nursing care pathways within an environment focusing on early recovery and various perioperative strategies to improve patient functional recovery (n=50) Comparator Conventional non-structured perioperative care (n=50)	Perspective Healthcare provider Primary outcomes Length of stay; Complications; Readmissions Direct Costs Total cost of protocol development, inpatient stay, outpatient appointments, treatment costs, readmission and complication costs were all considered. Data on patient resource use was collected from their records. Readmission costs and complication costs were based on hospital records/costs Productivity costs n/a	The costs and benefits were not synthesised The implementation of the intervention protocol cost approx. NZ$102,000 for the first 50 patients (set-up costs included) Cost per patient with NZ$16,052.35 Cost per patients without NZ$22,929.74 Cost-saving NZ$6,900 per patient Post-op LOS ERAS: 4 (3 to 34); C: 6.5 (3 to 18) (p<0.001) Total LOS ERAS: 4(3 to 34); C: 8(4 to 29) (p<0.001) Readmissions NS Complications – overall 54% in ERAS ≥1 compared with 66% comp Uncertainty n/a
King *et al*(2006)[50] UK Hospital setting Study Population Surgery for colorectal cancer Time horizon 2 years	Intervention Preoperative counselling, epidural analgesia, early feeding and mobilisation, predetermined discharge aim (n=60) Comparator Conventional care (fully reported) included no epidural, no formal mobilisation plan, no predetermined discharge (n=86)	Economic evaluation based on a single study Perspective UK NHS stated by author, although inclusion of productivity costs suggests wider societal perspective Primary outcomes Post-op length of stay; Complications; Readmissions Health-related quality-of-life EORTC QLQ-C30 Direct Costs Resource use data was reported to be individual patient level, but not reported. Direct costs included: theatre (including pre and recovery), hospital (including ICU), postoperative (including re-operation), chemotherapy and radiotherapy, follow –up at 3 months Productivity costs Average earnings based on employment status at commencement of trial	Results The costs and benefits were not synthesised Total costs of care for patients receiving the intervention: £7327.47; for those receiving comparator: £7998.18 Post-op LOS significantly reduced, intervention cohort staying 49% as long as comparator (95% CI: 39% to 61%; p<0.001) No-sig difference in quality-of-life, readmissions, re-operations or complications Uncertainty n/a
Neilson *et al*(2008)[51] Denmark Hospital setting	Intervention Integrated programme including: information and education, optimal operation technique, better pain reduction, early nutrition and aggressive	Economic evaluation based on a single study Perspective Societal	Results The costs and benefits were not synthesised Intervention direct cost 1,174 Euros per patient compared with 1,668 for standard care

Study Details	Study Comparators	Main Analytical Approaches, primary outcomes, and costs	Incremental cost-effectiveness (ICER) estimates and Decision Uncertainty
Study Population Lumbar fusion patients with degenerative lumbar disease Time horizon 6 months	post-op mobilisation (n=28) Comparator Standard care, not including components above (n=32)	Primary outcome Measured using 15D-score (self-reported at inclusion, day of surgery, day of discharge, and 1, 3 and 6 months post-op Direct Costs Three categories of cost considered: staff resources, equipment and purely bed costs. Bed costs included salary of nurses/porters, food, clothes, laundry and cleaning. Post-discharge for 3 months GP visits, physiotherapy appointments and emergency room contact was registered and included. Productivity costs Based on return to work rates & Danish average daily wage	Intervention productivity costs were 8,021 Euros compared with 9,152 for standard care NS difference in HR quality of life scores Uncertainty Optimistic and pessimistic scenarios varying individually pre-op costs, post-op hospital costs, direct costs, and productivity costs
Reilly *et al*(2005)[47] UK Hospital setting Study Population Patients undergoing unicompartmental knee arthroplasty Time horizon Unclear	Intervention Accelerated discharge: aim to discharge day after surgery (n=20) Comparator Standard discharge: approx. 5 days post-surgery (n=21)	Economic evaluation based on a single study Perspective Hospital Primary outcome Oxford Knee Assessment Direct Costs Fixed costs (surgical staff, anaesthetics, prosthesis, pharmacy), outpatient appointment, specialist registrar time. Productivity costs n/a	Results The costs and benefits were not synthesised Intervention resulted in a 6 month OKA score of 43.7 (SD 3.7) compared with 42.2 (SD 7.1) for standard care (NS) Total costs for intervention per patient £3,391 compared with £4,634 for standard care Uncertainty n/a
Archibald[48] USA Hospital setting Study Population Colorectal surgery patients Time horizon unclear	Intervention The availability of patient education, fluid managements, opioid-sparing strategies, tube and drain protocols, ambulation, feeding protocol, and discharge criteria. All based on surgeons choice. (n=1358, 588 enrolled in ERAS & 770 not enrolled) Comparator Standard care historical baseline (n=1673)	Economic evaluation based on a study comparing two time periods, where ERAS was available in one and not in the other. Primary outcome Length of stay ; POD; Readmission Direct Costs Hospital costs (total direct and indirect costs identified via hospital billing system) Productivity costs n/a	Results The costs and benefits were not synthesised Mean LOS for the intervention was 8.4 days compared with 6.9 days for the comparator (p<0.0001) Mean POD for the intervention was 7.6 days compared with 6.3 days (p<0.0001) Mean hospital cost for the intervention population was US$18,741 compared with US$16,978 for the comparator. Uncertainty n/a

Draft Protocol

3 December 1012

HS&DR Project: 11/1026/04

Initiatives to reduce length of stay in acute hospital settings. A rapid synthesis of evidence relating to enhanced recovery programmes by the CRD Knowledge Translation Service

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Aims and objectives

To conduct a rapid synthesis of the evidence relating to the effectiveness, cost effectiveness, implementation, delivery and impact of enhanced recovery programmes in acute hospital settings. The rapid review will aim to:

- Identify and review the effectiveness and cost effectiveness of enhanced recovery programmes designed to reduce length of stay in acute hospital settings.
- Identify and critically describe current knowledge on the impact of enhanced recovery programmes on the organisation of care, configuration of workforce, resource utilisation in UK settings.
- Identify and critically describe the key factors associated with successful adoption, implementation and sustainability of enhanced recovery programmes in UK settings.
- Summarise and describe the available evidence relating to patient experience of and equity of access to enhanced recovery programmes in UK settings.

Background

Enhanced Recovery Programmes in patients undergoing surgery involve the development of enhanced recovery multidisciplinary teams, agreed basic principles, improved efficiency around the surgical pathway, increased awareness of patients about the process, and early discharge planning using agreed criteria (Enhanced Recovery Partnership Programme, DH, 2011). Over the last two years the Department of Health's Enhanced Recovery Partnership Programme (ERPP) has sought to raise the profile and promote the benefits of enhanced recovery for elective surgical care across the NHS (ERPP; DH, 2011).

The underlying aim of Enhanced Recovery Programmes is to ensure patients are in optimal condition for treatment, receive innovative care during surgery, and experience optimal post-surgical rehabilitation (ERRP; DH, 2011). Programme components differ widely, but share common elements, such as patient education and involvement in pre-operative planning processes, pre-operative oral carbohydrates, improved anaesthetic and post-operative analgesic techniques to reduce the physical stress of the operation, early oral feeding and mobilisation (Sturm 2009; Kehlet 2003).

Enhanced recovery has the potential to deliver productivity gains through reduced length of stay, fewer post-operative complications, reduced readmissions and improved patient care and patient outcomes, and reduced risks, costs and length of stay (Wainwright and Middleton 2010).

The NHS is facing severe funding constraints both now and in the medium term. Rather than reducing management costs, it has been proposed that the greatest potential savings may be found in increasing efficiency by reducing variations in clinical practices (Ham, 2009). The Kings Fund emphasises that the NHS must focus on carefully identifying those initiatives that will produce more value from the finite resources available - 'doing things right and doing the right things' (Appleby, 2010). Evidence has shown that the cost of implementing Enhanced Recovery Programmes can be offset by costs saved in reduced post-operative resource use (Sammour 2010).

Before embarking on more whole scale adoption of this major initiative, NHS managers and clinicians therefore need to be fully aware of the strength of the underlying evidence base to support the use of such programmes. More crucially, they also need to have a clear understanding of how best to implement, as well as the likely implications they face relating to service delivery given finite budgets and need for equity of access.

The proposed research will aim to provide the first comprehensive rapid evidence synthesis of the evidence relating to the effectiveness, cost effectiveness, implementation, delivery and impact of enhanced recovery programmes and contextualise the findings to acute hospital settings in the NHS. Our dissemination activity will be designed to ensure that key individuals, NHS Trusts and organisations with an interest in enhanced recovery programmes are made aware of the research and its eventual findings.

Objectives

The project will address three main areas:

1. *Clinical and cost effectiveness:* We will evaluate the clinical and cost-effectiveness of enhanced recovery programmes designed to reduce length of stay in acute hospital settings in patients undergoing elective surgery, including the impact on the organisation of care, configuration of workforce, and resource utilisation in UK settings.

2. *Implementation:* We will identify and critically describe the key factors associated with successful adoption, implementation and sustainability of enhanced recovery programmes in UK settings.

3. *Patient experience:* We will summarise existing knowledge about patient experience of enhanced recovery programmes in UK settings, including issues surrounding equity of access to such programmes.

Review methods

We will conduct a rapid review of the evidence to inform the three objectives stated above. The review will be undertaken systematically following established principles (CRD, 2009; Moher, 2009) and adapted as appropriate to ensure they are relevant to this context.

Searching

- ***Clinical and cost-effectiveness***

We will search electronic databases (Cochrane Database of Systematic Reviews, DARE, NHS EED, and CRD HTA) from 1990 to present, to identify systematic reviews and economic evaluations. The PROSPERO database will be searched to identify unpublished and ongoing systematic reviews. We will also screen NIHR HTA and NIHR Health Services and Delivery Research Programme Reports, and NICE guidelines.

RCTs will be identified from the following sources: MEDLINE, Cochrane Controlled Trials Register, and ongoing trials registers (eg. ClinicalTrials.gov). Searches will be conducted from 1990 to present. Reference lists of retrieved articles, reviews and evaluations will be scanned to identify additional studies.

Search terms are reported in Appendix 1.

- ***Implementation and patient experience***

Evidence from case studies relating to the experiences of patients and clinical teams in implementing and delivering enhanced recovery programmes in UK settings will be identified from the following sources:

- Association of Surgeons of Great Britain and Ireland
- British Association of Day Surgery
- British Orthopedic Association
- British Association of Urology Surgeons
- British Association Breast Surgeons
- Department of Health Enhanced Recovery Partnership Programme
- Enhanced Recovery Partnership Programme Innovation sites
- ERAS (UK)
- NHS Evidence
- NHS Institute for Innovation and Improvement
- NHS Improvement - Enhanced Recovery
- NHS Cancer Action Team
- NICE
- Royal College of Anaesthetists
- Royal College of Obstetricians and Gynaecologists
- Royal College of Surgeons

Relevant individuals will also be identified and contacted for additional evidence, including Regional Leads at the NHS Institute for Innovation and Improvement, and ERAS (UK) society members.

Inclusion/exclusion criteria

Participants

Patients of any age undergoing any type of elective surgery in an acute hospital in the UK NHS or a comparable healthcare system. Patients undergoing emergency surgery will not be eligible for inclusion, but findings from the review will be discussed in terms of their transferability to emergency surgery settings.

Intervention

Reviews and studies of enhanced recovery programmes, as defined in the original articles, will be considered for inclusion. Eligible interventions could include enhanced recovery combined with other techniques to reduce the impact of any type of elective surgery.

Reviews and studies will then be assessed to identify which ones encompass the main components of the approach, as stated by the Enhanced Recovery Partnership Programme; there will be no restriction on the number of components, or individual elements within each component, needed for a study to be eligible for inclusion. The essential elements include providing support and information to ensure the patient is in the best possible condition for surgery (pre-operative), ensuring the patient has the best possible management during surgery (intra-operative), ensuring the patient

experiences the best post-operative rehabilitation (post-operative). See also Appendix 2 for example protocol.

Comparator
Usual/standard care without a multimodal enhanced recovery programme, as defined in the included studies.

Outcomes
All health and cost-related outcomes will be considered for inclusion; eligible studies must report at least one outcome. We will then distinguish between clinical outcomes (mobilisation, mortality and morbidity, pain, readmission rates, re-intervention rates, length of hospital stay), patient outcomes (eg. patient experience and satisfaction, quality of life), and resource use in acute and, where available, primary care settings (eg. workforce utilisation and costs, including involvement of an Enhanced Programme Facilitator and resource implications post-discharge).

Patient experience must be assessed using validated questionnaires and surveys (eg. 2011 National Inpatient Survey, Picker Institute Europe & Care Quality Commission).

Study design
Systematic reviews of primary studies and economic evaluations will be included if they evaluate enhanced recovery programmes in patients undergoing elective surgery. Other synthesised evidence, such as reviews of reviews, will be eligible for inclusion, but will be assessed separately.

Also eligible for inclusion will be individual RCTs not included in the above reviews, and UK NHS cost analysis studies identified from HEED. Case studies, impact assessments, or surveys of patient experience documenting the experience of implementing enhanced recovery in a UK setting will also be considered.

No language restrictions will be applied. Where feasible, foreign language papers will be translated and included in the synthesis. Where this is not feasible, the number of articles will be reported.

Selection

- ***Clinical and cost effectiveness and implementation***

Search results will be stored in a reference management database (Endnote). Two researchers will independently screen all titles and abstracts obtained through the searches for potentially relevant articles. Full manuscripts of potentially relevant articles will be ordered and two researchers will independently assess the relevance of each article using the criteria above. Disagreements between reviewers will be resolved by discussion or by recourse to a third reviewer if necessary.

Data extraction
Data will be extracted into review software (EPPI Reviewer 4.0). Data extraction forms will be piloted on a small selection of studies and adjusted as

necessary. Data extraction will be undertaken by one researcher and checked by another, with discrepancies resolved by consensus or recourse to a third researcher if necessary.

Study characteristics

Clinical effectiveness

Systematic review

Study reference

Review objective(s)

Inclusion criteria

- Participants
- Intervention
- Comparator
- Outcomes
- Study design

Review details

- Surgical speciality
- Country
- Follow-up duration

Participant characteristics (health professionals)

- Brief description of enhanced recovery team; including whether the team involved an Enhanced Recovery Programme Facilitator and whether the role was temporary to set up the programme, or permanent to sustain the programme over time

Participant characteristics (patients)

- Indication (including stage of condition and measure (eg. POSSUM))
- Mean age
- Co-morbidities

Enhanced recovery intervention

- Components of Enhanced Recovery Programme measured
- Number of elements of Enhanced Recovery Programme measured
- Elements most frequently reported
- Brief details of additional interventions
- Issues with implementation (including any reported information on intervention fidelity)?
- Number of patients included

Comparator group(s)

- Brief description of comparator(s)
- Number of patients included

RCTs

Study reference

Study details

- Study objective(s)
- Setting (e.g. inpatient, outpatient)
- Surgical speciality/type of operation
- Country
- Follow-up duration

Participant characteristics (health professionals)

- Brief description of enhanced recovery team; including whether the team involved an Enhanced Recovery Programme Facilitator and whether the role was temporary to set up the programme, or permanent to sustain the programme over time

Participant characteristics (patients)

- Indication (including stage of condition and measure (eg. POSSUM))
- Mean age
- Gender
- Ethnicity
- Co-morbidities
- How were participants selected?

Enhanced recovery intervention

- Objective(s) of the intervention (if not covered above)
- Brief description of components of intervention (pre-, intra-, and post-operative, including discharge elements and post-discharge support)
- Number of elements of Enhanced Recovery Programme measured
- Brief details of additional interventions
- Brief details on resources used (eg. personnel)
- Issues with implementation (including any reported information on intervention fidelity)?
- Number of patients randomised
- Number of patients analysed

Comparator group(s)

- Brief description of comparator(s)
- Number in patients randomised
- Number of patients analysed

Cost-effectiveness

Study reference

Study details

- Type of economic evaluation (cost-effectiveness, cost-utility, cost-benefit)
- Population
- Study objective(s)
- Setting (e.g. inpatient, outpatient)
- Surgical speciality/type of operation
- Country
- Time horizon/discount rate
- Perspective
- Price year/currency
- Intervention
- Comparator(s)
- Methods of deriving effectiveness data
- Measurement and valuation of resource data
- Measurement and valuation of utility data
- Method of synthesising costs and benefits

- Analysis of uncertainty

Cost

- Study reference
- Study details
- Population
- Setting (e.g. inpatient, outpatient)
- Surgical speciality/type of operation
- Intervention
- Comparator(s)
- Measurement and valuation of resource data

Implementation

NHS audits/ studies evaluating implementation

Study reference

NHS study details

- Setting (e.g. inpatient, outpatient)
- Surgical speciality/type of operation
- Date of study
- Objective(s)
- How were the cases selected
- How were data collected
- How was implementation fidelity measured
- What moderating factors were described? State which component(s) the moderating factors related to (pre-, intra-, post-operative) and which elements were implicated
- Were any limitations to implementation described (eg. resources, training issues)? State which component(s) the limitations related to (pre-, intra-, post-operative) and which elements were implicated

Patient experience

Survey reference

Survey details

- Type of healthcare system
- Setting (e.g. inpatient, outpatient)
- Surgical speciality/type of operation
- Country

Sample

- Clinical problem
- Co-morbidities
- Mean age
- Gender
- Ethnicity
- How was the sample obtained?

Administration

- Type of instrument used
- Copy of instrument available?
- Date of survey

- How many people received the instrument?
- Response rate

Results

- ***Clinical effectiveness***

We will extract study results for clinical, patient or resource outcomes into tables (see draft tables below), according to ITT and/or per protocol analysis, where relevant.

Systematic reviews/other synthesised evidence

Review details	Study designs	Comparison	Results
			Type of synthesis Type of analysis (ITT/per protocol) Number of studies <u>Clinical outcome</u>: Intervention group Control group Difference between groups Significance: <u>Patient outcome</u>: Intervention group Control group Difference between groups Significance: <u>Resource outcome</u>: Intervention group Control group Difference between groups Significance:

Individual RCTs

Study details	Comparison	Results
		Type of analysis (ITT/per protocol) Clinical outcome: Intervention group Control group Difference between groups Significance: Patient outcome: Intervention group Control group Difference between groups Significance: Resource outcome: Intervention group Control group Difference between groups Significance:

- ***Cost-effectiveness***

We will extract study results for clinical, patient or resource outcomes into tables (see draft tables below)

Study details	Results
	Outcomes: Intervention Comparator(s) Difference between groups: Costs: Intervention group Comparator(s) Difference between groups: Incremental results: Uncertainty results:

- ***Patient experience***

Patient details	Results
	Patient outcome: **Responses to standard questions from the 2010 National Inpatient Survey** Were you involved as much as you wanted to be in decisions about your care and treatment? How much information about your condition or treatment was given to you? Did you feel you were involved in decisions about your discharge from hospital? Did hospital staff tell you who to contact if you were worried about your condition or treatment after you left hospital?

Quality assessment

Quality assessment of systematic reviews, economic evaluations will be based on the existing critical appraisals provided by DARE and NHS EED. Identified RCTs will be appraised using criteria based on recent CRD guidance (CRD, 2009). Cost analysis studies will not be formally quality assessed.

The quality of the identified surveys will be assessed using a list of questions for the appraisal of surveys (Crombie 1996). The quality of audits will be assessed using similar methods to those stated in a previous systematic review of audits (Lewis, 2005). Implementation fidelity (the degree to which an ERAS programme was implemented as intended) will be assessed according to elements in Carroll's conceptual framework. No overall quality score will be calculated for case studies, but aspects of the quality assessment will be used to inform the results.

Quality assessment will be undertaken by one researcher and checked by a second with discrepancies resolved by consensus or recourse to a third researcher if necessary.

Data synthesis

- ***Clinical and cost-effectiveness***

We anticipate that the type and range of evidence to be included, and the expected heterogeneity in settings and interventions, will preclude meta-analysis. We will present a narrative synthesis by type of surgical pathway (differentiating between evidence from systematic reviews and additional RCTs), and by the main components that encompass the enhanced recovery approach (pre-, intra- and post-operative).

We will relate the evidence to the context of the NHS, by assessing the generalisability (i.e. external validity and applicability) of the evidence to the

NHS highlighting any potential limiting factors that might affect this. We will highlight any evidence as to which components of enhanced recovery programmes are most essential for achieving improvements in clinical and patient outcomes, and resource use.

- ***Implementation***

Based on the evidence in the systematic reviews and from UK case studies, we will consider the time taken to implement; any workforce implications; requirements for training; equipment etc.

Using evidence from the studies we will critically describe the key factors associated with successful (and unsuccessful) adoption, implementation and sustainability of enhanced recovery programmes in NHS acute hospital settings. We will also highlight any factors that are associated with minimising the postoperative burden of enhanced recovery programmes on general practice.

- ***Patient experience***

We will summarise what is currently known about patient experience and will attempt to assess any implications for health equity using the approach developed by the SUPPORT Collaboration (Oxman, 2010).

- Which groups or settings are likely to be disadvantaged in relation to enhanced recovery being considered?

- Are there plausible reasons for anticipating differences in the relative effectiveness of enhanced recovery for disadvantaged groups or settings?

- Are there likely to be different baseline conditions across groups or settings such that the absolute effectiveness of enhanced recovery would be different for disadvantaged groups or settings?

- Are there important considerations that should be made when implementing enhanced recovery to ensure that inequities are reduced, if possible, and that they are not increased?

Dissemination

The proposed research will seek to establish whether initiatives to reduce length of stay in acute hospital settings such as enhanced recovery programmes are 'the right thing to do' and more crucially shed light on 'how to do the right things right'. At the outset, a detailed dissemination strategy will be produced to ensure that key individuals, NHS Trusts and organisations with an interest in enhanced recovery programmes are made aware of the research and its eventual findings.

The selection of specific dissemination activities will be informed by the key messages generated by the research, and will take account of the needs and preferences of the audiences to be targeted. In developing plans, the project team will draw upon the expertise of the Centre for Reviews and

Dissemination, recent guidance (CRD, 2009) and lessons from recent research that has explored how best to disseminate (Wilson, 2010a, 2010b).

Dissemination activities will include the production and distribution of a short non-technical evidence briefing targeted at the end users (key individuals, NHS Trusts and organisations with an interest in enhanced recovery programmes), submission of papers for peer-reviewed publication and submission of abstracts to conferences. The results will also be made available on the NIHR HS&DR and CRD websites.

The project will take 9 months to complete. The key milestones are as follows:

	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	June	July
Protocol development and consultation										
Project team meeting 1		23 Nov								
Literature searches										
Contact with ERAS Leads and other NHS sources										
Data extraction and checking										
Project team meeting 2										
Submit progress report					18 Feb					
Data analysis and synthesis										
Project team meeting 3										
Draft report										
Draft non technical briefing for NHS audiences										
Peer review with external advisors										
Project team meeting 4										
Revise and finalise report										
Submit final report										18 July
Submit detailed financial reconciliation										18 July

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Appendix 1 – search strategy

#1 ERAS:ti,ab
#2 ((enhanced or early or accelerated or fast track or fast-track or rapid) near/1 (recover* or rehabilitat* or convalesc* or mobil* or ambulat* or walk* or feed* or nutrition* or eat*) near/3 (surger* or program* or protocol* or pathway*)):ti,ab
#3 ((multimodal or optimised or optimized) near/1 (recover* or rehabilitat* or convalesc*)):ti,ab
#4 #1 or #2 or #3

Appendix 2 – Enhanced Recovery After Surgery Protocol (example)
ERAS Society 2012

Preoperative

- Pre-admission counselling
- Fluid and carbohydrate loading
- No prolonged fasting
- No/selective bowel preparation
- Antibiotic prophylaxis
- Thromboprophylaxis
- No pre-medication

Intraoperative

- Short-acting anaesthetic agents
- Mid-thoracic epidural anaesthesia/analgesia
- No drains
- Avoidance of salt and water overload
- Maintenance of normothermia (body warmer/warm intravenous fluids)

Postoperative

- Mid-thoracic epidural anaesthesia/analgesia
- No nasogastric tubes
- Prevention of nausea and vomiting
- Avoidance of salt and water overload
- Early removal of catheter
- Early oral nutrition
- Non-opioid oral analgesia/NSAIDs
- Early mobilisation
- Stimulation of gut motility
- Audit of compliance and outcomes

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3-4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Full report – in press. Protocol attached to manuscript submission
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6

PRISMA 2009 Checklist

Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	N/A
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency ($e.g., I^2$) for each meta-analysis.	N/A

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	20
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	21-22
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	23-25
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	NA
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	NA
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	10-13
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	11-13
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13-14
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1-2

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097.

PRISMA 2009 Checklist

doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

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Effectiveness and implementation of enhanced recovery after surgery programmes: a rapid evidence synthesis

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Primary Subject Heading:	Surgery
Secondary Subject Heading:	Health services research
Keywords:	enhanced recovery, fast track, length of hospital stay

Effectiveness and implementation of enhanced recovery after surgery programmes: a rapid evidence synthesis

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Abstract

Objectives

To assess the evidence on the impact of enhanced recovery programmes for patients undergoing elective surgery in acute hospital settings in the UK.

Design

Rapid evidence synthesis. Eight databases were searched from 1990 to March 2013 without language restrictions. Relevant reports and guidelines, websites, and reference lists of retrieved articles were scanned to identify additional studies. Systematic reviews, RCTs not included in the systematic reviews, economic evaluations and UK NHS cost analysis, implementation case studies and surveys of patient experience in a UK setting were eligible for inclusion.

Primary and secondary outcome measures

We assessed the impact of enhanced recovery programmes on health or cost-related outcomes, and assessed implementation case studies and patient experience in UK settings. Studies were quality assessed where appropriate. using the CRD DARE critical appraisal process.

Results

Seventeen systematic reviews and 12 additional RCTs were included. Ten relevant economic evaluations were included. No cost analysis studies were identified. Most of the evidence focused on colorectal surgery. Fourteen innovation case studies and 15 implementation case studies undertaken in NHS settings described factors critical to the success of an enhanced recovery programme.

Evidence for colorectal surgery suggests that enhanced recovery programmes may reduce hospital stays by 0.5 to 3.5 days compared with conventional care. There were no significant differences in reported readmission rates. Other surgical specialties showed greater variation in reductions in length of stay reflecting the limited evidence identified.

Findings relating to other outcomes were hampered by a lack of robust evidence and poor reporting.

Conclusions

There is consistent, albeit limited, evidence that enhanced recovery programmes can reduce length of patient hospital stay without increasing readmission rates. The extent to which

managers and clinicians considering implementing enhanced recovery programmes in UK settings can realise savings will depend on length of stay achieved under their existing care pathway.

Word Count: 300

Strengths and limitations of the study

- Enhanced recovery programmes have been adopted with enthusiasm by the NHS as a means to achieving productivity gains and cost-savings. This evolution makes combining studies over different periods and interpreting results of earlier studies in relation to the current context more difficult.
- The evidence base to support such widespread implementation suggests possible benefits in terms of reduced length of hospital stay, fewer postoperative complications, reduced readmissions and improved patient outcomes.
- Althouth there is a reasonable volume of evidence evaluating enhanced recovery programmes in colorectal surgery, robust evidence is sparse. Optimal care is certainly the right thing to do, but the evidence does not identify which enhanced recovery programme elements and combinations of elements are most effective.
- Findings relating to other outcomes, costs of enhanced recovery programmes, experience in using the programmes, and patient experience were limited by generally poor quality evidence and poor reporting. As such, conclusions on which combinations provide greatest gains and how best to implement them cannot be made.

Introduction

The National Health Service (NHS) faces severe funding constraints now and in the medium term. The forecast reduction in resources provides an enormous challenge to NHS organisations and staff. Service redesign can save money and improve quality but much depends on how care is co-ordinated and the way services are implemented in a local setting.[1, 2] NHS decision makers need to consider not only the effectiveness and cost effectiveness of any initiative but also efficient implementation. Enhanced recovery programmes (also known as ERAS, fast track, multimodal, rapid or accelerated recovery programmes) seek to deliver an optimal pathway (covering the preoperative, intraoperative and postoperative periods) that is focused on optimal recovery and discharge for patients. The approach was pioneered in Denmark in the late 1990s for patients undergoing colorectal surgery[3] and is now spreading to other surgical pathways such as orthopaedic, urology and gynaecology.

Enhanced recovery programmes have been delivered in the UK NHS since the early 2000s. Implementation has to date been variable despite the support of the Department of Health and more recently the Royal Colleges. In 2011, 14 innovation sites were established as part of the Enhanced Recovery Partnership Programme. These sites acted as pathfinders for implementation; some sites were self-selecting and others were encouraged to join. The aim was to raise the profile, promote the benefits and inform the uptake of enhanced recovery for elective surgical care across the NHS. These sites had little or no experience in enhanced recovery pathways. It is likely that this variation seen across these sites reflects both the complexity of enhanced recovery programmes themselves and issues around implementing change in established surgical pathways . Differences in programme implementation may also reflect differences between surgical specialities. Set against the benefits of enhanced recovery programmes are concerns that discharging patients too soon after surgery could increase complications and readmissions, thereby worsening patient experience and potentially health outcomes, and increasing pressure on primary and/or secondary healthcare services.

Before embarking on adoption of an enhanced recovery programme, NHS managers and clinicians need to be fully aware of the strength of the underlying evidence. They need to have a clear understanding of how best to implement such programmes and the likely implications for service delivery within finite budgets and considering the need for equity of access. The aim of this project was to conduct a rapid synthesis of the evidence on the clinical and cost effectiveness of enhanced recovery programmes, and the implementation, delivery and impact of such programmes in secondary care settings in the UK.

Methods

Eight databases, including DARE, NHS EED and MEDLINE were searched to from 1990 to March 2013 without language restrictions. The PROSPERO database was searched to identify ongoing systematic reviews. Relevant reports and guidelines were screened for further studies. Reference lists of retrieved articles, reviews and evaluations were scanned, and relevant individuals contacted for additional evidence.

Systematic reviews, RCTs not included in the systematic reviews, economic evaluations, and UK NHS cost analysis studies were included if they evaluated the impact of enhanced recovery programmes (encompassing different combinations of the main preoperative, intraoperative and postoperative pathway elements described by the Enhanced Recovery Partnership Programme[4] on health or cost-related outcomes. Eligible studies included patients undergoing elective surgery in an acute hospital in the UK NHS or a comparable healthcare system. Comparators were only relevant to clinical and cost-effectiveness evaluations, and included conventional (usual/standard) care without a structured multimodal enhanced recovery patient pathway (as defined in the included studies). Case studies, impact assessments and surveys of patient experience that documented the experience of implementing enhanced recovery in a UK setting were also eligible.

Quality assessment of systematic reviews, RCTs and economic evaluations was based on existing CRD critical appraisal methods (http://www.crd.york.ac.uk/crdweb/HomePage.asp; CRD, 2009). Cost analysis studies, studies of patient experience, and case studies of implementation were not formally quality assessed.

All stages of the review process were performed by one researcher and checked by a second. Disagreements between reviewers were resolved by discussion or by recourse to a third reviewer where necessary.

The type and range of evidence precluded meta-analysis and we therefore performed a narrative synthesis, differentiating clinical outcomes (eg. mobilisation, mortality and morbidity, and length of hospital stay), patient-reported outcomes (eg. patient experience and satisfaction), resource use in secondary care (eg. workforce utilisation and costs), and implementation case studies.

Results

Seventeen systematic reviews[5-21] and 12 additional RCTs[22-34] were included in the evidence on clinical effectiveness (see Figure 1: flow diagram). The quality of the systematic reviews varied and the additional RCTs were considered to be at high risk of bias (see tables 1 and 2). One RCT was a four arm trial; this was the only multicentre trial, the remaining trials were small, single centre trials.[35] We included 15 case studies of implementation of ERAS in NHS settings, and evaluations of the 14 Enhanced Recovery Partnership Programme innovation sites. In addition, 10 relevant economic evaluations were also included (summary evidence tables are available on request from the review authors). Most of the evidence focussed on colorectal surgery.

Where reviews reported the number of included patients, sample sizes ranged between 99 and 5,747 patients in the ERAS group and between 99 and 1,062 in comparator groups. Most individual RCTs analysed fewer than 100 patients (range 44 to 597 patients). Where indications for surgery were reported in systematic reviews and individual RCTs, most trials were in patients with cancer. Where reported, patients were adults within similar age ranges.

The number and combination of ERAS elements varied considerably across all types of evidence; ranging from four to 14 elements across systematic reviews and from 10 to 14 elements across individual RCTs (see full report for details; in press). Follow-up was generally up to 30 days post discharge.

Despite the large number of studies, robust evidence was sparse (supplementary tables 1 and 2; full outcome details are available in the full review; in press). Seven reviews in colorectal surgery performed meta-analyses and showed a significant mean reduction in primary or total length of stay that ranged from 1.56 days (95% CI 0.50 to 2.61 days)(19) to 3.75 days (95% CI 5.11 to 2.40 days).(18) Evidence from individual RCTs in colorectal surgery also suggest reduced length of hostpital stay following an ERAS programme (mean length of stay 4.15 days to 6.43 days) compared to conventional care (mean length of stay 6.6 days to 11.7 days). There were no significant differences in reported readmission rates, but it was unclear how readmissions were defined and measured in the reviews and RCTs.

Other surgical specialties showed greater variation in reported reductions in length of stay, but this is likely to reflect the greater uncertainty due to the more limited evidence base for these specialties. Statistical heterogeneity varied between reviews and was often not formally explored, but may have reflected differences in ERAS protocols and surgical populations.

Deaths were rare and no significant differences between treatment groups were found in the systematic reviews and additional RCTs, regardless of surgical speciality. Morbidity was defined differently across systematic reviews and RCTs; rates between treatment groups were sometimes inconsistent, but generally indicated no statistically significant differences.

Mobilisation rates were inconsistent across systematic reviews, but most reported no significant differences in time to mobilisation between treatment groups. Mobilisation was rarely reported as an outcome in the additional RCTs.

Where systematic reviews and additional RCTs assessed quality of life and patient experience/satisfaction, equivocal findings were reported. Evidence on reintervention rates, pain and resource use was lacking in both systematic reviews and RCTs.

Other Reviews

A systematic review in colorectal surgery, identified after the last literature search, showed similar findings to the systematic reviews discussed above.[36] Mean length of primary hospital stay was statistically significantly reduced in ERAS patients; mean difference (MD) -2.44 (95% CI -3.06 to -1.83; 11 RCTs) but with significant statistical heterogeneity (I^2=88%). There was no evidence to suggest increased rates of readmissions, complications and mortality. Some of the individual RCT results for primary length of stay did not appear to be consistent with results reported in other systematic reviews, and this may have impacted on the estimated reduction in length of primary hospital stay.[36]

Two reviews[37, 38] focusing on individual ERAS elements were found and details can be found in the full review (in press).

Case studies

Ten of 14 UK NHS innovation sites provided adequate data for inclusion in this section.[39-41] Fifteen case studies of implementation of ERAS in NHS settings, and 11 NHS trusts (mostly in colorectal surgery) provided evidence relating to the implementation of an ERAS programme within their Trust.

There were variations in practice in terms of numbers and combinations of ERAS elements implemented; the most frequently implemented programme elements in the case studies were pre-admission information/counselling and early postoperative mobilisation. Available evidence did not address which enhanced recovery elements and combinations of elements were most effective. Substantial variation in what constitutes an enhanced recovery programme within and between different surgical specialities, and difficulties in implementing

certain ERAS components, suggest that the enhanced recovery pathway may be used as a framework and adapted to suit local situations. Evidence on compliance/adherence to enhanced recovery programmes was lacking.

Case studies identified the factors believed to act as barriers or facilitators to implementing an ERAS programme. Barriers to implementation included resistance to change from patients and staff, lack of funding or support from management,[39, 42-44] staff turnover, problems arising from poor documentation, the time required to complete documentation, and other practical issues.

Facilitators included the presence of a dedicated ERAS project lead/nurse to coordinate and sustain multidisciplinary working and continuity of the pathway, a multidisciplinary team approach, and continual education for staff and patients/patient representatives. One innovation site mentioned that it did not offer a seven day service for enhanced recovery due to staff resources. Patients operated on towards the end of the week may have to wait until after the weekend to be discharged if they need to be seen by any health care professionals or social services. The need to sustain multidisciplinary working means that, in the absence of 24/7 working for elective procedures, enhanced recovery programmes will tend to be front loaded into the start of the working week (typically Monday to Thursday). Recent evidence suggests a higher risk of death for patients who have elective surgical procedures carried out later in the working week and at the weekend,[45] the capcity to implement ERAS throughout the working week might ensure continuity of best care and help mitigate against such variation.

We included two published studies of patient experience of ERAS.[46, 47] Each study used qualitative research methods to analyse audiotaped material. The two studies provided limited evidence suggesting that patients who were willing to provide feedback took a positive view of their experience of treatment in an ERAS programme. The studies suggested that patients were willing to comment on their experience in a way that can help healthcare providers to identify areas for improvement.

Cost-effectiveness

Ten economic evaluations in adult populations undergoing various surgical procedures evaluated costs and outcomes over short time horizons (supplementary table 3).[48-57] All of the evaluations suggested that programmes that achieve a reduction in length of stay are cost saving, and are not to the detriment of patients in terms of complication rates, readmission and health-related quality-of-life. The quality of the clinical studies on which these evaluations were based was variable, but generally poor. The generalisability of the

results of these evaluations was limited by a lack of transparency in reporting, and the disparity in standard protocols and what had been evaluated across the settings made it unfeasible to select a cost-effective programme.

Discussion

Statement of Principal Findings

Overall, the systematic reviews and additional RCTs suggest that length of hospital stay is reduced in ERAS patients compared to patients receiving conventional care. The evidence was based mainly on colorectal surgery and the applicability of findings to other surgical specialities remains less clear. Evidence for colorectal surgery suggests that enhanced recovery programmes may reduce hospital stays by 0.5 to 3.5 days compared with conventional care.

There were marked differences in length of stay across reviews and individual studies regardless of speciality. These differences may reflect differences in ERAS protocols and health care systems and/or outcome definitions. This raises questions regarding the magnitude of effect of the ERAS protocols on length of stay, which may be overstated in some reviews.

The evidence suggests that ERAS programmes do not compromise patient morbidity, mortality and readmission rates but outcome definitions varied across reviews and individual studies. Such differences make it difficult to determine the reliability and generalisability of the findings.

Equivocal findings were reported for quality of life and patient experience/satisfaction but the evidence was based on few studies, which utilised various methods to measure these outcomes. The limited evidence precludes conclusions on the effects of ERAS protocols on pain, mobilisation and reintervention.

The implementation evidence included resource use in terms of the professionals involved in delivery of enhanced recovery programmes, but details were very limited and did not add to the evidence synthesis. Most case studies were uncontrolled and represent experiences of a sample of centres that chose to report their data; their outcomes may not be representative of those achieved elsewhere in the UK NHS. Their main value as evidence is the light they shed on NHS clinicians' perceptions of requirements for successful implementation and barriers to implementation of ERAS.

The impact of surgical experience and surgical volume on clinical outcomes was not explored and any implications of differences in these areas remain unknown. As enhanced recovery invariably targets the fitter, more mobile patient, frailer patients may not receive parity of access to what may be considered optimal treatment and management. Managers and clinicians considering implementing such programmes should think about the likely implication on equity of access. Whether inequity is an unintended outcome of enhanced recovery, merits further investigation.

Our review of the cost effectiveness literature suggests that enhanced recovery programmes that achieve a reduction in length of stay may save costs without detrimental effects on complication rates, readmission and health-related quality of life. However, generalisability of the results of the economic evaluations is limited by a lack of transparency in reporting, use of different settings and populations and variable methodology in analyses. Data were lacking for resource use associated with the programmes evaluated and could not usefully inform the review of economic evaluations. In addition, the clinical effectiveness of some of the programmes considered in economic evaluations was not based on robust evidence.

Strengths and weaknesses

The main strength of this study was our use of multiple approaches to acquire and synthesise evidence. The main limitations were poor methodological quality and poor reporting of the included studies, and the inherent difficulty of reviewing a complex intervention in different healthcare systems and surgical specialities. Current methods for synthesising such complex interventions are limited. The methodological limitations and are not discussed here as this was outside the scope of this project, but have been addressed in previous publications (eg. Noyes et al, 2013).[58] Another complication is that elements of early enhanced recovery programmes have become accepted practice within conventional care. This evolution makes combining studies over different periods and interpreting results of earlier studies in relation to the current context more difficult.

We found a large number of systematic reviews but there was substantial overlap in the included studies and evidence was not as abundant as the existence of multiple systematic reviews suggested. Most of the RCTs were small and not high quality. With the exception of one RCT, the remainder were single centre trials and therefore appear to have been undertaken to support implementation of an enhanced recovery programme in a specific setting rather than being planned as research studies. There were significant clinical and methodological differences between individual trials, and we therefore presented a narrative

synthesis. Relatively few trials were conducted in the UK and this may limit the generalisability of evidence to UK NHS settings.

Lack of evidence on important outcomes including pain and quality of life is also an issue for research in this field. Trials tended not to report on adherence to the planned enhanced recovery programme. Assessing adherence to interventions and the impact this has on health outcomes is an important issue which is often overlooked in studies, and is a limitation in the evidence base in this review.

Three additional systematic reviews of effectiveness were brought to our attention during manuscript submission. One systematic review incorporates RCTs in colorectal surgery (Greco, 2013),[59] one incorporates RCTs and cohort studies in abdominal surgery (Neville, 2014)[59] and one includes RCTs and quasi-RCTs across various surgical specialities (Nicholson, 2014).[59] The trials included in Greco (2013)[59] and Nicholson (2014)[59] overlap with those included in this review and the findings are consistent. The inclusion of these two reviews would therefore not have significantly altered the findings from this review. Neville (2014)[59] provides some additional data on patient-reported outcomes, including some evidence on post-discharge functional status. However, these outcomes were not frequently reported, and the additional evidence was mainly from study designs that would not have met the inclusion criteria for this review.

An important feature of our review is the inclusion of evidence on the implementation of enhanced recovery programmes in the UK NHS. This evidence has not been synthesised previously and the original programme webistes are archived, so future access is not assured. By summarising this evidence, we have ensured that the main findings continue to be publicly available. We sought evidence on the experience of health professionals and patients of a broad range of sources and study types. Important themes emerged from this evidence that may be of value for implementing and sustaining enhanced recovery programmes in UK NHS settings. Due to the rapid nature of the evidence synthesis, the list of sources searched to identify data on implementation and delivery of enhanced recovery programmes was not exhaustive and we acknowledge that relevant evidence may have been missed. Indeed, evidence from Scotland has been noted and eligible case studies have been identified from the NHS Scotland Quality Improvement Hub website. It should be noted that these are as limited as those included in the review. A qualititaive study was brought to our attention at peer review; the study was published after our final search date. Pearsall et al (2014)[60] conducted a qualitative study to explore the barriers and enablers in implementing an enhanced recovery after surgery programme in a University hospital in Canada. The themes identified are consistent with those reported in this review.

However, case studies are susceptible to risk of bias. Use of a standard reporting format was a potential strength of the case studies but variation in what each site actually reported (particularly in terms of evidence of benefit from the introduction of enhanced recovery programmes) reduced the usefulness of the evidence.

We sought to incorporate published and unpublished evidence on patient experiences and views of enhanced recovery programmes. Evaluation of patient experience of care is increasingly important for the NHS, especially in view of unacceptable failures of care such as those highlighted in the Francis Report.[61] Though the evidence was generally positive for enhanced recovery, it was limited by a shortage of studies that used validated measures of patient experience and by study designs that could bias results in favour of enhanced recovery.

A further strength of this study was the consideration of cost-effectiveness evidence, but the nature of the evidence did not permit any analyses. There is a clear need to capture better evaluated data on costs and benefits of enhanced recovery programmes from a clearly stated perspective. A systematic review of economic evaluations (Lee, 2014)[59] was brought to our attention during manuscript publication. The review confirmed the need for well-designed trials to determine the cost-effectiveness of enhanced recovery programmes from both the institutional and societal perspectives.

Implications for healthcare

Overall, there is consistent, albeit limited, evidence that enhanced recovery programmes can reduce length of patient hospital stay without increasing readmission rates. Data on re-intervention rates and patient-reported outcomes did not suggest significant differences between enhanced recovery and conventional care, but the evidence was very limited and based on small numbers of patients. The lack of evidence on patient outcomes, resource use and costs precludes firm conclusions on the overall value of enhanced recovery programmes.

ERAS does not appear to reduce complication or readmission rates; the only cost benefit may lie in a reduction in post-operative bed days. Optimal care is certainly the right thing to do, but the evidence does not identify which enhanced recovery programme elements and combinations of elements are most effective. As such, conclusions on which combinations provide greatest gains and how best to implement them cannot be made.

The extent to which managers and clinicians considering implementing enhanced recovery programmes can realise reductions and cost savings will therefore depend on length of stays achieved under their existing care pathway. Important themes emerged from the relevant evidence identified on implementation, including the role of ERAS facilitators and the need for full support from management. It appears that these components are essential for the successful implementation and sustained delivery of enhanced recovery programmes in NHS settings. Consideration of potential benefit also needs to take account of the costs of service redesign, the resource use associated with programmes of this nature, the potential for improvement in patient outcomes and the impact on equity of access.

Implications for research

RCTs comparing an enhanced recovery programme with conventional care continue to be conducted and published, although mostly not in the UK. Given the available evidence, further single centre RCTs of this kind are not a priority. Rather, what is needed is improved collection and reporting of how enhanced recovery programmes are implemented, resourced and experienced in NHS settings. Also, exploration into the effect that varying levels of surgical volume and surgical experience, and different discharge protocols might have on the success of an enhanced recovery pathway and subsequent outcomes.This will enhance our existing knowledge and understanding and provide evidence to support local decision-making about whether to adopt and how best to implement.

The two groups of implementation case studies included in our synthesis, although all were conducted in the UK, provide very limited information on how enhanced recovery programmes have actually been implemented in UK NHS settings. The standard reporting format originally proposed by The Enhanced Recovery Partnership Programme would enhance the value of future case studies if adhered to. Knowledge of how well the intervention has been implemented (fidelity) is essential for understanding how and why the intervention works and hence how outcomes can be further improved. Assessing fidelity may involve considering not only adherence to the requirements of the programme but also potential moderating factors, such as strategies used to assist delivery of the intervention, quality of delivery and participant responsiveness to new practices.[62] It would be helpful if future innovation programmes used standardised reporting. For multi-site programmes, a formal synthesis of findings from all participating sites should be undertaken as part of the evaluative process. This would ensure that the insights and contextual information which can inform the wider spread and adoption (or indeed discontinuation) would be systematically captured in a generalisable format.

Adherence/compliance to elements by staff and patients also requires further investigation. Rigorous data on patients' experiences of enhanced recovery programmes are lacking. Validated tools should be used and administered independently of those providing the service. Efforts should be made to obtain data from representative samples of patients receiving conventional care as well as those treated with enhanced recovery protocols, along with evidence on the experiences of their families/carers.

Evidence relating to the cost-effectiveness of enhanced recovery programmes in UK NHS settings is lacking. Whist enhanced recovery programmes have the potential to deliver cost savings, improved measurement of costs and benefits is crucial to help decision-makers decide how best to make optimal use of limited resources.

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Transparency declaration: The lead author (the manuscript's guarantor) affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Data sharing: No additional data available.

Table 1: Systematic review risk of bias assessment

Author	Adequate search	Risk of bias assessed	Quality score accounted for in analysis	Study details reported and differences accounted for	Statistical heterogeneity investigated	Gaps in research identified	Conclusions justified
Colorectal/Colon surgery							
Adamina (2011)[6]	✓	✓	UC	✓	UC	✓	✓
Ahmed (2012)[7]	✓	X	X	X	X	X	✓
Eskicioglu (2009)[10]	✓	✓	X	✓	✓	✓	✓
Gouvas (2009)[11]	✓	✓	X	✓	✓	✓	✓
Khan (2010)[13]	✓	✓	X	✓	X	✓	✓
Lv (2012a)[21]	✓	✓	X	X	✓	✓	✓
Rawlinson (2011)[15]	✓	X	X	✓	UC	X	UC
Spanjersberg (2011)[16]	✓	✓	✓	✓	✓	✓	✓
Varadhan (2010)[17]	✓	✓	X	✓	✓	✓	✓
Walter (2009)[18]	✓	✓	✓	✓	✓	✓	✓
Wind (2006)[19]	✓	✓	✓	✓	✓	✓	✓
Gynaecological surgery							
Lv (2012b)[20]	✓	X	X	X	X	✓	✓
Liver/pancreatic surgery							
Coolsen (2012)[8]	✓	✓	X	✓	X	✓	✓
Coolsen (2013)[9] Link to [63]	✓	✓	✓	✓	✓	✓	✓
Hall (2012)[12]	X	X	X	✓	X	✓	✓
Various surgical specialities							
Lemmens (2009)[14]	✓	X	X	✓	X	✓	✓
Sturm (2009)[5]	✓	X	X	✓	UC	✓	✓

UC=unclear reporting

Table 2: RCT quality assessment

Author	Adequate random allocation	Adequate allocation concealment	Blinding of healthcare professional	Blinding of participants	Blinding of outcome assessor	Unexpected imbalances in drop-outs between groups	Imbalances accounted/adjusted for	Intention to treat analysis	ITT appropriate and appropriate methods used to account for missing data
Bariatric surgery									
Lemanu (2013)[27]	✓	✓	X	X	X	X	NA	UC	UC
Colorectal/colon surgery									
Garcia-Botello (2011)[24]	UC	X	UC	X	UC	X	NA	UC	✓
Ionescu (2009)[25]	✓	✓	X	X	UC	X	NA	UC	UC
Lee (2011)[26]	✓	✓	UC	X	UC	X	NA	UC	UC
Ren (2012)[29]	✓	✓	X	X	✓	X	NA	UC	UC
Wang (2011)[31]	UC	UC	UC	X	UC	X	NA	✓	✓
Wang (2012)[32]	UC	UC	X	X	✓	UC	UC	UC	UC
Yang (2012)[33, 34]	✓	UC	X	X	UC	X	NA	X	X
Gastric surgery									
Chen (2012)[22]	UC	UC	X	✓	✓	X	NA	UC	UC
Kim (2012)[23]	UC	UC	X	X	X	X	NA	UC	UC
Liu (2010)[28]	UC	X	X	X	X	X	NA	UC	UC
Wang (2010)[30]	UC	UC	X	X	UC	X	NA	X	X

UC: unclear reporting; NA: not applicable

Figure legend:

Figure 1: Study flow diagram

Effectiveness and implementation of enhanced recovery after surgery programmes: a rapid evidence synthesis

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Data sharing: No additional data available.

Abstract

Objectives

To assess the evidence on the impact of enhanced recovery programmes for patients undergoing elective surgery in acute hospital settings in the UK.

Design

Rapid evidence synthesis. Eight databases were searched from 1990 to March 2013 without language restrictions. Relevant reports and guidelines, websites, and reference lists of retrieved articles were scanned to identify additional studies. Systematic reviews, RCTs not included in the systematic reviews, economic evaluations and UK NHS cost analysis, implementation case studies and surveys of patient experience in a UK setting were eligible for inclusion.

Primary and secondary outcome measures

We assessed the impact of enhanced recovery programmes on health or cost-related outcomes, and assessed implementation case studies and patient experience in UK settings. Studies were quality assessed where appropriate. using the CRD DARE critical appraisal process.

Results

Seventeen systematic reviews and 12 additional RCTs were included. Ten relevant economic evaluations were included. No cost analysis studies were identified. Most of the evidence focused on colorectal surgery. Fourteen innovation case studies and 15 implementation case studies undertaken in NHS settings described factors critical to the success of an enhanced recovery programme.

Evidence for colorectal surgery suggests that enhanced recovery programmes may reduce hospital stays by 0.5 to 3.5 days compared with conventional care. There were no significant differences in reported readmission rates. Other surgical specialties showed greater variation in reductions in length of stay reflecting the limited evidence identified.

Findings relating to other outcomes were hampered by a lack of robust evidence and poor reporting.

Conclusions

There is consistent, albeit limited, evidence that enhanced recovery programmes can reduce length of patient hospital stay without increasing readmission rates. The extent to which managers and clinicians considering implementing enhanced recovery programmes in UK settings can realise savings will depend on length of stay achieved under their existing care pathway.

Word Count: ~~290~~ 300

Strengths and limitations of the study

- Enhanced recovery programmes have been adopted with enthusiasm by the NHS as a means to achieving productivity gains and cost-savings. This evolution makes combining studies over different periods and interpreting results of earlier studies in relation to the current context more difficult.
- The evidence base to support such widespread implementation suggests possible benefits in terms of reduced length of hospital stay, fewer postoperative complications, reduced readmissions and improved patient outcomes.
- Althouth there is a reasonable volume of evidence evaluating enhanced recovery programmes in colorectal surgery, robust evidence is sparse. Optimal care is certainly the right thing to do, but the evidence does not identify which enhanced recovery programme elements and combinations of elements are most effective.
- Findings relating to other outcomes, costs of enhanced recovery programmes, experience in using the programmes, and patient experience were limited by generally poor quality evidence and poor reporting. As such, conclusions on which combinations provide greatest gains and how best to implement them cannot be made.

Introduction

The National Health Service (NHS) faces severe funding constraints now and in the medium term. The forecast reduction in resources provides an enormous challenge to NHS organisations and staff. Service redesign can save money and improve quality but much depends on how care is co-ordinated and the way services are implemented in a local setting.[1, 2] NHS decision makers need to consider not only the effectiveness and cost effectiveness of any initiative but also efficient implementation. Enhanced recovery programmes (also known as ERAS, fast track, multimodal, rapid or accelerated recovery programmes) seek to deliver an optimal pathway (covering the preoperative, intraoperative and postoperative periods) that is focused on optimal recovery and discharge for patients. The approach was pioneered in Denmark in the late 1990s for patients undergoing colorectal surgery[3] and is now spreading to other surgical pathways such as orthopaedic, urology and gynaecology.

Enhanced recovery programmes have been delivered in the UK NHS since the early 2000s. Implementation has to date been variable despite the support of the Department of Health and more recently the Royal Colleges. In 2011, 14 innovation sites were established as part of the Enhanced Recovery Partnership Programme. These sites acted as pathfinders for implementation; some sites were self-selecting and others were encouraged to join. The aim was to raise the profile, promote the benefits and inform the uptake of enhanced recovery for elective surgical care across the NHS. These sites had little or no experience in enhanced recovery pathways. It is likely that this variation seen across these sites reflects both the complexity of enhanced recovery programmes themselves and issues around implementing change in established surgical pathways . Differences in programme implementation may also reflect differences between surgical specialities. Set against the benefits of enhanced recovery programmes are concerns that discharging patients too soon after surgery could increase complications and readmissions, thereby worsening patient experience and potentially health outcomes, and increasing pressure on primary and/or secondary healthcare services.

Before embarking on adoption of an enhanced recovery programme, NHS managers and clinicians need to be fully aware of the strength of the underlying evidence. They need to have a clear understanding of how best to implement such programmes and the likely implications for service delivery within finite budgets and considering the need for equity of access. The aim of this project was to conduct a rapid synthesis of the evidence on the

clinical and cost effectiveness of enhanced recovery programmes, and the implementation, delivery and impact of such programmes in secondary care settings in the UK.

Methods

Eight databases, including DARE, NHS EED and MEDLINE were searched to from 1990 to March 2013 without language restrictions. The PROSPERO database was searched to identify ongoing systematic reviews. Relevant reports and guidelines were screened for further studies. Reference lists of retrieved articles, reviews and evaluations were scanned, and relevant individuals contacted for additional evidence.

Systematic reviews, RCTs not included in the systematic reviews, economic evaluations, and UK NHS cost analysis studies were included if they evaluated the impact of enhanced recovery programmes (encompassing different combinations of the main preoperative, intraoperative and postoperative pathway elements described by the Enhanced Recovery Partnership Programme[4] on health or cost-related outcomes. Eligible studies included patients undergoing elective surgery in an acute hospital in the UK NHS or a comparable healthcare system. Comparators were only relevant to clinical and cost-effectiveness evaluations, and included conventional (usual/standard) care without a structured multimodal enhanced recovery patient pathway (as defined in the included studies). Case studies, impact assessments and surveys of patient experience that documented the experience of implementing enhanced recovery in a UK setting were also eligible.

Quality assessment of systematic reviews, RCTs and economic evaluations was based on existing CRD critical appraisal methods (http://www.crd.york.ac.uk/crdweb/HomePage.asp; CRD, 2009). Cost analysis studies, studies of patient experience, and case studies of implementation were not formally quality assessed.

All stages of the review process were performed by one researcher and checked by a second. Disagreements between reviewers were resolved by discussion or by recourse to a third reviewer where necessary.

The type and range of evidence precluded meta-analysis and we therefore performed a narrative synthesis, differentiating clinical outcomes (eg. mobilisation, mortality and morbidity, and length of hospital stay), patient-reported outcomes (eg. patient experience and satisfaction), resource use in secondary care (eg. workforce utilisation and costs), and implementation case studies.

Results

Seventeen systematic reviews[5-21] and 12 additional RCTs[22-34] were included in the evidence on clinical effectiveness (see Figure 1: flow diagram). The quality of the systematic reviews varied and the additional RCTs were considered to be at high risk of bias (see tables 1 and 2). One RCT was a four arm trial; this was the only multicentre trial, the remaining trials were small, single centre trials.[35] We included 15 case studies of implementation of ERAS in NHS settings, and evaluations of the 14 Enhanced Recovery Partnership Programme innovation sites. In addition, 10 relevant economic evaluations were also included (summary evidence tables are available on request from the review authors). Most of the evidence focussed on colorectal surgery.

Where reviews reported the number of included patients, sample sizes ranged between 99 and 5,747 patients in the ERAS group and between 99 and 1,062 in comparator groups. Most individual RCTs analysed fewer than 100 patients (range 44 to 597 patients). Where indications for surgery were reported in systematic reviews and individual RCTs, most trials were in patients with cancer. Where reported, patients were adults within similar age ranges.

The number and combination of ERAS elements varied considerably across all types of evidence; ranging from four to 14 elements across systematic reviews and from 10 to 14 elements across individual RCTs (see full report for details; in press). Follow-up was generally up to 30 days post discharge.

Despite the large number of studies, robust evidence was sparse (~~see tables 3 and 4~~ supplementary tables 1 and 2; full outcome details are available in the full review; in press). Seven reviews in colorectal surgery performed meta-analyses and showed a significant mean reduction in primary or total length of stay that ranged from 1.56 days (95% CI 0.50 to 2.61 days)(19) to 3.75 days (95% CI 5.11 to 2.40 days).(18)~~(Walter 2009)~~ Evidence from individual RCTs in colorectal surgery also suggest reduced length of hostpital stay following an ERAS programme (mean length of stay 4.15 days to 6.43 days) compared to conventional care (mean length of stay 6.6 days to 11.7 days). There were no significant differences in reported readmission rates, but it was unclear how readmissions were defined and measured in the reviews and RCTs.

Other surgical specialties showed greater variation in reported reductions in length of stay, but this is likely to reflect the greater uncertainty due to the more limited evidence base for these specialties. Statistical heterogeneity varied between reviews and was often not

formally explored, but may have reflected differences in ERAS protocols and surgical populations.

Deaths were rare and no significant differences between treatment groups were found in the systematic reviews and additional RCTs, regardless of surgical speciality. Morbidity was defined differently across systematic reviews and RCTs; rates between treatment groups were sometimes inconsistent, but generally indicated no statistically significant differences.

Mobilisation rates were inconsistent across systematic reviews, but most reported no significant differences in time to mobilisation between treatment groups. Mobilisation was rarely reported as an outcome in the additional RCTs.

Where systematic reviews and additional RCTs assessed quality of life and patient experience/satisfaction, equivocal findings were reported. Evidence on reintervention rates, pain and resource use was lacking in both systematic reviews and RCTs.

Other Reviews

A systematic review in colorectal surgery, identified after the last literature search, showed similar findings to the systematic reviews discussed above.[36] Mean length of primary hospital stay was statistically significantly reduced in ERAS patients; mean difference (MD) -2.44 (95% CI -3.06 to -1.83; 11 RCTs) but with significant statistical heterogeneity (I^2=88%). There was no evidence to suggest increased rates of readmissions, complications and mortality. Some of the individual RCT results for primary length of stay did not appear to be consistent with results reported in other systematic reviews, and this may have impacted on the estimated reduction in length of primary hospital stay.[36]

Two reviews[37, 38] focusing on individual ERAS elements were found and details can be found in the full review (in press).

Case studies

Ten of 14 UK NHS innovation sites provided adequate data for inclusion in this section.[39-41] Fifteen case studies of implementation of ERAS in NHS settings, and 11 NHS trusts (mostly in colorectal surgery) provided evidence relating to the implementation of an ERAS programme within their Trust.

There were variations in practice in terms of numbers and combinations of ERAS elements implemented; the most frequently implemented programme elements in the case studies

were pre-admission information/counselling and early postoperative mobilisation. Available evidence did not address which enhanced recovery elements and combinations of elements were most effective. Substantial variation in what constitutes an enhanced recovery programme within and between different surgical specialities, and difficulties in implementing certain ERAS components, suggest that the enhanced recovery pathway may be used as a framework and adapted to suit local situations. Evidence on compliance/adherence to enhanced recovery programmes was lacking.

Case studies identified the factors believed to act as barriers or facilitators to implementing an ERAS programme. Barriers to implementation included resistance to change from patients and staff, lack of funding or support from management,[39, 42-44] staff turnover, problems arising from poor documentation, the time required to complete documentation, and other practical issues.

Facilitators included the presence of a dedicated ERAS project lead/nurse to coordinate and sustain multidisciplinary working and continuity of the pathway, a multidisciplinary team approach, and continual education for staff and patients/patient representatives. One innovation site mentioned that it did not offer a seven day service for enhanced recovery due to staff resources. Patients operated on towards the end of the week may have to wait until after the weekend to be discharged if they need to be seen by any health care professionals or social services. The need to sustain multidisciplinary working means that, in the absence of 24/7 working for elective procedures, enhanced recovery programmes will tend to be front loaded into the start of the working week (typically Monday to Thursday). Recent evidence suggests a higher risk of death for patients who have elective surgical procedures carried out later in the working week and at the weekend,[45] the capcity to implement ERAS throughout the working week might ensure continuity of best care and help mitigate against such variation.

We included two published studies of patient experience of ERAS.[46, 47] Each study used qualitative research methods to analyse audiotaped material. The two studies provided limited evidence suggesting that patients who were willing to provide feedback took a positive view of their experience of treatment in an ERAS programme. The studies suggested that patients were willing to comment on their experience in a way that can help healthcare providers to identify areas for improvement.

Cost-effectiveness

Ten economic evaluations in adult populations undergoing various surgical procedures evaluated costs and outcomes over short time horizons (~~see Table 5~~ supplementary table 3).[48-57] All of the evaluations suggested that programmes that achieve a reduction in length of stay are cost saving, and are not to the detriment of patients in terms of complication rates, readmission and health-related quality-of-life. The quality of the clinical studies on which these evaluations were based was variable, but generally poor. The generalisability of the results of these evaluations was limited by a lack of transparency in reporting, and the disparity in standard protocols and what had been evaluated across the settings made it unfeasible to select a cost-effective programme.

Discussion

Statement of Principal Findings

Overall, the systematic reviews and additional RCTs suggest that length of hospital stay is reduced in ERAS patients compared to patients receiving conventional care. The evidence was based mainly on colorectal surgery and the applicability of findings to other surgical specialities remains less clear. Evidence for colorectal surgery suggests that enhanced recovery programmes may reduce hospital stays by 0.5 to 3.5 days compared with conventional care.

There were marked differences in length of stay across reviews and individual studies regardless of speciality. These differences may reflect differences in ERAS protocols and health care systems and/or outcome definitions. This raises questions regarding the magnitude of effect of the ERAS protocols on length of stay, which may be overstated in some reviews.

The evidence suggests that ERAS programmes do not compromise patient morbidity, mortality and readmission rates but outcome definitions varied across reviews and individual studies. Such differences make it difficult to determine the reliability and generalisability of the findings.

Equivocal findings were reported for quality of life and patient experience/satisfaction but the evidence was based on few studies, which utilised various methods to measure these outcomes. The limited evidence precludes conclusions on the effects of ERAS protocols on pain, mobilisation and reintervention.

The implementation evidence included resource use in terms of the professionals involved in delivery of enhanced recovery programmes, but details were very limited and did not add to the evidence synthesis. Most case studies were uncontrolled and represent experiences of a sample of centres that chose to report their data; their outcomes may not be representative of those achieved elsewhere in the UK NHS. Their main value as evidence is the light they shed on NHS clinicians' perceptions of requirements for successful implementation and barriers to implementation of ERAS.

The impact of surgical experience and surgical volume on clinical outcomes was not explored and any implications of differences in these areas remain unknown. As enhanced recovery invariably targets the fitter, more mobile patient, frailer patients may not receive parity of access to what may be considered optimal treatment and management. Managers and clinicians considering implementing such programmes should think about the likely implication on equity of access. Whether inequity is an unintended outcome of enhanced recovery, merits further investigation.

Our review of the cost effectiveness literature suggests that enhanced recovery programmes that achieve a reduction in length of stay may save costs without detrimental effects on complication rates, readmission and health-related quality of life. However, generalisability of the results of the economic evaluations is limited by a lack of transparency in reporting, use of different settings and populations and variable methodology in analyses. Data were lacking for resource use associated with the programmes evaluated and could not usefully inform the review of economic evaluations. In addition, the clinical effectiveness of some of the programmes considered in economic evaluations was not based on robust evidence.

Strengths and weaknesses

The main strength of this study was our use of multiple approaches to acquire and synthesise evidence. The main limitations were poor methodological quality and poor reporting of the included studies, and the inherent difficulty of reviewing a complex intervention in different healthcare systems and surgical specialities. Current methods for synthesising such complex interventions are limited. The methodological limitations and are not discussed here as this was outside the scope of this project, but have been addressed in previous publications (eg. Noyes et al, 2013).[58] Another complication is that elements of early enhanced recovery programmes have become accepted practice within conventional care. This evolution makes combining studies over different periods and interpreting results of earlier studies in relation to the current context more difficult.

We found a large number of systematic reviews but there was substantial overlap in the included studies and evidence was not as abundant as the existence of multiple systematic reviews suggested. Most of the RCTs were small and not high quality. With the exception of one RCT, the remainder were single centre trials and therefore appear to have been undertaken to support implementation of an enhanced recovery programme in a specific setting rather than being planned as research studies. There were significant clinical and methodological differences between individual trials, and we therefore presented a narrative synthesis. Relatively few trials were conducted in the UK and this may limit the generalisability of evidence to UK NHS settings.

Lack of evidence on important outcomes including pain and quality of life is also an issue for research in this field. Trials tended not to report on adherence to the planned enhanced recovery programme. Assessing adherence to interventions and the impact this has on health outcomes is an important issue which is often overlooked in studies, and is a limitation in the evidence base in this review.

Three additional systematic reviews of effectiveness were brought to our attention during manuscript submission. One systematic review incorporates RCTs in colorectal surgery (Greco, 2013),[59] one incorporates RCTs and cohort studies in abdominal surgery (Neville, 2014)[59] and one includes RCTs and quasi-RCTs across various surgical specialities (Nicholson, 2014).[59] The trials included in Greco (2013)[59] and Nicholson (2014)[59] overlap with those included in this review and the findings are consistent. The inclusion of these two reviews would therefore not have significantly altered the findings from this review. Neville (2014)[59] provides some additional data on patient-reported outcomes, including some evidence on post-discharge functional status. However, these outcomes were not frequently reported, and the additional evidence was mainly from study designs that would not have met the inclusion criteria for this review.

An important feature of our review is the inclusion of evidence on the implementation of enhanced recovery programmes in the UK NHS. This evidence has not been synthesised previously and the original programme webistes are archived, so future access is not assured. By summarising this evidence, we have ensured that the main findings continue to be publicly available. We sought evidence on the experience of health professionals and patients of a broad range of sources and study types. Important themes emerged from this evidence that may be of value for implementing and sustaining enhanced recovery programmes in UK NHS settings. Due to the rapid nature of the evidence synthesis, the list

of sources searched to identify data on implementation and delivery of enhanced recovery programmes was not exhaustive and we acknowledge that relevant evidence may have been missed. Indeed, evidence from Scotland has been noted and eligible case studies have been identified from the NHS Scotland Quality Improvement Hub website. It should be noted that these are as limited as those included in the review. A qualititaive study was brought to our attention at peer review; the study was published after our final search date. Pearsall et al (2014)[60] conducted a qualitative study to explore the barriers and enablers in implementing an enhanced recovery after surgery programme in a University hospital in Canada. The themes identified are consistent with those reported in this review.

However, case studies are susceptible to risk of bias. Use of a standard reporting format was a potential strength of the case studies but variation in what each site actually reported (particularly in terms of evidence of benefit from the introduction of enhanced recovery programmes) reduced the usefulness of the evidence.

We sought to incorporate published and unpublished evidence on patient experiences and views of enhanced recovery programmes. Evaluation of patient experience of care is increasingly important for the NHS, especially in view of unacceptable failures of care such as those highlighted in the Francis Report.[61] Though the evidence was generally positive for enhanced recovery, it was limited by a shortage of studies that used validated measures of patient experience and by study designs that could bias results in favour of enhanced recovery.

A further strength of this study was the consideration of cost-effectiveness evidence, but the nature of the evidence did not permit any analyses. There is a clear need to capture better evaluated data on costs and benefits of enhanced recovery programmes from a clearly stated perspective. A systematic review of economic evaluations (Lee, 2014)[59] was brought to our attention during manuscript publication. The review confirmed the need for well-designed trials to determine the cost-effectiveness of enhanced recovery programmes from both the institutional and societal perspectives.

Implications for healthcare

Overall, there is consistent, albeit limited, evidence that enhanced recovery programmes can reduce length of patient hospital stay without increasing readmission rates. Data on re-intervention rates and patient-reported outcomes did not suggest significant differences between enhanced recovery and conventional care, but the evidence was very limited and

based on small numbers of patients. The lack of evidence on patient outcomes, resource use and costs precludes firm conclusions on the overall value of enhanced recovery programmes.

ERAS does not appear to reduce complication or readmission rates; the only cost benefit may lie in a reduction in post-operative bed days. Optimal care is certainly the right thing to do, but the evidence does not identify which enhanced recovery programme elements and combinations of elements are most effective. As such, conclusions on which combinations provide greatest gains and how best to implement them cannot be made.

The extent to which managers and clinicians considering implementing enhanced recovery programmes can realise reductions and cost savings will therefore depend on length of stays achieved under their existing care pathway. Important themes emerged from the relevant evidence identified on implementation, including the role of ERAS facilitators and the need for full support from management. It appears that these components are essential for the successful implementation and sustained delivery of enhanced recovery programmes in NHS settings. Consideration of potential benefit also needs to take account of the costs of service redesign, the resource use associated with programmes of this nature, the potential for improvement in patient outcomes and the impact on equity of access.

Implications for research

RCTs comparing an enhanced recovery programme with conventional care continue to be conducted and published, although mostly not in the UK. Given the available evidence, further single centre RCTs of this kind are not a priority. Rather, what is needed is improved collection and reporting of how enhanced recovery programmes are implemented, resourced and experienced in NHS settings. Also, exploration into the effect that varying levels of surgical volume and surgical experience, and different discharge protocols might have on the success of an enhanced recovery pathway and subsequent outcomes.This will enhance our existing knowledge and understanding and provide evidence to support local decision-making about whether to adopt and how best to implement.

The two groups of implementation case studies included in our synthesis, although all were conducted in the UK, provide very limited information on how enhanced recovery programmes have actually been implemented in UK NHS settings. The standard reporting format originally proposed by The Enhanced Recovery Partnership Programme would enhance the value of future case studies if adhered to. Knowledge of how well the

intervention has been implemented (fidelity) is essential for understanding how and why the intervention works and hence how outcomes can be further improved. Assessing fidelity may involve considering not only adherence to the requirements of the programme but also potential moderating factors, such as strategies used to assist delivery of the intervention, quality of delivery and participant responsiveness to new practices.[62] It would be helpful if future innovation programmes used standardised reporting. For multi-site programmes, a formal synthesis of findings from all participating sites should be undertaken as part of the evaluative process. This would ensure that the insights and contextual information which can inform the wider spread and adoption (or indeed discontinuation) would be systematically captured in a generalisable format.

Adherence/compliance to elements by staff and patients also requires further investigation. Rigorous data on patients' experiences of enhanced recovery programmes are lacking. Validated tools should be used and administered independently of those providing the service. Efforts should be made to obtain data from representative samples of patients receiving conventional care as well as those treated with enhanced recovery protocols, along with evidence on the experiences of their families/carers.

Evidence relating to the cost-effectiveness of enhanced recovery programmes in UK NHS settings is lacking. Whist enhanced recovery programmes have the potential to deliver cost savings, improved measurement of costs and benefits is crucial to help decision-makers decide how best to make optimal use of limited resources.

Word Count: ~~3,732~~4,179

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Figure 1: Study flow diagram

Table 1: Systematic review risk of bias assessment

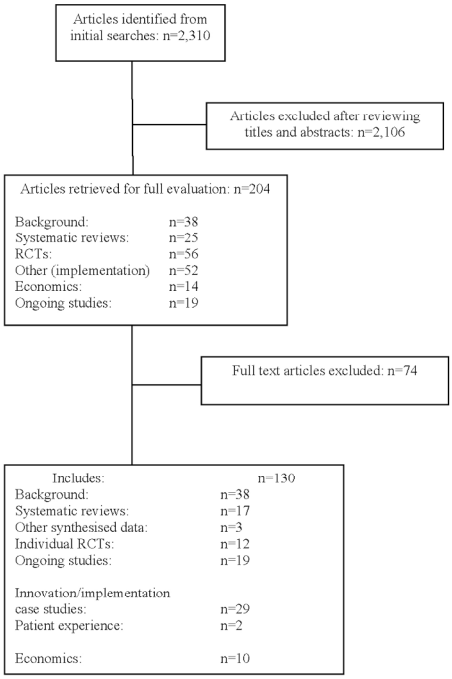
Author	Adequate search	Risk of bias assessed	Quality score accounted for in analysis	Study details reported and differences accounted for	Statistical heterogeneity investigated	Gaps in research identified	Conclusions justified
Colorectal/Colon surgery							
Adamina (2011)[6]	✓	✓	UC	✓	UC	✓	✓
Ahmed (2012)[7]	✓	X	X	X	X	X	✓
Eskicioglu (2009)[10]	✓	✓	X	✓	✓	✓	✓
Gouvas (2009)[11]	✓	✓	X	✓	✓	✓	✓
Khan (2010)[13]	✓	✓	X	✓	X	✓	✓
Lv (2012a)[21]	✓	✓	X	X	✓	✓	✓
Rawlinson (2011)[15]	✓	X	X	✓	UC	X	UC
Spanjersberg (2011)[16]	✓	✓	✓	✓	✓	✓	✓
Varadhan (2010)[17]	✓	✓	X	✓	✓	✓	✓
Walter (2009)[18]	✓	✓	✓	✓	✓	✓	✓
Wind (2006)[19]	✓	✓	✓	✓	✓	✓	✓
Gynaecological surgery							
Lv (2012b)[20]	✓	X	X	X	X	✓	✓
Liver/pancreatic surgery							
Coolsen (2012)[8]	✓	✓	X	✓	X	✓	✓
Coolsen (2013)[9] Link to [63]	✓	✓	✓	✓	✓	✓	✓
Hall (2012)[12]	X	X	X	✓	X	✓	✓
Various surgical specialities							
Lemmens (2009)[14]	✓	X	X	✓	X	✓	✓
Sturm (2009)[5]	✓	X	X	✓	UC	✓	✓

UC=unclear reporting

Table 2: RCT quality assessment

Author	Adequate random allocation	Adequate allocation concealment	Blinding of healthcare professional	Blinding of participants	Blinding of outcome assessor	Unexpected imbalances in drop-outs between groups	Imbalances accounted/adjusted for	Intention to treat analysis	ITT appropriate and appropriate methods used to account for missing data
Bariatric surgery									
Lemanu (2013)[27]	✓	✓	X	X	X	X	NA	UC	UC
Colorectal/colon surgery									
Garcia-Botello (2011)[24]	UC	X	UC	X	UC	X	NA	UC	✓
Ionescu (2009)[25]	✓	✓	X	X	UC	X	NA	UC	UC
Lee (2011)[26]	✓	✓	UC	X	UC	X	NA	UC	UC
Ren (2012)[29]	✓	✓	X	X	✓	X	NA	UC	UC
Wang (2011)[31]	UC	UC	UC	X	UC	X	NA	✓	✓
Wang (2012)[32]	UC	UC	X	X	✓	UC	UC	UC	UC
Yang (2012)[33, 34]	✓	UC	X	X	UC	X	NA	X	X
Gastric surgery									
Chen (2012)[22]	UC	UC	X	✓	✓	X	NA	UC	UC
Kim (2012)[23]	UC	UC	X	X	X	X	NA	UC	UC
Liu (2010)[28]	UC	X	X	X	X	X	NA	UC	UC
Wang (2010)[30]	UC	UC	X	X	UC	X	NA	X	X

UC: unclear reporting; NA: not applicable



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Supplementary table 1: Systematic reviews – main clinical outcomes

Author & no. included studies	Length of hospital stay (days)	Readmission rates (N/%)
Colorectal/colon surgery		
Adamina (2011)[6] *6 RCTs*	Primary length of stay: ERAS reduced stay by 2.5 days (95 CrI -3.92 to -1.11)	ERAS did not increase readmission rates (RR 0.59, 95% CrI 0.14 to 1.43)
Ahmed (2012)[7] *11 studies; study designs not reported*	2 to 11 days (10 studies)	0 to 22% (8 studies) Shortest length of stay (2 days) associated with highest readmission rate (22%)
Eskicioglu (2009)[10] *4 RCTs*	Three out of four trials reported a significantly shorter length of primary hospital stay in the ERAS group. Two trials reported overall hospital stay, both of which found a significantly reduced length of stay in the ERAS group.	7/99 ERAS, 11/99 control; no significant difference between groups (RR 0.67, 95% CI 0.20 to 2.19, 4 trials; I^2= 24%)
Gouvas (2009)[11] *11 studies; 4 RCTs,* *7 non-randomised case control studies*	Significantly reduced primary hospital stay with fast track: 3.3 to 6.7/5.8 to 10 days (WMD -2.35, 95% CI -3.24 to -1.46; I^2=75% , 9 studies). Similar results in subgroup analysis. Significantly reduced total hospital stay with fast track: 4 to 5.5 days/6.5 to 13 days (WMD -2.46, 95% CI -3.43 to -1.48; I^2= 0%, 5 studies). Similar results for subgroup analysis.	0 to 24%/0 to 20%: NS (RR 1.37, 95% 0.97 to 1.92; I^2=0%, 10 studies). Subgroup analysis showed that non-RCTs had significantly lower readmission rates in the control group.
Khan (2010)[13] *10 studies; 4 RCTS, 6 non-randomised comparative studies*	Not applicable	Not applicable
Lv (2012a)[21] *7 RCTs (one multi-arm RCT analysed as 2 separate comparisons)*	Total length of stay significantly shorter for ERAS treated patients (MD -1.88 days, 95% CI -2.91 to -0.86; 7 RCTs/8 comparisons, I^2=75%). Sensitivity analysis did not significantly alter the results.	No statistically significant differences between groups (RR 0.90, 95% CI 0.52 to 1.53; 7 RCTS/8 comparisons, I^2=0%).
Rawlinson (2011)[15] *13 studies; 6 RCTs and 7 non-randomised clinical trials*	Eleven studies reported on primary hospital stay, of which 10 reported a significantly shorter stay in the ERAS group.	Readmissions ranged from 0 to 24% with ERAS and from 0 to 20% with traditional care; 12 studies; no significant difference between groups.
Spanjersberg (2011)[16] *6 RCTs (2 did not meet inclusion criteria and were not included in primary analyses)*	Statistically significantly reduced in ERAS patients (MD -2.94 days, 95% CI -3.69 to -2.19 days; I^2=0%, 4 RCTs) Subgroup analyses including the 2 RCTs involving limited number of ERAS elements did not significantly alter the findings.	ERAS 4 (3.3%); control 5 (4.2%) No significant difference between groups (I^2=59%, 4 RCTs) Subgroup analyses including the 2 RCTs involving limited number of ERAS elements did not significantly alter the findings.
Varadhan (2010)[17] *6 RCTs*	Primary hospital stay was significantly shorter in the ERAS group (WMD -2.51 days, 95% CI -3.54 to -1.47, 6 trials; I^2 = 55%).	10/226 ERAS, 13/226 control; no significant difference between groups (RR 0.80, 95% CI 0.32 to 1.98, 4 trials with events; I^2 = 9%
Walter (2009)[18] *4 studies; 2 RCTs, one quasi-randomised trial, 1 cohort*	Total length of stay (mean (SD) days) Statistically significant reduction in ERAS compared to control groups WMD -3.75 days (95% CI -5.11 to -2.40 days; I^2=0%, 2 RCTs) Primary length of stay (mean (SD) days) Statistically significant reduction in ERAS compared to control groups WMD -3.64 days (95% CI -4.98 to -2.29 days; I^2=0%, 2 RCTs)	No statistically significant difference between groups (RR 0.26, 95% CI 0.03 to 2.25; one RCT) and (RR 1.73, 95% CI 1.00 to 3.01; I^2=0%, 2 CCTs). (p=0.05 which the authors consider significant).

Author & no. included studies	Length of hospital stay (days)	Readmission rates (N/%)
Wind (2006)[19] *6 studies; 3 RCTs, 3 CCTs*	Primary hospital stay (mean) Primary hospital stay statistically significantly lower in the ERAS group (WMD -1.56, 95% CI -2.61 to -0.50; I^2=52.9%, 3 RCTs, 3 CCTs). Subgroup analyses showed similar results for RCTs and CCTs. Overall hospital stay (mean) All three trials showed statistically significantly shorter overall hospital stay in ERAS patients (p<0.05)	No statistically significant differences between groups (RR 1.17, 95 %CI 0.73 to 1.86; I^2=23.6%, 2 RCTs, 3 CCTs). Subgroup analyses showed similar results in favour of ERAS in RCTs, but in favour of traditional care in CCTs.
Gynaecological surgery		
Lv (2012b)[20] *0 studies*	Not applicable	Not applicable
Liver/pancreatic surgery		
Coolsen (2012)[8] *6 studies; 3 case-control, 2 RCTs (both arms ERAS elements; equivalent to prospective case series), one retrospective case series.*	3 comparative studies: ERAS 5 to 7 days; control 7 to 11 days: difference (NS one study, p<0.001 2 studies) Non-comparative studies: 4 to 7 days	3 comparative studies: ERAS 0 to 13%; control 0 to 10%: difference (NS 3 studies) 3 non-comparative studies: 0 to 5%
Coolsen (2013)[9] **Link to** [63] *8 studies; 5 case-control (historical controls receiving traditional care); 2 retrospective case series; 1 prospective case series.*	It was unclear whether results were mean or median number of days. Comparative studies ERAS 6.7 to 13.5 days; control 8 to 16.4 days (4 of 5 studies reported statistically significant differences in favour of ERAS) Non-comparative studies 10 days (range 4 to 115), three studies	No significant differences (RD 0.8%, 95% CI -2.6% to 4.1%; I^2=0%, 4 studies)
Hall (2012)[12] *10 studies; Two studies with a single intervention in one parameter of peri-operative care but within an ERAS programme (including one RCT); 6 prospective case series comparing ERAS programmes versus historical controls, one retrospective case study, and one multicentre study.*	Reduced with ERAS programme: Pancreatic 10 to 13 days (range 4 to 115 days; 4 studies); liver 4 to 7.2 days (range 2 to 82 days; 5 studies).	Pancreatic 3.5 to14.6% (4 studies); liver 0 to 13 % (5 studies)
Various surgical specialities		
Lemmens (2009)[14] *13 studies; One RCT, 3 controlled clinical trials, 2 case-control, one retrospective case series, 6 pre- post-pathway studies*	Statistically significant decrease in clinical pathway group in 11 studies; mean number of days decreased from between 5.9 and 21.7 days to between 3.3 and 18.5 days (9 studies). Median number of days decreased from between 5 and 13 days to between 2 and 7 days (4 studies). 2 studies reported no significant difference between groups.	One study reported statistically significant reduction (13% to 6%); 2 studies not reported; 10 studies NS
Sturm (2009)[5] *11 RCTs plus one systematic review*	Length of stay was clearly significantly shorter in the ERAS group in 6 trials (3 colorectal, 3 other). There was no significant difference in 1 trial (lung surgery). In the remaining trials, significance was unclear or was not reported.	Eight trials reported on readmission rates. Rates ranged from 0 to 9.7% in the ERAS groups and 0 to 20% in the control groups. Only one trial reported a statistically significant difference and this favoured the ERAS group (p = 0.022).

Supplementary table 2: RCTs – main clinical outcomes

Author	Length of hospital stay (days)	Readmission rates (N/%)
Bariatric surgery		
Lemanu (2013)[27]	Median days (interquartile range) Length of index admission: ERAS 1 (1 to 2); control 2 (o), p<0.001 Total hospital stay (including admission plus subsequent readmissions): ERAS 1 (1 to 3); control 2 (2 to 3), p<0.001	Defined as presentation to hospital within 30 days of surgery after the day of discharge; subsequent hospital stay had to be more than 24 hours. ERAS 8/40 (20%); control 8/38 (21%) Median length of readmission was 6 days with no difference between groups.
Colorectal/colon surgery		
Ionescu (2009)[25]	Mean (SD) ERAS 4.15 (2.2); control 9.23 (7), p<0.001	ERAS 3 (5%); control 2 (3%), p=0.51
Lee (2011)[26]	ERAS 6.43 (3.41); control 9.16 (2.67), p=0.001	ERAS 0 (0); control 0 (0)
Ren (2012)[29]	Post-operative: Rehabilitation 7 (6 to 8); control 8 (7 to 9), p=0.065 Total: Rehabilitation 9 (8 to 10); control 10 (9 to 11), p=0.054	30-day: rehabilitation 0; control 0
Wang (2011)[31]	*Mean (SD) ERAS 5.7 (1.6); control 6.6 (2.4), p<0.001*	*Not reported*
Wang (2012)[32]	*Median (range) post-operative hospital stay ERAS 5 (2 to 41); control 7 (3 to 55), p<0.01*	*No statistically significant differences between groups within 30 days after resection. ERAS 4 (4%) patients re-admitted for wound infection; control 9 (9%) readmitted due to bowel obstruction, vomiting, and wound infection.*
Yang (2012)[33, 34]	*Median days: ERAS 5.5 (5 to 6); control 7.0 (6 to 8), p<0.001*	*Not reported*
Ionescu (2009)[25]	*Mean (SD) ERAS 6.0 (1.0); control 11.7 (3.8), p<0.05*	*No hospital readmissions due to complications.*
Gastric surgery		
Chen (2012)[22]	Median days (range) Compared with ODG, the remaining three groups had shorter post-operative hospital stay (p<0.05) FTS + LADG 7 (5.5 to 10); LADG 7.5 (6 to 11); FTS + ODG 7.5 (6 to 11); ODG 8.75 (7 to 14)	Not reported
Kim (2012)[23]	Possible post-operative hospital stay (mean days, SD) ERAS 4.68 (0.65) (range 4 to 6); control 7.05 (0.65) (range 6 to 9), p<0.001 Post-operative hospital stay (mean days, SD) ERAS 5.36 (1.46) (range 4 to 11); control 7.95 (1.98) (range 6 to 15), p<0.001	ERAS 1/22 (4.5%); control 0/22 (0%)
Liu (2010)[28]	*Primary length of stay (mean (SD)): ERAS 6.2 (1.9); control 9.8 (2.8), p<0.001*	*Readmitted within 30 days after surgery ERAS 1/33 (3%); control 0/30 (0%)*
Wang (2010)[30]	*Median (quartile range) ERAS 6 days (6 to 7); control 8 (7 to 8), p<0.001. Primary clinical endpoint of the trial.*	*ERAS 1/45 (2.2%); control 1/47 (2.1%), no significant difference between groups*

Supplementary table 3: Economic evaluations meeting the inclusion criteria

Study Details	Study Comparators	Main Analytical Approaches, primary outcomes, and costs	Incremental cost-effectiveness (ICER) estimates and Decision Uncertainty
Salihiyyah *et al* (2011)[56] UK Hospital setting Study Population Cardiac surgery Inpatients Time horizon 6 months	Intervention Fast-track transfer post-surgery to an independent theatre recovery unit 1-2-1 nursing (n=84) Comparator Transfer post-surgery to hospital intensive care unit (n=52)	Economic evaluation based on a single study Perspective Hospital Primary outcomes Length of stay; Duration of intubation Direct Costs Total expenditure of unit divided by number of patients Productivity Costs n/a	Results The costs and benefits were not synthesised mean cost FT: £4182 (SD:2284) mean cost C: £4553 (SD:1355) (p<0.001) total LOS NSD 8 patients failed FT & were transferred to ICU 5 patients (4 FT & 1 C) required readmission Uncertainty One-way & multi-way sensitivity analysis demonstrated robustness in result that FT costs less than C
Lin *et al* (2011)[53] China Hospital setting Study Population Liver resection Inpatients Time horizon Not reported	Intervention Multidisciplinary team, streamlining of preoperative evaluation, education of patients and families, earlier oral feeding, earlier discontinuation of IV, no drains or naso-gastric tubes, early ambulation, urinary catheter <24 hours, planned discharge 6 days post-surgery (n=56) Comparator Conventional pathway (limited reporting) (n=61)	Economic evaluation based on a single study Perspective Hospital Primary outcomes Length of stay; Complications; Mortality; Readmission Direct Costs Hospital charges: operation and anaesthesia; pharmacy; auxiliary examination; other Productivity Costs n/a	Results The costs and benefits were not synthesised mean charge pre-pathway RMB 26,626 mean charge post-pathway RMB 21,004 (p<0.05) LOS reduced from 11 days to 7 days (p<0.005) Complications, mortality & readmissions NSD Uncertainty n/a
Kariv *et al* (2006)[55] USA Hospital setting Study Population Patients undergoing open ileoanal pouch surgery	Intervention Presurgery patients provided with FT protocol and documentation of post-surgery milestones. Epidural or analgesia were not used; early food and mobilisation (day of surgery/anaesthesia), patients who lived 100 to 150 miles from hospital discharged to hotel for 1 to 3 days. Success defined as discharge within 5	Economic evaluation based on a single study Perspective Hospital Primary outcomes Length of stay; Readmission; Reoperation Direct Costs Total costs for each of the categories were presented:	Results The costs and benefits were not synthesised total per case cost FT US$ 5,692 total per case cost C US$ 6672 diff US$980 (p=0.001) median postoperative los FT = 4 days C= 5 days (p=0.012) NSD in readmission outcomes

Study Details	Study Comparators	Main Analytical Approaches, primary outcomes, and costs	Incremental cost-effectiveness (ICER) estimates and Decision Uncertainty
Time horizon 30 days	days (n=97) Comparator Based on professional preferences of surgeon; no supporting documentation; sat out of bed on POD 1, walked POD 2; food withheld until stool or flatus (n=97)	per case of hospitalisation; operating room; radiology; anaesthesia; pharmacy; laboratory; ICU; and nursing care Productivity Costs n/a	Uncertainty n/a
Yanatori *et al* (2007)[57] Japan Hospital setting Study Population Cardiovascular surgery (cardiac arrest requiring cardiopulmonary bypass) Time horizon 2 years	Intervention Admitted 4 days prior to surgery, preoperative education by nurses, surgeons and rehab staff; discharge at day 7 post surgery Comparator Conventional protocol – details not reported	Economic evaluation based on a single study Perspective Healthcare provider/hospital Primary outcomes Length of stay; Complications Direct Costs Only total costs were presented Productivity Costs n/a	Results The costs and benefits were not synthesised Total mean cost for FT YEN 712,545 Total mean cost for C YEN 383,268 (p=0.038) Mean post-op LOS FT=15(12.4) C=36.7(6) (p=0.01) Uncertainty n/a
Larsen *et al* (2009)[54] Denmark Hospital setting Study Population All patients for elective primary total hip/knee arthroplasty or unicompartmental knee arthroplasty Time horizon One year	Intervention Patients receive info pre-hospitalisation; separate ward; one nurse in charge of multidisciplinary nurses, occupational therapists, and physiotherapists; nutrition screening and special focus on daily consumption of 1.5L fluid (including 2 protein beverages); mobilisation and exercise started on day of surgery; intensive mobilisation of patients in teams; eight hours of mobilisation daily (n=45: 28 total hip; 15 total knee; 2 unicompartmental knee) Comparator Patients receive info on day of admission; patients randomly among wards, various nurses in charge of care; and various occupational and physio-therapists responsible for mobilisation; mobilisation and exercise started on first postoperative day; individual and gradual mobilisation according to patient tolerance; four hours mobilisation daily (n=42: 28 total hip; 12 total knee; 2 unicompartmental knee)	Economic evaluation based on a single study Perspective Societal Primary outcomes Length of stay; Adverse events (first 3months) Health-related quality-of-life QALYS (EQ-5D) (baseline to 3 months) Direct Costs Patients followed over one-year. Resource use: based on patient level mix of activity based costing and step down methods. Discharge to 3 months cost diary Productivity Costs Average wage rate for age-specific groups	Results Accelerated intervention was both more effective and less costly than the comparator Average total cost for I DKK90,227 (+/- 47,475) Average total cost for C DKK71,344 (+/- 39,958) Average QALYs was 0.83 for the intervention and 0.78 in the comparator. Average QALY gain for hip patients I v C = 0.08 (CI: 0.02 to 0.05) (p=0.006) Average QALY gain for knee patients was NS Uncertainty Bootstrapping, uni and multivariate

Study Details	Study Comparators	Main Analytical Approaches, primary outcomes, and costs	Incremental cost-effectiveness (ICER) estimates and Decision Uncertainty
Sammour *et al* (2010)[50] New Zealand Hospital setting Study Population Elective colonic resection patients >15 years old Time horizon Unclear	Intervention Emphasised structured nursing care pathways within an environment focusing on early recovery and various perioperative strategies to improve patient functional recovery (n=50) Comparator Conventional non-structured perioperative care (n=50)	Economic evaluation based on a single study Perspective Healthcare provider Primary outcomes Length of stay; Complications; Readmissions Direct Costs Total cost of protocol development, inpatient stay, outpatient appointments, treatment costs, readmission and complication costs were all considered. Data on patient resource use was collected from their records. Readmission costs and complication costs were based on hospital records/costs Productivity costs n/a	Results The costs and benefits were not synthesised The implementation of the intervention protocol cost approx. NZ$102,000 for the first 50 patients (set-up costs included) Cost per patient with NZ$16,052.35 Cost per patients without NZ$22,929.74 Cost-saving NZ$6,900 per patient Post-op LOS ERAS: 4 (3 to 34); C: 6.5 (3 to 18) (p<0.001) Total LOS ERAS: 4(3 to 34); C: 8(4 to 29) (p<0.001) Readmissions NS Complications – overall 54% in ERAS ≥1 compared with 66% comp Uncertainty n/a
King *et al*(2006)[51] UK Hospital setting Study Population Surgery for colorectal cancer Time horizon 2 years	Intervention Preoperative counselling, epidural analgesia, early feeding and mobilisation, predetermined discharge aim (n=60) Comparator Conventional care (fully reported) included no epidural, no formal mobilisation plan, no predetermined discharge (n=86)	Economic evaluation based on a single study Perspective UK NHS stated by author, although inclusion of productivity costs suggests wider societal perspective Primary outcomes Post-op length of stay; Complications; Readmissions Health-related quality-of-life EORTC QLQ-C30 Direct Costs Resource use data was reported to be individual patient level, but not reported. Direct costs included: theatre (including pre and recovery), hospital (including ICU), postoperative (including re-operation), chemotherapy and radiotherapy, follow –up at 3 months Productivity costs Average earnings based on employment status at commencement of trial	Results The costs and benefits were not synthesised Total costs of care for patients receiving the intervention: £7327.47; for those receiving comparator: £7998.18 Post-op LOS significantly reduced, intervention cohort staying 49% as long as comparator (95% CI: 39% to 61%; p<0.001) No-sig difference in quality-of-life, readmissions, re-operations or complications Uncertainty n/a
Neilson *et al*(2008)[52] Denmark	Intervention Integrated programme including: information and education, optimal	Economic evaluation based on a single study Perspective	Results The costs and benefits were not synthesised

Study Details	Study Comparators	Main Analytical Approaches, primary outcomes, and costs	Incremental cost-effectiveness (ICER) estimates and Decision Uncertainty
Hospital setting Study Population Lumbar fusion patients with degenerative lumbar disease Time horizon 6 months	operation technique, better pain reduction, early nutrition and aggressive post-op mobilisation (n=28) Comparator Standard care, not including components above (n=32)	Societal Primary outcome Measured using 15D-score (self-reported at inclusion, day of surgery, day of discharge, and 1, 3 and 6 months post-op Direct Costs Three categories of cost considered: staff resources, equipment and purely bed costs. Bed costs included salary of nurses/porters, food, clothes, laundry and cleaning. Post-discharge for 3 months GP visits, physiotherapy appointments and emergency room contact was registered and included. Productivity costs Based on return to work rates & Danish average daily wage	Intervention direct cost 1,174 Euros per patient compared with 1,668 for standard care Intervention productivity costs were 8,021 Euros compared with 9,152 for standard care NS difference in HR quality of life scores Uncertainty Optimistic and pessimistic scenarios varying individually pre-op costs, post-op hospital costs, direct costs, and productivity costs
Reilly *et al*(2005)[48] UK Hospital setting Study Population Patients undergoing unicompartmental knee arthroplasty Time horizon Unclear	Intervention Accelerated discharge: aim to discharge day after surgery (n=20) Comparator Standard discharge: approx. 5 days post-surgery (n=21)	Economic evaluation based on a single study Perspective Hospital Primary outcome Oxford Knee Assessment Direct Costs Fixed costs (surgical staff, anaesthetics, prosthesis, pharmacy), outpatient appointment, specialist registrar time. Productivity costs n/a	Results The costs and benefits were not synthesised Intervention resulted in a 6 month OKA score of 43.7 (SD 3.7) compared with 42.2 (SD 7.1) for standard care (NS) Total costs for intervention per patient £3,391 compared with £4,634 for standard care Uncertainty n/a
Archibald[49] USA Hospital setting Study Population Colorectal surgery patients Time horizon unclear	Intervention The availability of patient education, fluid managements, opioid-sparing strategies, tube and drain protocols, ambulation, feeding protocol, and discharge criteria. All based on surgeons choice. (n=1358, 588 enrolled in ERAS & 770 not enrolled) Comparator Standard care historical baseline (n=1673)	Economic evaluation based on a study comparing two time periods, where ERAS was available in one and not in the other. Primary outcome Length of stay ; POD; Readmission Direct Costs Hospital costs (total direct and indirect costs identified via hospital billing system) Productivity costs n/a	Results The costs and benefits were not synthesised Mean LOS for the intervention was 8.4 days compared with 6.9 days for the comparator (p<0.0001); Mean POD for the intervention was 7.6 days compared with 6.3 days (p<0.0001) Mean hospital cost for the intervention population was US$18,741 compared with US$16,978 for the comparator. Uncertainty n/a

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3-4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Full report – in press. Protocol attached to manuscript submission
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6

PRISMA 2009 Checklist

Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	N/A
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency ($e.g., I^2$) for each meta-analysis.	N/A

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	20
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	21-22
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	23-25
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	NA
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	NA
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	10-13
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	11-13
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13-14
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1-2

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097.

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Effectiveness and implementation of enhanced recovery after surgery programmes: a rapid evidence synthesis

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Effectiveness and implementation of enhanced recovery after surgery programmes: a rapid evidence synthesis

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Abstract

Objectives

To assess the evidence on the impact of enhanced recovery programmes for patients undergoing elective surgery in acute hospital settings in the UK.

Design

Rapid evidence synthesis. Eight databases were searched from 1990 to March 2013 without language restrictions. Relevant reports and guidelines, websites, and reference lists of retrieved articles were scanned to identify additional studies. Systematic reviews, RCTs not included in the systematic reviews, economic evaluations and UK NHS cost analysis, implementation case studies and surveys of patient experience in a UK setting were eligible for inclusion.

Primary and secondary outcome measures

We assessed the impact of enhanced recovery programmes on health or cost-related outcomes, and assessed implementation case studies and patient experience in UK settings. Studies were quality assessed where appropriate. using the CRD DARE critical appraisal process.

Results

Seventeen systematic reviews and 12 additional RCTs were included. Ten relevant economic evaluations were included. No cost analysis studies were identified. Most of the evidence focused on colorectal surgery. Fourteen innovation case studies and 15 implementation case studies undertaken in NHS settings described factors critical to the success of an enhanced recovery programme.

Evidence for colorectal surgery suggests that enhanced recovery programmes may reduce hospital stays by 0.5 to 3.5 days compared with conventional care. There were no significant differences in reported readmission rates. Other surgical specialties showed greater variation in reductions in length of stay reflecting the limited evidence identified.

Findings relating to other outcomes were hampered by a lack of robust evidence and poor reporting.

Conclusions

There is consistent, albeit limited, evidence that enhanced recovery programmes can reduce length of patient hospital stay without increasing readmission rates. The extent to which managers and clinicians considering implementing enhanced recovery programmes in UK settings can realise savings will depend on length of stay achieved under their existing care pathway.

Word Count: 300

Strengths and limitations of the study

- Enhanced recovery programmes have been adopted with enthusiasm by the NHS as a means to achieving productivity gains and cost-savings. This evolution makes combining studies over different periods and interpreting results of earlier studies in relation to the current context more difficult.
- The evidence base to support such widespread implementation suggests possible benefits in terms of reduced length of hospital stay, fewer postoperative complications, reduced readmissions and improved patient outcomes.
- Althouth there is a reasonable volume of evidence evaluating enhanced recovery programmes in colorectal surgery, robust evidence is sparse. Optimal care is certainly the right thing to do, but the evidence does not identify which enhanced recovery programme elements and combinations of elements are most effective.
- Findings relating to other outcomes, costs of enhanced recovery programmes, experience in using the programmes, and patient experience were limited by generally poor quality evidence and poor reporting. As such, conclusions on which combinations provide greatest gains and how best to implement them cannot be made.

Introduction

The National Health Service (NHS) faces severe funding constraints now and in the medium term. The forecast reduction in resources provides an enormous challenge to NHS organisations and staff. Service redesign can save money and improve quality but much depends on how care is co-ordinated and the way services are implemented in a local setting.[1, 2] NHS decision makers need to consider not only the effectiveness and cost effectiveness of any initiative but also efficient implementation. Enhanced recovery programmes (also known as ERAS, fast track, multimodal, rapid or accelerated recovery programmes) seek to deliver an optimal pathway (covering the preoperative, intraoperative and postoperative periods) that is focused on optimal recovery and discharge for patients. The approach was pioneered in Denmark in the late 1990s for patients undergoing colorectal surgery[3] and is now spreading to other surgical pathways such as orthopaedic, urology and gynaecology.

Enhanced recovery programmes have been delivered in the UK NHS since the early 2000s. Implementation has to date been variable despite the support of the Department of Health and more recently the Royal Colleges. In 2011, 14 innovation sites were established as part of the Enhanced Recovery Partnership Programme. These sites acted as pathfinders for implementation; some sites were self-selecting and others were encouraged to join. The aim was to raise the profile, promote the benefits and inform the uptake of enhanced recovery for elective surgical care across the NHS. These sites had little or no experience in enhanced recovery pathways. It is likely that this variation seen across these sites reflects both the complexity of enhanced recovery programmes themselves and issues around implementing change in established surgical pathways . Differences in programme implementation may also reflect differences between surgical specialities. Set against the benefits of enhanced recovery programmes are concerns that discharging patients too soon after surgery could increase complications and readmissions, thereby worsening patient experience and potentially health outcomes, and increasing pressure on primary and/or secondary healthcare services.

Before embarking on adoption of an enhanced recovery programme, NHS managers and clinicians need to be fully aware of the strength of the underlying evidence. They need to have a clear understanding of how best to implement such programmes and the likely implications for service delivery within finite budgets and considering the need for equity of access. The aim of this project was to conduct a rapid synthesis of the evidence on the

clinical and cost effectiveness of enhanced recovery programmes, and the implementation, delivery and impact of such programmes in secondary care settings in the UK.

Methods
Eight databases, including DARE, NHS EED and MEDLINE were searched to from 1990 to March 2013 without language restrictions. The PROSPERO database was searched to identify ongoing systematic reviews. Relevant reports and guidelines were screened for further studies. Reference lists of retrieved articles, reviews and evaluations were scanned, and relevant individuals contacted for additional evidence.

Systematic reviews, RCTs not included in the systematic reviews, economic evaluations, and UK NHS cost analysis studies were included if they evaluated the impact of enhanced recovery programmes (encompassing different combinations of the main preoperative, intraoperative and postoperative pathway elements described by the Enhanced Recovery Partnership Programme[4] on health or cost-related outcomes. Eligible studies included patients undergoing elective surgery in an acute hospital in the UK NHS or a comparable healthcare system. Comparators were only relevant to clinical and cost-effectiveness evaluations, and included conventional (usual/standard) care without a structured multimodal enhanced recovery patient pathway (as defined in the included studies). Case studies, impact assessments and surveys of patient experience that documented the experience of implementing enhanced recovery in a UK setting were also eligible.

Quality assessment of systematic reviews, RCTs and economic evaluations was based on existing CRD critical appraisal methods (http://www.crd.york.ac.uk/crdweb/HomePage.asp; CRD, 2009). Cost analysis studies, studies of patient experience, and case studies of implementation were not formally quality assessed.

All stages of the review process were performed by one researcher and checked by a second. Disagreements between reviewers were resolved by discussion or by recourse to a third reviewer where necessary.

The type and range of evidence precluded meta-analysis and we therefore performed a narrative synthesis, differentiating clinical outcomes (eg. mobilisation, mortality and morbidity, and length of hospital stay), patient-reported outcomes (eg. patient experience and satisfaction), resource use in secondary care (eg. workforce utilisation and costs), and implementation case studies.

Results

Seventeen systematic reviews[5-21] and 12 additional RCTs[22-34] were included in the evidence on clinical effectiveness (see Figure 1: flow diagram). The quality of the systematic reviews varied and the additional RCTs were considered to be at high risk of bias (see tables 1 and 2). One RCT was a four arm trial; this was the only multicentre trial, the remaining trials were small, single centre trials.[35] We included 15 case studies of implementation of ERAS in NHS settings, and evaluations of the 14 Enhanced Recovery Partnership Programme innovation sites. In addition, 10 relevant economic evaluations were also included (summary evidence tables are available on request from the review authors). Most of the evidence focussed on colorectal surgery.

Where reviews reported the number of included patients, sample sizes ranged between 99 and 5,747 patients in the ERAS group and between 99 and 1,062 in comparator groups. Most individual RCTs analysed fewer than 100 patients (range 44 to 597 patients). Where indications for surgery were reported in systematic reviews and individual RCTs, most trials were in patients with cancer. Where reported, patients were adults within similar age ranges. Follow-up was generally up to 30 days post discharge.

The number and combination of ERAS elements varied considerably across all types of evidence; ranging from four to 14 elements across systematic reviews and from 10 to 14 elements across individual RCTs (see full report for details; in press). This highlights the lack of standardisation across ERAS programmes and agreement on what constitutes an ERAS pathway, and will have implications on the overall findings. Only one review assessed compliance with ERAS elements.[7] Ahmed (2012)[7] noted that, in general, compliance fell during the postoperative period in most of the studies (from around 100% to around 20%). Use of epidural analgesia had the highest levels of compliance across all studies (67% to 100%). Use of transverse incisions had the lowest levels of compliance (around 25%). Reasons for differences in compliance and waning of compliance were not measured in the reviews. None of the reviews assessed patient compliance, including adherence to preoperative advice to ensure fitness for surgery.

Despite the large number of studies, robust evidence was sparse (supplementary tables 1 and 2; full outcome details are available in the full review; in press). Seven reviews in colorectal surgery performed meta-analyses and showed a significant mean reduction in primary or total length of stay that ranged from 1.56 days (95% CI 0.50 to 2.61 days)(19) to 3.75 days (95% CI 5.11 to 2.40 days).(18) Evidence from individual RCTs in colorectal

surgery also suggest reduced length of hostpital stay following an ERAS programme (mean length of stay 4.15 days to 6.43 days) compared to conventional care (mean length of stay 6.6 days to 11.7 days). There were no significant differences in reported readmission rates, but it was unclear how readmissions were defined and measured in the reviews and RCTs.

Other surgical specialties showed greater variation in reported reductions in length of stay, but this is likely to reflect the greater uncertainty due to the more limited evidence base for these specialties. Statistical heterogeneity varied between reviews and was often not formally explored, but may have reflected differences in ERAS protocols, lack of compliance with important ERAS elements, and differences in surgical populations and procedures.

Deaths were rare and no significant differences between treatment groups were found in the systematic reviews and additional RCTs, regardless of surgical speciality. Morbidity was defined differently across systematic reviews and RCTs; rates between treatment groups were sometimes inconsistent, but generally indicated no statistically significant differences.

Mobilisation rates were inconsistent across systematic reviews, but most reported no significant differences in time to mobilisation between treatment groups. Mobilisation was rarely reported as an outcome in the additional RCTs.

Where systematic reviews and additional RCTs assessed quality of life and patient experience/satisfaction, equivocal findings were reported. Evidence on reintervention rates, pain and resource use was lacking in both systematic reviews and RCTs.

Other Reviews

A systematic review in colorectal surgery, identified after the last literature search, showed similar findings to the systematic reviews discussed above.[36] Mean length of primary hospital stay was statistically significantly reduced in ERAS patients; mean difference (MD) -2.44 (95% CI -3.06 to -1.83; 11 RCTs) but with significant statistical heterogeneity (I^2=88%). There was no evidence to suggest increased rates of readmissions, complications and mortality. Some of the individual RCT results for primary length of stay did not appear to be consistent with results reported in other systematic reviews, and this may have impacted on the estimated reduction in length of primary hospital stay.[36]

Two reviews[37, 38] focusing on individual ERAS elements were identified, both of which highlighted the lack of evidence on the full ERAS pathway and the lack of compliance with ERAS protocols. Details can be found in the full review (in press).

Case studies

Ten of 14 UK NHS innovation sites provided adequate data for inclusion in this section.[39-41] Fifteen case studies of implementation of ERAS in NHS settings, and 11 NHS trusts (mostly in colorectal surgery) provided evidence relating to the implementation of an ERAS programme within their Trust. Full results and evidence tables are presented in the full review (in press).

There were variations in practice in terms of numbers and combinations of ERAS elements implemented; the most frequently implemented programme elements in the case studies were pre-admission information/counselling and early postoperative mobilisation. Available evidence did not address which enhanced recovery elements and combinations of elements were most effective. Substantial variation in what constitutes an enhanced recovery programme within and between different surgical specialities, and difficulties in implementing certain ERAS components, suggest that the enhanced recovery pathway may be used as a framework and adapted to suit local situations. Evidence on compliance/adherence to enhanced recovery programmes was lacking.

Case studies identified the factors believed to act as barriers or facilitators to implementing an ERAS programme. Barriers to implementation included resistance to change from patients and staff, lack of funding or support from management,[39, 42-44] staff turnover, problems arising from poor documentation, the time required to complete documentation, and other practical issues.

Facilitators included the presence of a dedicated ERAS project lead/nurse to coordinate and sustain multidisciplinary working and continuity of the pathway, a multidisciplinary team approach, and continual education for staff and patients/patient representatives. One innovation site mentioned that it did not offer a seven day service for enhanced recovery due to staff resources. Patients operated on towards the end of the week may have to wait until after the weekend to be discharged if they need to be seen by any health care professionals or social services. The need to sustain multidisciplinary working means that, in the absence of 24/7 working for elective procedures, enhanced recovery programmes will tend to be front loaded into the start of the working week (typically Monday to Thursday). Recent evidence suggests a higher risk of death for patients who have elective surgical procedures carried out later in the working week and at the weekend,[45] the capcity to implement ERAS throughout the working week might ensure continuity of best care and help mitigate against such variation.

We included two published studies of patient experience of ERAS.[46, 47] Each study used qualitative research methods to analyse audiotaped material. The two studies provided limited evidence suggesting that patients who were willing to provide feedback took a positive view of their experience of treatment in an ERAS programme. The studies suggested that patients were willing to comment on their experience in a way that can help healthcare providers to identify areas for improvement.

Cost-effectiveness

Ten economic evaluations in adult populations undergoing various surgical procedures evaluated costs and outcomes over short time horizons (supplementary table 3).[48-57] All of the evaluations suggested that programmes that achieve a reduction in length of stay are cost saving, and are not to the detriment of patients in terms of complication rates, readmission and health-related quality-of-life. The quality of the clinical studies on which these evaluations were based was variable, but generally poor. The generalisability of the results of these evaluations was limited by a lack of transparency in reporting, and the disparity in standard protocols and what had been evaluated across the settings made it unfeasible to select a cost-effective programme.

Discussion

Statement of Principal Findings

Overall, the systematic reviews and additional RCTs suggest that length of hospital stay is reduced in ERAS patients compared to patients receiving conventional care. The evidence was based mainly on colorectal surgery and the applicability of findings to other surgical specialities remains less clear. Evidence for colorectal surgery suggests that enhanced recovery programmes may reduce hospital stays by 0.5 to 3.5 days compared with conventional care.

There were marked differences in length of stay across reviews and individual studies regardless of speciality. These differences may reflect differences in ERAS protocols, compliance to ERAS programmes, health care systems and procedures, and/or outcome definitions. This raises questions regarding the magnitude of effect of the ERAS protocols on length of stay, which may be overstated in some reviews.

The evidence suggests that ERAS programmes do not compromise patient morbidity, mortality and readmission rates but outcome definitions varied across reviews and individual studies. Such differences make it difficult to determine the reliability and generalisability of the findings.

Equivocal findings were reported for quality of life and patient experience/satisfaction but the evidence was based on few studies, which utilised various methods to measure these outcomes. The limited evidence precludes conclusions on the effects of ERAS protocols on pain, mobilisation and reintervention.

The implementation evidence included resource use in terms of the professionals involved in delivery of enhanced recovery programmes, but details were very limited and did not add to the evidence synthesis. Most case studies were uncontrolled and represent experiences of a sample of centres that chose to report their data; their outcomes may not be representative of those achieved elsewhere in the UK NHS. Their main value as evidence is the light they shed on NHS clinicians' perceptions of requirements for successful implementation and barriers to implementation of ERAS.

The impact of surgical experience and surgical volume on clinical outcomes was not explored and any implications of differences in these areas remain unknown. As enhanced recovery invariably targets the fitter, more mobile patient, frailer patients may not receive parity of access to what may be considered optimal treatment and management. Managers and clinicians considering implementing such programmes should think about the likely implication on equity of access. Whether inequity is an unintended outcome of enhanced recovery, merits further investigation.

Our review of the cost effectiveness literature suggests that enhanced recovery programmes that achieve a reduction in length of stay may save costs without detrimental effects on complication rates, readmission and health-related quality of life. However, generalisability of the results of the economic evaluations is limited by a lack of transparency in reporting, use of different settings and populations and variable methodology in analyses. Data were lacking for resource use associated with the programmes evaluated and could not usefully inform the review of economic evaluations. In addition, the clinical effectiveness of some of the programmes considered in economic evaluations was not based on robust evidence.

Strengths and weaknesses

The main strength of this study was our use of multiple approaches to acquire and synthesise evidence. The main limitations were poor methodological quality and poor reporting of the included studies, and the inherent difficulty of reviewing a complex intervention in different healthcare systems and surgical specialities. Current methods for

synthesising such complex interventions are limited. The methodological limitations and are not discussed here as this was outside the scope of this project, but have been addressed in previous publications (eg. Noyes et al, 2013).[58] Another complication is that elements of early enhanced recovery programmes have become accepted practice within conventional care. This evolution makes combining studies over different periods and interpreting results of earlier studies in relation to the current context more difficult.

We found a large number of systematic reviews but there was substantial overlap in the included studies and evidence was not as abundant as the existence of multiple systematic reviews suggested. Most of the RCTs were small and not high quality. With the exception of one RCT, the remainder were single centre trials and therefore appear to have been undertaken to support implementation of an enhanced recovery programme in a specific setting rather than being planned as research studies. There were significant clinical and methodological differences between individual trials, and we therefore presented a narrative synthesis. Relatively few trials were conducted in the UK and this may limit the generalisability of evidence to UK NHS settings.

Lack of evidence on important outcomes including pain and quality of life is also an issue for research in this field. Trials tended not to report on adherence to the planned enhanced recovery programme. Assessing adherence to interventions and the impact this has on health outcomes is an important issue which is often overlooked in studies, and is a limitation in the evidence base in this review.

Three additional systematic reviews of effectiveness were brought to our attention during manuscript submission. One systematic review incorporates RCTs in colorectal surgery (Greco, 2013),[59] one incorporates RCTs and cohort studies in abdominal surgery (Neville, 2014)[59] and one includes RCTs and quasi-RCTs across various surgical specialities (Nicholson, 2014).[59] The trials included in Greco (2013)[59] and Nicholson (2014)[59] overlap with those included in this review and the findings are consistent. The inclusion of these two reviews would therefore not have significantly altered the findings from this review. Neville (2014)[59] provides some additional data on patient-reported outcomes, including some evidence on post-discharge functional status. However, these outcomes were not frequently reported, and the additional evidence was mainly from study designs that would not have met the inclusion criteria for this review.

An important feature of our review is the inclusion of evidence on the implementation of enhanced recovery programmes in the UK NHS. This evidence has not been synthesised

previously and the original programme webistes are archived, so future access is not assured. By summarising this evidence, we have ensured that the main findings continue to be publicly available. We sought evidence on the experience of health professionals and patients of a broad range of sources and study types. Important themes emerged from this evidence that may be of value for implementing and sustaining enhanced recovery programmes in UK NHS settings. Due to the rapid nature of the evidence synthesis, the list of sources searched to identify data on implementation and delivery of enhanced recovery programmes was not exhaustive and we acknowledge that relevant evidence may have been missed. Indeed, evidence from Scotland has been noted and eligible case studies have been identified from the NHS Scotland Quality Improvement Hub website. It should be noted that these are as limited as those included in the review. A qualitative study was brought to our attention at peer review; the study was published after our final search date. Pearsall et al (2014)[60] conducted a qualitative study to explore the barriers and enablers in implementing an enhanced recovery after surgery programme in a University hospital in Canada. The themes identified are consistent with those reported in this review.

However, case studies are susceptible to risk of bias. Use of a standard reporting format was a potential strength of the case studies but variation in what each site actually reported (particularly in terms of evidence of benefit from the introduction of enhanced recovery programmes) reduced the usefulness of the evidence.

We sought to incorporate published and unpublished evidence on patient experiences and views of enhanced recovery programmes. Evaluation of patient experience of care is increasingly important for the NHS, especially in view of unacceptable failures of care such as those highlighted in the Francis Report.[61] Though the evidence was generally positive for enhanced recovery, it was limited by a shortage of studies that used validated measures of patient experience and by study designs that could bias results in favour of enhanced recovery.

A further strength of this study was the consideration of cost-effectiveness evidence, but the nature of the evidence did not permit any analyses. There is a clear need to capture better evaluated data on costs and benefits of enhanced recovery programmes from a clearly stated perspective. A systematic review of economic evaluations (Lee, 2014)[62] was brought to our attention during manuscript publication. The review confirmed the need for well-designed research to determine the cost-effectiveness of enhanced recovery programmes from both the institutional and societal perspectives.

Implications for healthcare

Overall, there is consistent, albeit limited, evidence that enhanced recovery programmes can reduce length of patient hospital stay without increasing readmission rates. Data on re-intervention rates and patient-reported outcomes did not suggest significant differences between enhanced recovery and conventional care, but the evidence was very limited and based on small numbers of patients. The lack of evidence on patient outcomes, resource use and costs precludes firm conclusions on the overall value of enhanced recovery programmes.

ERAS does not appear to reduce complication or readmission rates; the only cost benefit may lie in a reduction in post-operative bed days. Optimal care is certainly the right thing to do, but the evidence does not identify which enhanced recovery programme elements and combinations of elements are most effective. As such, conclusions on which combinations provide greatest gains and how best to implement them cannot be made.

The extent to which managers and clinicians considering implementing enhanced recovery programmes can realise reductions and cost savings will therefore depend on length of stays achieved under their existing care pathway. Important themes emerged from the relevant evidence identified on implementation, including the role of ERAS facilitators and the need for full support from management. It appears that these components are essential for the successful implementation and sustained delivery of enhanced recovery programmes in NHS settings. Consideration of potential benefit also needs to take account of the costs of service redesign, the resource use associated with programmes of this nature, the potential for improvement in patient outcomes and the impact on equity of access.

Implications for research

RCTs comparing an enhanced recovery programme with conventional care continue to be conducted and published, although mostly not in the UK. Given the available evidence, further single centre RCTs of this kind are not a priority. Rather, what is needed is improved collection and reporting of how enhanced recovery programmes are implemented, resourced and experienced in NHS settings. Also, exploration into the effect that varying levels of surgical volume and surgical experience, and different discharge protocols might have on the success of an enhanced recovery pathway and subsequent outcomes.This will enhance our existing knowledge and understanding and provide evidence to support local decision-making about whether to adopt and how best to implement.

The two groups of implementation case studies included in our synthesis, although all were conducted in the UK, provide very limited information on how enhanced recovery programmes have actually been implemented in UK NHS settings. The standard reporting format originally proposed by The Enhanced Recovery Partnership Programme would enhance the value of future case studies if adhered to. Knowledge of how well the intervention has been implemented (fidelity) is essential for understanding how and why the intervention works and hence how outcomes can be further improved. Assessing fidelity may involve considering not only adherence to the requirements of the programme but also potential moderating factors, such as strategies used to assist delivery of the intervention, quality of delivery and participant responsiveness to new practices.[63] It would be helpful if future innovation programmes used standardised reporting. For multi-site programmes, a formal synthesis of findings from all participating sites should be undertaken as part of the evaluative process. This would ensure that the insights and contextual information which can inform the wider spread and adoption (or indeed discontinuation) would be systematically captured in a generalisable format.

Adherence/compliance to elements by staff and patients also requires further investigation. Rigorous data on patients' experiences of enhanced recovery programmes are lacking. Validated tools should be used and administered independently of those providing the service. Efforts should be made to obtain data from representative samples of patients receiving conventional care as well as those treated with enhanced recovery protocols, along with evidence on the experiences of their families/carers.

Evidence relating to the cost-effectiveness of enhanced recovery programmes in UK NHS settings is lacking. Whist enhanced recovery programmes have the potential to deliver cost savings, improved measurement of costs and benefits is crucial to help decision-makers decide how best to make optimal use of limited resources.

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Contributors: PW took overall responsibility for the rapid synthesis. AE provided input at all stages. D Craig was involved in all stages of the economic evaluation including production of the final review write-up. D Chambers and FP were involved in all stages of the rapid synthesis including production of the final review write-up. DF conducted literature searches and contributed to the methods section of the review. DJ and EMcG provided advice throughout the rapid synthesis and commented on the draft review.

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Transparency declaration: The lead author (the manuscript's guarantor) affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Data sharing: No additional data available.

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Table 1: Systematic review risk of bias assessment

Author	Adequate search	Risk of bias assessed	Quality score accounted for in analysis	Study details reported and differences accounted for	Statistical heterogeneity investigated	Gaps in research identified	Conclusions justified
Colorectal/Colon surgery							
Adamina (2011)[6]	✓	✓	UC	✓	UC	✓	✓
Ahmed (2012)[7]	✓	X	X	X	X	X	✓
Eskicioglu (2009)[10]	✓	✓	X	✓	✓	✓	✓
Gouvas (2009)[11]	✓	✓	X	✓	✓	✓	✓
Khan (2010)[13]	✓	✓	X	✓	X	✓	✓
Lv (2012a)[21]	✓	✓	X	X	✓	✓	✓
Rawlinson (2011)[15]	✓	X	X	✓	UC	X	UC
Spanjersberg (2011)[16]	✓	✓	✓	✓	✓	✓	✓
Varadhan (2010)[17]	✓	✓	X	✓	✓	✓	✓
Walter (2009)[18]	✓	✓	✓	✓	✓	✓	✓
Wind (2006)[19]	✓	✓	✓	✓	✓	✓	✓
Gynaecological surgery							
Lv (2012b)[20]	✓	X	X	X	X	✓	✓
Liver/pancreatic surgery							
Coolsen (2012)[8]	✓	✓	X	✓	X	✓	✓
Coolsen (2013)[9] Link to [64]	✓	✓	✓	✓	✓	✓	✓
Hall (2012)[12]	X	X	X	✓	X	✓	✓
Various surgical specialities							
Lemmens (2009)[14]	✓	X	X	✓	X	✓	✓
Sturm (2009)[5]	✓	X	X	✓	UC	✓	✓

UC=unclear reporting

Table 2: RCT quality assessment

Author	Adequate random allocation	Adequate allocation concealment	Blinding of healthcare professional	Blinding of participants	Blinding of outcome assessor	Unexpected imbalances in drop-outs between groups	Imbalances accounted/adjusted for	Intention to treat analysis	ITT appropriate and appropriate methods used to account for missing data
Bariatric surgery									
Lemanu (2013)[27]	✓	✓	X	X	X	X	NA	UC	UC
Colorectal/colon surgery									
Garcia-Botello (2011)[24]	UC	X	UC	X	UC	X	NA	UC	✓
Ionescu (2009)[25]	✓	✓	X	X	UC	X	NA	UC	UC
Lee (2011)[26]	✓	✓	UC	X	UC	X	NA	UC	UC
Ren (2012)[29]	✓	✓	X	X	✓	X	NA	UC	UC
Wang (2011)[31]	UC	UC	UC	X	UC	X	NA	✓	✓
Wang (2012)[32]	UC	UC	X	X	✓	UC	UC	UC	UC
Yang (2012)[33, 34]	✓	UC	X	X	UC	X	NA	X	X
Gastric surgery									
Chen (2012)[22]	UC	UC	X	✓	✓	X	NA	UC	UC
Kim (2012)[23]	UC	UC	X	X	X	X	NA	UC	UC
Liu (2010)[28]	UC	X	X	X	X	X	NA	UC	UC
Wang (2010)[30]	UC	UC	X	X	UC	X	NA	X	X

UC: unclear reporting; NA: not applicable

Figure 1: Study flow diagram

Effectiveness and implementation of enhanced recovery after surgery programmes: a rapid evidence synthesis

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Transparency declaration: The lead author (the manuscript's guarantor) affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Data sharing: No additional data available.

Abstract

Objectives

To assess the evidence on the impact of enhanced recovery programmes for patients undergoing elective surgery in acute hospital settings in the UK.

Design

Rapid evidence synthesis. Eight databases were searched from 1990 to March 2013 without language restrictions. Relevant reports and guidelines, websites, and reference lists of retrieved articles were scanned to identify additional studies. Systematic reviews, RCTs not included in the systematic reviews, economic evaluations and UK NHS cost analysis, implementation case studies and surveys of patient experience in a UK setting were eligible for inclusion.

Primary and secondary outcome measures

We assessed the impact of enhanced recovery programmes on health or cost-related outcomes, and assessed implementation case studies and patient experience in UK settings. Studies were quality assessed where appropriate. using the CRD DARE critical appraisal process.

Results

Seventeen systematic reviews and 12 additional RCTs were included. Ten relevant economic evaluations were included. No cost analysis studies were identified. Most of the evidence focused on colorectal surgery. Fourteen innovation case studies and 15 implementation case studies undertaken in NHS settings described factors critical to the success of an enhanced recovery programme.

Evidence for colorectal surgery suggests that enhanced recovery programmes may reduce hospital stays by 0.5 to 3.5 days compared with conventional care. There were no significant differences in reported readmission rates. Other surgical specialties showed greater variation in reductions in length of stay reflecting the limited evidence identified.

Findings relating to other outcomes were hampered by a lack of robust evidence and poor reporting.

Conclusions

There is consistent, albeit limited, evidence that enhanced recovery programmes can reduce length of patient hospital stay without increasing readmission rates. The extent to which managers and clinicians considering implementing enhanced recovery programmes in UK settings can realise savings will depend on length of stay achieved under their existing care pathway.

Word Count: ~~290~~ 300

Strengths and limitations of the study

- Enhanced recovery programmes have been adopted with enthusiasm by the NHS as a means to achieving productivity gains and cost-savings. This evolution makes combining studies over different periods and interpreting results of earlier studies in relation to the current context more difficult.
- The evidence base to support such widespread implementation suggests possible benefits in terms of reduced length of hospital stay, fewer postoperative complications, reduced readmissions and improved patient outcomes.
- Althouth there is a reasonable volume of evidence evaluating enhanced recovery programmes in colorectal surgery, robust evidence is sparse. Optimal care is certainly the right thing to do, but the evidence does not identify which enhanced recovery programme elements and combinations of elements are most effective.
- Findings relating to other outcomes, costs of enhanced recovery programmes, experience in using the programmes, and patient experience were limited by generally poor quality evidence and poor reporting. As such, conclusions on which combinations provide greatest gains and how best to implement them cannot be made.

Introduction

The National Health Service (NHS) faces severe funding constraints now and in the medium term. The forecast reduction in resources provides an enormous challenge to NHS organisations and staff. Service redesign can save money and improve quality but much depends on how care is co-ordinated and the way services are implemented in a local setting.[1, 2] NHS decision makers need to consider not only the effectiveness and cost effectiveness of any initiative but also efficient implementation. Enhanced recovery programmes (also known as ERAS, fast track, multimodal, rapid or accelerated recovery programmes) seek to deliver an optimal pathway (covering the preoperative, intraoperative and postoperative periods) that is focused on optimal recovery and discharge for patients. The approach was pioneered in Denmark in the late 1990s for patients undergoing colorectal surgery[3] and is now spreading to other surgical pathways such as orthopaedic, urology and gynaecology.

Enhanced recovery programmes have been delivered in the UK NHS since the early 2000s. Implementation has to date been variable despite the support of the Department of Health and more recently the Royal Colleges. In 2011, 14 innovation sites were established as part of the Enhanced Recovery Partnership Programme. These sites acted as pathfinders for implementation; some sites were self-selecting and others were encouraged to join. The aim was to raise the profile, promote the benefits and inform the uptake of enhanced recovery for elective surgical care across the NHS. These sites had little or no experience in enhanced recovery pathways. It is likely that this variation seen across these sites reflects both the complexity of enhanced recovery programmes themselves and issues around implementing change in established surgical pathways . Differences in programme implementation may also reflect differences between surgical specialities. Set against the benefits of enhanced recovery programmes are concerns that discharging patients too soon after surgery could increase complications and readmissions, thereby worsening patient experience and potentially health outcomes, and increasing pressure on primary and/or secondary healthcare services.

Before embarking on adoption of an enhanced recovery programme, NHS managers and clinicians need to be fully aware of the strength of the underlying evidence. They need to have a clear understanding of how best to implement such programmes and the likely implications for service delivery within finite budgets and considering the need for equity of access. The aim of this project was to conduct a rapid synthesis of the evidence on the

clinical and cost effectiveness of enhanced recovery programmes, and the implementation, delivery and impact of such programmes in secondary care settings in the UK.

Methods

Eight databases, including DARE, NHS EED and MEDLINE were searched to from 1990 to March 2013 without language restrictions. The PROSPERO database was searched to identify ongoing systematic reviews. Relevant reports and guidelines were screened for further studies. Reference lists of retrieved articles, reviews and evaluations were scanned, and relevant individuals contacted for additional evidence.

Systematic reviews, RCTs not included in the systematic reviews, economic evaluations, and UK NHS cost analysis studies were included if they evaluated the impact of enhanced recovery programmes (encompassing different combinations of the main preoperative, intraoperative and postoperative pathway elements described by the Enhanced Recovery Partnership Programme[4] on health or cost-related outcomes. Eligible studies included patients undergoing elective surgery in an acute hospital in the UK NHS or a comparable healthcare system. Comparators were only relevant to clinical and cost-effectiveness evaluations, and included conventional (usual/standard) care without a structured multimodal enhanced recovery patient pathway (as defined in the included studies). Case studies, impact assessments and surveys of patient experience that documented the experience of implementing enhanced recovery in a UK setting were also eligible.

Quality assessment of systematic reviews, RCTs and economic evaluations was based on existing CRD critical appraisal methods (http://www.crd.york.ac.uk/crdweb/HomePage.asp; CRD, 2009). Cost analysis studies, studies of patient experience, and case studies of implementation were not formally quality assessed.

All stages of the review process were performed by one researcher and checked by a second. Disagreements between reviewers were resolved by discussion or by recourse to a third reviewer where necessary.

The type and range of evidence precluded meta-analysis and we therefore performed a narrative synthesis, differentiating clinical outcomes (eg. mobilisation, mortality and morbidity, and length of hospital stay), patient-reported outcomes (eg. patient experience and satisfaction), resource use in secondary care (eg. workforce utilisation and costs), and implementation case studies.

Results

Seventeen systematic reviews[5-21] and 12 additional RCTs[22-34] were included in the evidence on clinical effectiveness (see Figure 1: flow diagram). The quality of the systematic reviews varied and the additional RCTs were considered to be at high risk of bias (see tables 1 and 2). One RCT was a four arm trial; this was the only multicentre trial, the remaining trials were small, single centre trials.[35] We included 15 case studies of implementation of ERAS in NHS settings, and evaluations of the 14 Enhanced Recovery Partnership Programme innovation sites. In addition, 10 relevant economic evaluations were also included (summary evidence tables are available on request from the review authors). Most of the evidence focussed on colorectal surgery.

Where reviews reported the number of included patients, sample sizes ranged between 99 and 5,747 patients in the ERAS group and between 99 and 1,062 in comparator groups. Most individual RCTs analysed fewer than 100 patients (range 44 to 597 patients). Where indications for surgery were reported in systematic reviews and individual RCTs, most trials were in patients with cancer. Where reported, patients were adults within similar age ranges. Follow-up was generally up to 30 days post discharge.

The number and combination of ERAS elements varied considerably across all types of evidence; ranging from four to 14 elements across systematic reviews and from 10 to 14 elements across individual RCTs (see full report for details; in press). This highlights the lack of standardisation across ERAS programmes and agreement on what constitutes an ERAS pathway, and will have implications on the overall findings. Only one review assessed compliance with ERAS elements.[7] Ahmed (2012)[7] noted that, in general, compliance fell during the postoperative period in most of the studies (from around 100% to around 20%). Use of epidural analgesia had the highest levels of compliance across all studies (67% to 100%). Use of transverse incisions had the lowest levels of compliance (around 25%). Reasons for differences in compliance and waning of compliance were not measured in the reviews. None of the reviews assessed patient compliance, including adherence to preoperative advice to ensure fitness for surgery.

~~Follow-up was generally up to 30 days post discharge.~~

Despite the large number of studies, robust evidence was sparse (~~see tables 3 and 4~~ supplementary tables 1 and 2; full outcome details are available in the full review; in press). Seven reviews in colorectal surgery performed meta-analyses and showed a significant mean reduction in primary or total length of stay that ranged from 1.56 days (95% CI 0.50 to 2.61 days)(19) to 3.75 days (95% CI 5.11 to 2.40 days).(18)~~(Walter 2009)~~ Evidence from

individual RCTs in colorectal surgery also suggest reduced length of hostpital stay following an ERAS programme (mean length of stay 4.15 days to 6.43 days) compared to conventional care (mean length of stay 6.6 days to 11.7 days). There were no significant differences in reported readmission rates, but it was unclear how readmissions were defined and measured in the reviews and RCTs.

Other surgical specialties showed greater variation in reported reductions in length of stay, but this is likely to reflect the greater uncertainty due to the more limited evidence base for these specialties. Statistical heterogeneity varied between reviews and was often not formally explored, but may have reflected differences in ERAS protocols, lack of compliance with important ERAS elements, and differences in surgical populations and procedures.

Deaths were rare and no significant differences between treatment groups were found in the systematic reviews and additional RCTs, regardless of surgical speciality. Morbidity was defined differently across systematic reviews and RCTs; rates between treatment groups were sometimes inconsistent, but generally indicated no statistically significant differences.

Mobilisation rates were inconsistent across systematic reviews, but most reported no significant differences in time to mobilisation between treatment groups. Mobilisation was rarely reported as an outcome in the additional RCTs.

Where systematic reviews and additional RCTs assessed quality of life and patient experience/satisfaction, equivocal findings were reported. Evidence on reintervention rates, pain and resource use was lacking in both systematic reviews and RCTs.

Other Reviews

A systematic review in colorectal surgery, identified after the last literature search, showed similar findings to the systematic reviews discussed above.[36] Mean length of primary hospital stay was statistically significantly reduced in ERAS patients; mean difference (MD) -2.44 (95% CI -3.06 to -1.83; 11 RCTs) but with significant statistical heterogeneity (I^2=88%). There was no evidence to suggest increased rates of readmissions, complications and mortality. Some of the individual RCT results for primary length of stay did not appear to be consistent with results reported in other systematic reviews, and this may have impacted on the estimated reduction in length of primary hospital stay.[36]

Two reviews[37, 38] focusing on individual ERAS elements were ~~found~~ identified, both of which highlighted the lack of evidence on the full ERAS pathway and the lack of compliance with ERAS protocols. D~~and d~~etails can be found in the full review (in press).

Case studies

Ten of 14 UK NHS innovation sites provided adequate data for inclusion in this section.[39-41] Fifteen case studies of implementation of ERAS in NHS settings, and 11 NHS trusts (mostly in colorectal surgery) provided evidence relating to the implementation of an ERAS programme within their Trust. Full results and evidence tables are presented in the full review (in press).

There were variations in practice in terms of numbers and combinations of ERAS elements implemented; the most frequently implemented programme elements in the case studies were pre-admission information/counselling and early postoperative mobilisation. Available evidence did not address which enhanced recovery elements and combinations of elements were most effective. Substantial variation in what constitutes an enhanced recovery programme within and between different surgical specialities, and difficulties in implementing certain ERAS components, suggest that the enhanced recovery pathway may be used as a framework and adapted to suit local situations. Evidence on compliance/adherence to enhanced recovery programmes was lacking.

Case studies identified the factors believed to act as barriers or facilitators to implementing an ERAS programme. Barriers to implementation included resistance to change from patients and staff, lack of funding or support from management,[39, 42-44] staff turnover, problems arising from poor documentation, the time required to complete documentation, and other practical issues.

Facilitators included the presence of a dedicated ERAS project lead/nurse to coordinate and sustain multidisciplinary working and continuity of the pathway, a multidisciplinary team approach, and continual education for staff and patients/patient representatives. One innovation site mentioned that it did not offer a seven day service for enhanced recovery due to staff resources. Patients operated on towards the end of the week may have to wait until after the weekend to be discharged if they need to be seen by any health care professionals or social services. The need to sustain multidisciplinary working means that, in the absence of 24/7 working for elective procedures, enhanced recovery programmes will tend to be front loaded into the start of the working week (typically Monday to Thursday). Recent evidence suggests a higher risk of death for patients who have elective surgical procedures carried out later in the working week and at the weekend,[45] the capcity to implement ERAS

throughout the working week might ensure continuity of best care and help mitigate against such variation.

We included two published studies of patient experience of ERAS.[46, 47] Each study used qualitative research methods to analyse audiotaped material. The two studies provided limited evidence suggesting that patients who were willing to provide feedback took a positive view of their experience of treatment in an ERAS programme. The studies suggested that patients were willing to comment on their experience in a way that can help healthcare providers to identify areas for improvement.

Cost-effectiveness

Ten economic evaluations in adult populations undergoing various surgical procedures evaluated costs and outcomes over short time horizons (~~see Table 5~~ supplementary table 3).[48-57] All of the evaluations suggested that programmes that achieve a reduction in length of stay are cost saving, and are not to the detriment of patients in terms of complication rates, readmission and health-related quality-of-life. The quality of the clinical studies on which these evaluations were based was variable, but generally poor. The generalisability of the results of these evaluations was limited by a lack of transparency in reporting, and the disparity in standard protocols and what had been evaluated across the settings made it unfeasible to select a cost-effective programme.

Discussion

Statement of Principal Findings

Overall, the systematic reviews and additional RCTs suggest that length of hospital stay is reduced in ERAS patients compared to patients receiving conventional care. The evidence was based mainly on colorectal surgery and the applicability of findings to other surgical specialities remains less clear. Evidence for colorectal surgery suggests that enhanced recovery programmes may reduce hospital stays by 0.5 to 3.5 days compared with conventional care.

There were marked differences in length of stay across reviews and individual studies regardless of speciality. These differences may reflect differences in ERAS protocols, compliance to ERAS programmes, ~~and~~ health care systems and procedures, and/or outcome definitions. This raises questions regarding the magnitude of effect of the ERAS protocols on length of stay, which may be overstated in some reviews.

The evidence suggests that ERAS programmes do not compromise patient morbidity, mortality and readmission rates but outcome definitions varied across reviews and individual studies. Such differences make it difficult to determine the reliability and generalisability of the findings.

Equivocal findings were reported for quality of life and patient experience/satisfaction but the evidence was based on few studies, which utilised various methods to measure these outcomes. The limited evidence precludes conclusions on the effects of ERAS protocols on pain, mobilisation and reintervention.

The implementation evidence included resource use in terms of the professionals involved in delivery of enhanced recovery programmes, but details were very limited and did not add to the evidence synthesis. Most case studies were uncontrolled and represent experiences of a sample of centres that chose to report their data; their outcomes may not be representative of those achieved elsewhere in the UK NHS. Their main value as evidence is the light they shed on NHS clinicians' perceptions of requirements for successful implementation and barriers to implementation of ERAS.

The impact of surgical experience and surgical volume on clinical outcomes was not explored and any implications of differences in these areas remain unknown. As enhanced recovery invariably targets the fitter, more mobile patient, frailer patients may not receive parity of access to what may be considered optimal treatment and management. Managers and clinicians considering implementing such programmes should think about the likely implication on equity of access. Whether inequity is an unintended outcome of enhanced recovery, merits further investigation.

Our review of the cost effectiveness literature suggests that enhanced recovery programmes that achieve a reduction in length of stay may save costs without detrimental effects on complication rates, readmission and health-related quality of life. However, generalisability of the results of the economic evaluations is limited by a lack of transparency in reporting, use of different settings and populations and variable methodology in analyses. Data were lacking for resource use associated with the programmes evaluated and could not usefully inform the review of economic evaluations. In addition, the clinical effectiveness of some of the programmes considered in economic evaluations was not based on robust evidence.

Strengths and weaknesses

The main strength of this study was our use of multiple approaches to acquire and synthesise evidence. The main limitations were poor methodological quality and poor reporting of the included studies, and the inherent difficulty of reviewing a complex intervention in different healthcare systems and surgical specialities. Current methods for synthesising such complex interventions are limited. The methodological limitations and are not discussed here as this was outside the scope of this project, but have been addressed in previous publications (eg. Noyes et al, 2013).[58] Another complication is that elements of early enhanced recovery programmes have become accepted practice within conventional care. This evolution makes combining studies over different periods and interpreting results of earlier studies in relation to the current context more difficult.

We found a large number of systematic reviews but there was substantial overlap in the included studies and evidence was not as abundant as the existence of multiple systematic reviews suggested. Most of the RCTs were small and not high quality. With the exception of one RCT, the remainder were single centre trials and therefore appear to have been undertaken to support implementation of an enhanced recovery programme in a specific setting rather than being planned as research studies. There were significant clinical and methodological differences between individual trials, and we therefore presented a narrative synthesis. Relatively few trials were conducted in the UK and this may limit the generalisability of evidence to UK NHS settings.

Lack of evidence on important outcomes including pain and quality of life is also an issue for research in this field. Trials tended not to report on adherence to the planned enhanced recovery programme. Assessing adherence to interventions and the impact this has on health outcomes is an important issue which is often overlooked in studies, and is a limitation in the evidence base in this review.

Three additional systematic reviews of effectiveness were brought to our attention during manuscript submission. One systematic review incorporates RCTs in colorectal surgery (Greco, 2013),[59] one incorporates RCTs and cohort studies in abdominal surgery (Neville, 2014)[59] and one includes RCTs and quasi-RCTs across various surgical specialities (Nicholson, 2014).[59] The trials included in Greco (2013)[59] and Nicholson (2014)[59] overlap with those included in this review and the findings are consistent. The inclusion of these two reviews would therefore not have significantly altered the findings from this review. Neville (2014)[59] provides some additional data on patient-reported outcomes, including some evidence on post-discharge functional status. However, these outcomes were not frequently

reported, and the additional evidence was mainly from study designs that would not have met the inclusion criteria for this review.

An important feature of our review is the inclusion of evidence on the implementation of enhanced recovery programmes in the UK NHS. This evidence has not been synthesised previously and the original programme webistes are archived, so future access is not assured. By summarising this evidence, we have ensured that the main findings continue to be publicly available. We sought evidence on the experience of health professionals and patients of a broad range of sources and study types. Important themes emerged from this evidence that may be of value for implementing and sustaining enhanced recovery programmes in UK NHS settings. Due to the rapid nature of the evidence synthesis, the list of sources searched to identify data on implementation and delivery of enhanced recovery programmes was not exhaustive and we acknowledge that relevant evidence may have been missed. Indeed, evidence from Scotland has been noted and eligible case studies have been identified from the NHS Scotland Quality Improvement Hub website. It should be noted that these are as limited as those included in the review. A qualitative study was brought to our attention at peer review; the study was published after our final search date. Pearsall et al (2014)[60] conducted a qualitative study to explore the barriers and enablers in implementing an enhanced recovery after surgery programme in a University hospital in Canada. The themes identified are consistent with those reported in this review.

However, case studies are susceptible to risk of bias. Use of a standard reporting format was a potential strength of the case studies but variation in what each site actually reported (particularly in terms of evidence of benefit from the introduction of enhanced recovery programmes) reduced the usefulness of the evidence.

We sought to incorporate published and unpublished evidence on patient experiences and views of enhanced recovery programmes. Evaluation of patient experience of care is increasingly important for the NHS, especially in view of unacceptable failures of care such as those highlighted in the Francis Report.[61] Though the evidence was generally positive for enhanced recovery, it was limited by a shortage of studies that used validated measures of patient experience and by study designs that could bias results in favour of enhanced recovery.

A further strength of this study was the consideration of cost-effectiveness evidence, but the nature of the evidence did not permit any analyses. There is a clear need to capture better evaluated data on costs and benefits of enhanced recovery programmes from a clearly

stated perspective. A systematic review of economic evaluations (Lee, 2014)[62] was brought to our attention during manuscript publication. The review confirmed the need for well-designed research to determine the cost-effectiveness of enhanced recovery programmes from both the institutional and societal perspectives.

Implications for healthcare

Overall, there is consistent, albeit limited, evidence that enhanced recovery programmes can reduce length of patient hospital stay without increasing readmission rates. Data on re-intervention rates and patient-reported outcomes did not suggest significant differences between enhanced recovery and conventional care, but the evidence was very limited and based on small numbers of patients. The lack of evidence on patient outcomes, resource use and costs precludes firm conclusions on the overall value of enhanced recovery programmes.

ERAS does not appear to reduce complication or readmission rates; the only cost benefit may lie in a reduction in post-operative bed days. Optimal care is certainly the right thing to do, but the evidence does not identify which enhanced recovery programme elements and combinations of elements are most effective. As such, conclusions on which combinations provide greatest gains and how best to implement them cannot be made.

The extent to which managers and clinicians considering implementing enhanced recovery programmes can realise reductions and cost savings will therefore depend on length of stays achieved under their existing care pathway. Important themes emerged from the relevant evidence identified on implementation, including the role of ERAS facilitators and the need for full support from management. It appears that these components are essential for the successful implementation and sustained delivery of enhanced recovery programmes in NHS settings. Consideration of potential benefit also needs to take account of the costs of service redesign, the resource use associated with programmes of this nature, the potential for improvement in patient outcomes and the impact on equity of access.

Implications for research

RCTs comparing an enhanced recovery programme with conventional care continue to be conducted and published, although mostly not in the UK. Given the available evidence, further single centre RCTs of this kind are not a priority. Rather, what is needed is improved collection and reporting of how enhanced recovery programmes are implemented, resourced

and experienced in NHS settings. Also, exploration into the effect that varying levels of surgical volume and surgical experience, and different discharge protocols might have on the success of an enhanced recovery pathway and subsequent outcomes.This will enhance our existing knowledge and understanding and provide evidence to support local decision-making about whether to adopt and how best to implement.

The two groups of implementation case studies included in our synthesis, although all were conducted in the UK, provide very limited information on how enhanced recovery programmes have actually been implemented in UK NHS settings. The standard reporting format originally proposed by The Enhanced Recovery Partnership Programme would enhance the value of future case studies if adhered to. Knowledge of how well the intervention has been implemented (fidelity) is essential for understanding how and why the intervention works and hence how outcomes can be further improved. Assessing fidelity may involve considering not only adherence to the requirements of the programme but also potential moderating factors, such as strategies used to assist delivery of the intervention, quality of delivery and participant responsiveness to new practices.[63] It would be helpful if future innovation programmes used standardised reporting. For multi-site programmes, a formal synthesis of findings from all participating sites should be undertaken as part of the evaluative process. This would ensure that the insights and contextual information which can inform the wider spread and adoption (or indeed discontinuation) would be systematically captured in a generalisable format.

Adherence/compliance to elements by staff and patients also requires further investigation. Rigorous data on patients' experiences of enhanced recovery programmes are lacking. Validated tools should be used and administered independently of those providing the service. Efforts should be made to obtain data from representative samples of patients receiving conventional care as well as those treated with enhanced recovery protocols, along with evidence on the experiences of their families/carers.

Evidence relating to the cost-effectiveness of enhanced recovery programmes in UK NHS settings is lacking. Whist enhanced recovery programmes have the potential to deliver cost savings, improved measurement of costs and benefits is crucial to help decision-makers decide how best to make optimal use of limited resources.

Word Count: ~~3,732~~4,179

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Figure 1: Study flow diagram

Table 1: Systematic review risk of bias assessment

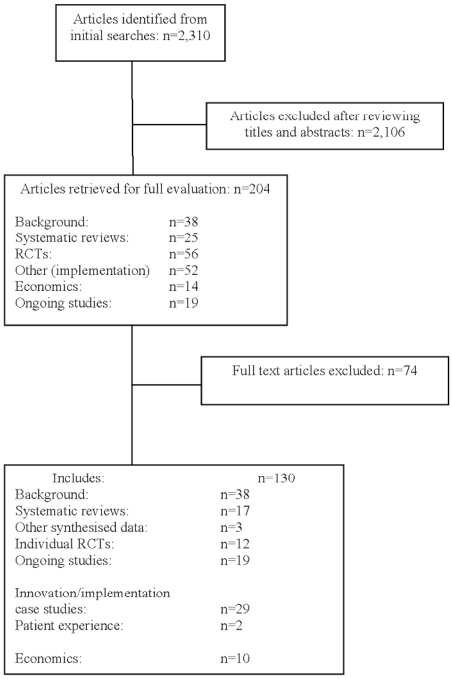
Author	Adequate search	Risk of bias assessed	Quality score accounted for in analysis	Study details reported and differences accounted for	Statistical heterogeneity investigated	Gaps in research identified	Conclusions justified
Colorectal/Colon surgery							
Adamina (2011)[6]	✓	✓	UC	✓	UC	✓	✓
Ahmed (2012)[7]	✓	X	X	X	X	X	✓
Eskicioglu (2009)[10]	✓	✓	X	✓	✓	✓	✓
Gouvas (2009)[11]	✓	✓	X	✓	✓	✓	✓
Khan (2010)[13]	✓	✓	X	✓	X	✓	✓
Lv (2012a)[21]	✓	✓	X	X	✓	✓	✓
Rawlinson (2011)[15]	✓	X	X	✓	UC	X	UC
Spanjersberg (2011)[16]	✓	✓	✓	✓	✓	✓	✓
Varadhan (2010)[17]	✓	✓	X	✓	✓	✓	✓
Walter (2009)[18]	✓	✓	✓	✓	✓	✓	✓
Wind (2006)[19]	✓	✓	✓	✓	✓	✓	✓
Gynaecological surgery							
Lv (2012b)[20]	✓	X	X	X	X	✓	✓
Liver/pancreatic surgery							
Coolsen (2012)[8]	✓	✓	X	✓	X	✓	✓
Coolsen (2013)[9] Link to [64]	✓	✓	✓	✓	✓	✓	✓
Hall (2012)[12]	X	X	X	✓	X	✓	✓
Various surgical specialities							
Lemmens (2009)[14]	✓	X	X	✓	X	✓	✓
Sturm (2009)[5]	✓	X	X	✓	UC	✓	✓

UC=unclear reporting

Table 2: RCT quality assessment

Author	Adequate random allocation	Adequate allocation concealment	Blinding of healthcare professional	Blinding of participants	Blinding of outcome assessor	Unexpected imbalances in drop-outs between groups	Imbalances accounted/adjusted for	Intention to treat analysis	ITT appropriate and appropriate methods used to account for missing data
Bariatric surgery									
Lemanu (2013)[27]	✓	✓	X	X	X	X	NA	UC	UC
Colorectal/colon surgery									
Garcia-Botello (2011)[24]	UC	X	UC	X	UC	X	NA	UC	✓
Ionescu (2009)[25]	✓	✓	X	X	UC	X	NA	UC	UC
Lee (2011)[26]	✓	✓	UC	X	UC	X	NA	UC	UC
Ren (2012)[29]	✓	✓	X	X	✓	X	NA	UC	UC
Wang (2011)[31]	UC	UC	UC	X	UC	X	NA	✓	✓
Wang (2012)[32]	UC	UC	X	X	✓	UC	UC	UC	UC
Yang (2012)[33, 34]	✓	UC	X	X	UC	X	NA	X	X
Gastric surgery									
Chen (2012)[22]	UC	UC	X	✓	✓	X	NA	UC	UC
Kim (2012)[23]	UC	UC	X	X	X	X	NA	UC	UC
Liu (2010)[28]	UC	X	X	X	X	X	NA	UC	UC
Wang (2010)[30]	UC	UC	X	X	UC	X	NA	X	X

UC: unclear reporting; NA: not applicable



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Supplementary table 1: Systematic reviews – main clinical outcomes

Author & no. included studies	Length of hospital stay (days)	Readmission rates (N/%)
Colorectal/colon surgery		
Adamina (2011)[6] *6 RCTs*	Primary length of stay: ERAS reduced stay by 2.5 days (95 CrI -3.92 to -1.11)	ERAS did not increase readmission rates (RR 0.59, 95% CrI 0.14 to 1.43)
Ahmed (2012)[7] *11 studies; study designs not reported*	2 to 11 days (10 studies)	0 to 22% (8 studies) Shortest length of stay (2 days) associated with highest readmission rate (22%)
Eskicioglu (2009)[10] *4 RCTs*	Three out of four trials reported a significantly shorter length of primary hospital stay in the ERAS group. Two trials reported overall hospital stay, both of which found a significantly reduced length of stay in the ERAS group.	7/99 ERAS, 11/99 control; no significant difference between groups (RR 0.67, 95% CI 0.20 to 2.19, 4 trials; I^2= 24%)
Gouvas (2009)[11] *11 studies; 4 RCTs,* *7 non-randomised case control studies*	Significantly reduced primary hospital stay with fast track: 3.3 to 6.7/5.8 to 10 days (WMD -2.35, 95% CI -3.24 to -1.46; I^2=75% , 9 studies). Similar results in subgroup analysis. Significantly reduced total hospital stay with fast track: 4 to 5.5 days/6.5 to 13 days (WMD -2.46, 95% CI -3.43 to -1.48; I^2= 0%, 5 studies). Similar results for subgroup analysis.	0 to 24%/0 to 20%: NS (RR 1.37, 95% 0.97 to 1.92; I^2=0%, 10 studies). Subgroup analysis showed that non-RCTs had significantly lower readmission rates in the control group.
Khan (2010)[13] *10 studies; 4 RCTS, 6 non-randomised comparative studies*	Not applicable	Not applicable
Lv (2012a)[21] *7 RCTs (one multi-arm RCT analysed as 2 separate comparisons)*	Total length of stay significantly shorter for ERAS treated patients (MD -1.88 days, 95% CI -2.91 to -0.86; 7 RCTs/8 comparisons, I^2=75%). Sensitivity analysis did not significantly alter the results.	No statistically significant differences between groups (RR 0.90, 95% CI 0.52 to 1.53; 7 RCTS/8 comparisons, I^2=0%).
Rawlinson (2011)[15] *13 studies; 6 RCTs and 7 non-randomised clinical trials*	Eleven studies reported on primary hospital stay, of which 10 reported a significantly shorter stay in the ERAS group.	Readmissions ranged from 0 to 24% with ERAS and from 0 to 20% with traditional care; 12 studies; no significant difference between groups.
Spanjersberg (2011)[16] *6 RCTs (2 did not meet inclusion criteria and were not included in primary analyses)*	Statistically significantly reduced in ERAS patients (MD -2.94 days, 95% CI -3.69 to -2.19 days; I^2=0%, 4 RCTs) Subgroup analyses including the 2 RCTs involving limited number of ERAS elements did not significantly alter the findings.	ERAS 4 (3.3%); control 5 (4.2%) No significant difference between groups (I^2=59%, 4 RCTs) Subgroup analyses including the 2 RCTs involving limited number of ERAS elements did not significantly alter the findings.
Varadhan (2010)[17] *6 RCTs*	Primary hospital stay was significantly shorter in the ERAS group (WMD -2.51 days, 95% CI -3.54 to -1.47, 6 trials; I^2 = 55%).	10/226 ERAS, 13/226 control; no significant difference between groups (RR 0.80, 95% CI 0.32 to 1.98, 4 trials with events; I^2 = 9%
Walter (2009)[18] *4 studies; 2 RCTs, one quasi-randomised trial, 1 cohort*	Total length of stay (mean (SD) days) Statistically significant reduction in ERAS compared to control groups WMD -3.75 days (95% CI -5.11 to -2.40 days; I^2=0%, 2 RCTs) Primary length of stay (mean (SD) days) Statistically significant reduction in ERAS compared to control groups WMD -3.64 days (95% CI -4.98 to -2.29 days; I^2=0%, 2 RCTs)	No statistically significant difference between groups (RR 0.26, 95% CI 0.03 to 2.25; one RCT) and (RR 1.73, 95% CI 1.00 to 3.01; I^2=0%, 2 CCTs). (p=0.05 which the authors consider significant).

Author & no. included studies	Length of hospital stay (days)	Readmission rates (N/%)
Wind (2006)[19] *6 studies; 3 RCTs, 3 CCTs*	Primary hospital stay (mean) Primary hospital stay statistically significantly lower in the ERAS group (WMD -1.56, 95% CI -2.61 to -0.50; I^2=52.9%, 3 RCTs, 3 CCTs). Subgroup analyses showed similar results for RCTs and CCTs. Overall hospital stay (mean) All three trials showed statistically significantly shorter overall hospital stay in ERAS patients (p<0.05)	No statistically significant differences between groups (RR 1.17, 95 %CI 0.73 to 1.86; I^2=23.6%, 2 RCTs, 3 CCTs). Subgroup analyses showed similar results in favour of ERAS in RCTs, but in favour of traditional care in CCTs.
Gynaecological surgery		
Lv (2012b)[20] *0 studies*	Not applicable	Not applicable
Liver/pancreatic surgery		
Coolsen (2012)[8] *6 studies; 3 case-control, 2 RCTs (both arms ERAS elements; equivalent to prospective case series), one retrospective case series.*	3 comparative studies: ERAS 5 to 7 days; control 7 to 11 days: difference (NS one study, p<0.001 2 studies) Non-comparative studies: 4 to 7 days	3 comparative studies: ERAS 0 to 13%; control 0 to 10%: difference (NS 3 studies) 3 non-comparative studies: 0 to 5%
Coolsen (2013)[9] **Link to** [63] *8 studies; 5 case-control (historical controls receiving traditional care); 2 retrospective case series; 1 prospective case series.*	It was unclear whether results were mean or median number of days. Comparative studies ERAS 6.7 to 13.5 days; control 8 to 16.4 days (4 of 5 studies reported statistically significant differences in favour of ERAS) Non-comparative studies 10 days (range 4 to 115), three studies	No significant differences (RD 0.8%, 95% CI -2.6% to 4.1%; I^2=0%, 4 studies)
Hall (2012)[12] *10 studies; Two studies with a single intervention in one parameter of peri-operative care but within an ERAS programme (including one RCT); 6 prospective case series comparing ERAS programmes versus historical controls, one retrospective case study, and one multicentre study.*	Reduced with ERAS programme: Pancreatic 10 to 13 days (range 4 to 115 days; 4 studies); liver 4 to 7.2 days (range 2 to 82 days; 5 studies).	Pancreatic 3.5 to14.6% (4 studies); liver 0 to 13 % (5 studies)
Various surgical specialities		
Lemmens (2009)[14] *13 studies; One RCT, 3 controlled clinical trials, 2 case-control, one retrospective case series, 6 pre- post-pathway studies*	Statistically significant decrease in clinical pathway group in 11 studies; mean number of days decreased from between 5.9 and 21.7 days to between 3.3 and 18.5 days (9 studies). Median number of days decreased from between 5 and 13 days to between 2 and 7 days (4 studies). 2 studies reported no significant difference between groups.	One study reported statistically significant reduction (13% to 6%); 2 studies not reported; 10 studies NS
Sturm (2009)[5] *11 RCTs plus one systematic review*	Length of stay was clearly significantly shorter in the ERAS group in 6 trials (3 colorectal, 3 other). There was no significant difference in 1 trial (lung surgery). In the remaining trials, significance was unclear or was not reported.	Eight trials reported on readmission rates. Rates ranged from 0 to 9.7% in the ERAS groups and 0 to 20% in the control groups. Only one trial reported a statistically significant difference and this favoured the ERAS group (p = 0.022).

Supplementary table 2: RCTs – main clinical outcomes

Author	Length of hospital stay (days)	Readmission rates (N/%)
Bariatric surgery		
Lemanu (2013)[27]	Median days (interquartile range) Length of index admission: ERAS 1 (1 to 2); control 2 (o), p<0.001 Total hospital stay (including admission plus subsequent readmissions): ERAS 1 (1 to 3); control 2 (2 to 3), p<0.001	Defined as presentation to hospital within 30 days of surgery after the day of discharge; subsequent hospital stay had to be more than 24 hours. ERAS 8/40 (20%); control 8/38 (21%) Median length of readmission was 6 days with no difference between groups.
Colorectal/colon surgery		
Ionescu (2009)[25]	Mean (SD) ERAS 4.15 (2.2); control 9.23 (7), p<0.001	ERAS 3 (5%); control 2 (3%), p=0.51
Lee (2011)[26]	ERAS 6.43 (3.41); control 9.16 (2.67), p=0.001	ERAS 0 (0); control 0 (0)
Ren (2012)[29]	Post-operative: Rehabilitation 7 (6 to 8); control 8 (7 to 9), p=0.065 Total: Rehabilitation 9 (8 to 10); control 10 (9 to 11), p=0.054	30-day: rehabilitation 0; control 0
Wang (2011)[31]	*Mean (SD) ERAS 5.7 (1.6); control 6.6 (2.4), p<0.001*	*Not reported*
Wang (2012)[32]	*Median (range) post-operative hospital stay ERAS 5 (2 to 41); control 7 (3 to 55), p<0.01*	*No statistically significant differences between groups within 30 days after resection. ERAS 4 (4%) patients re-admitted for wound infection; control 9 (9%) readmitted due to bowel obstruction, vomiting, and wound infection.*
Yang (2012)[33, 34]	*Median days: ERAS 5.5 (5 to 6); control 7.0 (6 to 8), p<0.001*	*Not reported*
Ionescu (2009)[25]	*Mean (SD) ERAS 6.0 (1.0); control 11.7 (3.8), p<0.05*	*No hospital readmissions due to complications.*
Gastric surgery		
Chen (2012)[22]	Median days (range) Compared with ODG, the remaining three groups had shorter post-operative hospital stay (p<0.05) FTS + LADG 7 (5.5 to 10); LADG 7.5 (6 to 11); FTS + ODG 7.5 (6 to 11); ODG 8.75 (7 to 14)	Not reported
Kim (2012)[23]	Possible post-operative hospital stay (mean days, SD) ERAS 4.68 (0.65) (range 4 to 6); control 7.05 (0.65) (range 6 to 9), p<0.001 Post-operative hospital stay (mean days, SD) ERAS 5.36 (1.46) (range 4 to 11); control 7.95 (1.98) (range 6 to 15), p<0.001	ERAS 1/22 (4.5%); control 0/22 (0%)
Liu (2010)[28]	*Primary length of stay (mean (SD)): ERAS 6.2 (1.9); control 9.8 (2.8), p<0.001*	*Readmitted within 30 days after surgery ERAS 1/33 (3%); control 0/30 (0%)*
Wang (2010)[30]	*Median (quartile range) ERAS 6 days (6 to 7); control 8 (7 to 8), p<0.001. Primary clinical endpoint of the trial.*	*ERAS 1/45 (2.2%); control 1/47 (2.1%), no significant difference between groups*

Supplementary table 3: Economic evaluations meeting the inclusion criteria

Study Details	Study Comparators	Main Analytical Approaches, primary outcomes, and costs	Incremental cost-effectiveness (ICER) estimates and Decision Uncertainty
Salihiyyah *et al* (2011)[56] UK Hospital setting Study Population Cardiac surgery Inpatients Time horizon 6 months	Intervention Fast-track transfer post-surgery to an independent theatre recovery unit 1-2-1 nursing (n=84) Comparator Transfer post-surgery to hospital intensive care unit (n=52)	Economic evaluation based on a single study Perspective Hospital Primary outcomes Length of stay; Duration of intubation Direct Costs Total expenditure of unit divided by number of patients Productivity Costs n/a	Results The costs and benefits were not synthesised mean cost FT: £4182 (SD:2284) mean cost C: £4553 (SD:1355) (p<0.001) total LOS NSD 8 patients failed FT & were transferred to ICU 5 patients (4 FT & 1 C) required readmission Uncertainty One-way & multi-way sensitivity analysis demonstrated robustness in result that FT costs less than C
Lin *et al* (2011)[53] China Hospital setting Study Population Liver resection Inpatients Time horizon Not reported	Intervention Multidisciplinary team, streamlining of preoperative evaluation, education of patients and families, earlier oral feeding, earlier discontinuation of IV, no drains or naso-gastric tubes, early ambulation, urinary catheter <24 hours, planned discharge 6 days post-surgery (n=56) Comparator Conventional pathway (limited reporting) (n=61)	Economic evaluation based on a single study Perspective Hospital Primary outcomes Length of stay; Complications; Mortality; Readmission Direct Costs Hospital charges: operation and anaesthesia; pharmacy; auxiliary examination; other Productivity Costs n/a	Results The costs and benefits were not synthesised mean charge pre-pathway RMB 26,626 mean charge post-pathway RMB 21,004 (p<0.05) LOS reduced from 11 days to 7 days (p<0.005) Complications, mortality & readmissions NSD Uncertainty n/a
Kariv *et al* (2006)[55] USA Hospital setting Study Population Patients undergoing open ileoanal pouch surgery	Intervention Presurgery patients provided with FT protocol and documentation of post-surgery milestones. Epidural or analgesia were not used; early food and mobilisation (day of surgery/anaesthesia), patients who lived 100 to 150 miles from hospital discharged to hotel for 1 to 3 days. Success defined as discharge within 5	Economic evaluation based on a single study Perspective Hospital Primary outcomes Length of stay; Readmission; Reoperation Direct Costs Total costs for each of the categories were presented:	Results The costs and benefits were not synthesised total per case cost FT US$ 5,692 total per case cost C US$ 6672 diff US$980 (p=0.001) median postoperative los FT = 4 days C= 5 days (p=0.012) NSD in readmission outcomes

Study Details	Study Comparators	Main Analytical Approaches, primary outcomes, and costs	Incremental cost-effectiveness (ICER) estimates and Decision Uncertainty
Time horizon 30 days	days (n=97) Comparator Based on professional preferences of surgeon; no supporting documentation; sat out of bed on POD 1, walked POD 2; food withheld until stool or flatus (n=97)	per case of hospitalisation; operating room; radiology; anaesthesia; pharmacy; laboratory; ICU; and nursing care Productivity Costs n/a	Uncertainty n/a
Yanatori *et al* (2007)[57] Japan Hospital setting Study Population Cardiovascular surgery (cardiac arrest requiring cardiopulmonary bypass) Time horizon 2 years	Intervention Admitted 4 days prior to surgery, preoperative education by nurses, surgeons and rehab staff; discharge at day 7 post surgery Comparator Conventional protocol – details not reported	Economic evaluation based on a single study Perspective Healthcare provider/hospital Primary outcomes Length of stay; Complications Direct Costs Only total costs were presented Productivity Costs n/a	Results The costs and benefits were not synthesised Total mean cost for FT YEN 712,545 Total mean cost for C YEN 383,268 (p=0.038) Mean post-op LOS FT=15(12.4) C=36.7(6) (p=0.01) Uncertainty n/a
Larsen *et al* (2009)[54] Denmark Hospital setting Study Population All patients for elective primary total hip/knee arthroplasty or unicompartmental knee arthroplasty Time horizon One year	Intervention Patients receive info pre-hospitalisation; separate ward; one nurse in charge of multidisciplinary nurses, occupational therapists, and physiotherapists; nutrition screening and special focus on daily consumption of 1.5L fluid (including 2 protein beverages); mobilisation and exercise started on day of surgery; intensive mobilisation of patients in teams; eight hours of mobilisation daily (n=45: 28 total hip; 15 total knee; 2 unicompartmental knee) Comparator Patients receive info on day of admission; patients randomly among wards, various nurses in charge of care; and various occupational and physio-therapists responsible for mobilisation; mobilisation and exercise started on first postoperative day; individual and gradual mobilisation according to patient tolerance; four hours mobilisation daily (n=42: 28 total hip; 12 total knee; 2 unicompartmental knee)	Economic evaluation based on a single study Perspective Societal Primary outcomes Length of stay; Adverse events (first 3months) Health-related quality-of-life QALYS (EQ-5D) (baseline to 3 months) Direct Costs Patients followed over one-year. Resource use: based on patient level mix of activity based costing and step down methods. Discharge to 3 months cost diary Productivity Costs Average wage rate for age-specific groups	Results Accelerated intervention was both more effective and less costly than the comparator Average total cost for I DKK90,227 (+/- 47,475) Average total cost for C DKK71,344 (+/- 39,958) Average QALYs was 0.83 for the intervention and 0.78 in the comparator. Average QALY gain for hip patients I v C = 0.08 (CI: 0.02 to 0.05) (p=0.006) Average QALY gain for knee patients was NS Uncertainty Bootstrapping, uni and multivariate

Study Details	Study Comparators	Main Analytical Approaches, primary outcomes, and costs	Incremental cost-effectiveness (ICER) estimates and Decision Uncertainty
Sammour *et al* (2010)[50] New Zealand Hospital setting Study Population Elective colonic resection patients >15 years old Time horizon Unclear	Intervention Emphasised structured nursing care pathways within an environment focusing on early recovery and various perioperative strategies to improve patient functional recovery (n=50) Comparator Conventional non-structured perioperative care (n=50)	Economic evaluation based on a single study Perspective Healthcare provider Primary outcomes Length of stay; Complications; Readmissions Direct Costs Total cost of protocol development, inpatient stay, outpatient appointments, treatment costs, readmission and complication costs were all considered. Data on patient resource use was collected from their records. Readmission costs and complication costs were based on hospital records/costs Productivity costs n/a	Results The costs and benefits were not synthesised The implementation of the intervention protocol cost approx. NZ$102,000 for the first 50 patients (set-up costs included) Cost per patient with NZ$16,052.35 Cost per patients without NZ$22,929.74 Cost-saving NZ$6,900 per patient Post-op LOS ERAS: 4 (3 to 34); C: 6.5 (3 to 18) (p<0.001) Total LOS ERAS: 4(3 to 34); C: 8(4 to 29) (p<0.001) Readmissions NS Complications – overall 54% in ERAS ≥1 compared with 66% comp Uncertainty n/a
King *et al*(2006)[51] UK Hospital setting Study Population Surgery for colorectal cancer Time horizon 2 years	Intervention Preoperative counselling, epidural analgesia, early feeding and mobilisation, predetermined discharge aim (n=60) Comparator Conventional care (fully reported) included no epidural, no formal mobilisation plan, no predetermined discharge (n=86)	Economic evaluation based on a single study Perspective UK NHS stated by author, although inclusion of productivity costs suggests wider societal perspective Primary outcomes Post-op length of stay; Complications; Readmissions Health-related quality-of-life EORTC QLQ-C30 Direct Costs Resource use data was reported to be individual patient level, but not reported. Direct costs included: theatre (including pre and recovery), hospital (including ICU), postoperative (including re-operation), chemotherapy and radiotherapy, follow –up at 3 months Productivity costs Average earnings based on employment status at commencement of trial	Results The costs and benefits were not synthesised Total costs of care for patients receiving the intervention: £7327.47; for those receiving comparator: £7998.18 Post-op LOS significantly reduced, intervention cohort staying 49% as long as comparator (95% CI: 39% to 61%; p<0.001) No-sig difference in quality-of-life, readmissions, re-operations or complications Uncertainty n/a
Neilson *et al*(2008)[52] Denmark	Intervention Integrated programme including: information and education, optimal	Economic evaluation based on a single study Perspective	Results The costs and benefits were not synthesised

Study Details	Study Comparators	Main Analytical Approaches, primary outcomes, and costs	Incremental cost-effectiveness (ICER) estimates and Decision Uncertainty
Hospital setting Study Population Lumbar fusion patients with degenerative lumbar disease Time horizon 6 months	operation technique, better pain reduction, early nutrition and aggressive post-op mobilisation (n=28) Comparator Standard care, not including components above (n=32)	Societal Primary outcome Measured using 15D-score (self-reported at inclusion, day of surgery, day of discharge, and 1, 3 and 6 months post-op Direct Costs Three categories of cost considered: staff resources, equipment and purely bed costs. Bed costs included salary of nurses/porters, food, clothes, laundry and cleaning. Post-discharge for 3 months GP visits, physiotherapy appointments and emergency room contact was registered and included. Productivity costs Based on return to work rates & Danish average daily wage	Intervention direct cost 1,174 Euros per patient compared with 1,668 for standard care Intervention productivity costs were 8,021 Euros compared with 9,152 for standard care NS difference in HR quality of life scores Uncertainty Optimistic and pessimistic scenarios varying individually pre-op costs, post-op hospital costs, direct costs, and productivity costs
Reilly *et al*(2005)[48] UK Hospital setting Study Population Patients undergoing unicompartmental knee arthroplasty Time horizon Unclear	Intervention Accelerated discharge: aim to discharge day after surgery (n=20) Comparator Standard discharge: approx. 5 days post-surgery (n=21)	Economic evaluation based on a single study Perspective Hospital Primary outcome Oxford Knee Assessment Direct Costs Fixed costs (surgical staff, anaesthetics, prosthesis, pharmacy), outpatient appointment, specialist registrar time. Productivity costs n/a	Results The costs and benefits were not synthesised Intervention resulted in a 6 month OKA score of 43.7 (SD 3.7) compared with 42.2 (SD 7.1) for standard care (NS) Total costs for intervention per patient £3,391 compared with £4,634 for standard care Uncertainty n/a
Archibald[49] USA Hospital setting Study Population Colorectal surgery patients Time horizon unclear	Intervention The availability of patient education, fluid managements, opioid-sparing strategies, tube and drain protocols, ambulation, feeding protocol, and discharge criteria. All based on surgeons choice. (n=1358, 588 enrolled in ERAS & 770 not enrolled) Comparator Standard care historical baseline (n=1673)	Economic evaluation based on a study comparing two time periods, where ERAS was available in one and not in the other. Primary outcome Length of stay ; POD; Readmission Direct Costs Hospital costs (total direct and indirect costs identified via hospital billing system) Productivity costs n/a	Results The costs and benefits were not synthesised Mean LOS for the intervention was 8.4 days compared with 6.9 days for the comparator (p<0.0001); Mean POD for the intervention was 7.6 days compared with 6.3 days (p<0.0001) Mean hospital cost for the intervention population was US$18,741 compared with US$16,978 for the comparator. Uncertainty n/a

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3-4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Full report – in press. Protocol attached to manuscript submission
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6

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Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	N/A
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency ($e.g., I^2$) for each meta-analysis.	N/A

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	20
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	21-22
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	23-25
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	NA
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	NA
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	10-13
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	11-13
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13-14
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1-2

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