



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

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4 **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

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3 managers and clinicians considering implementing enhanced recovery programmes can  
4 realise savings will depend on length of stay achieved under their existing care pathway.  
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9 Word Count: 290  
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### 11 **Strengths and limitations of the study**

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- 14 • Enhanced recovery programmes have been adopted with enthusiasm by the NHS as  
15 a means to achieving productivity gains and cost-savings. This evolution makes  
16 combining studies over different periods and interpreting results of earlier studies in  
17 relation to the current context more difficult.  
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- 20 • The evidence base to support such widespread implementation suggests possible  
21 benefits in terms of reduced length of hospital stay, fewer postoperative  
22 complications, reduced readmissions and improved patient outcomes.  
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- 25 • Although there is a reasonable volume of evidence evaluating enhanced recovery  
26 programmes in colorectal surgery, robust evidence is sparse. Optimal care is  
27 certainly the right thing to do, but the evidence does not identify which enhanced  
28 recovery programme elements and combinations of elements are most effective.  
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- 31 • Findings relating to other outcomes, costs of enhanced recovery programmes,  
32 experience in using the programmes, and patient experience were limited by  
33 generally poor quality evidence and poor reporting. As such, conclusions on which  
34 combinations provide greatest gains and how best to implement them cannot be  
35 made.  
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## 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.<sup>(1, 2)</sup> 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<sup>(3)</sup> and is now spreading<sup>(3)</sup> 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<sup>(4-20)</sup> and 12 additional RCTs<sup>(21-33)</sup> 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.<sup>(34)</sup> 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)<sup>(18)</sup> to 3.75 days (95% CI 5.11 to 2.40 days).<sup>(Walter 2009)</sup> Evidence from individual RCTs in colorectal surgery also suggest reduced length of hospital 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.

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3 Deaths were rare and no significant differences between treatment groups were found in the  
4 systematic reviews and additional RCTs, regardless of surgical speciality. Morbidity was  
5 defined differently across systematic reviews and RCTs; rates between treatment groups  
6 were sometimes inconsistent, but generally indicated no statistically significant differences.  
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10 Mobilisation rates were inconsistent across systematic reviews, but most reported no  
11 significant differences in time to mobilisation between treatment groups. Mobilisation was  
12 rarely reported as an outcome in the additional RCTs.  
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16 Where systematic reviews and additional RCTs assessed quality of life and patient  
17 experience/satisfaction, equivocal findings were reported. Evidence on reintervention rates,  
18 pain and resource use was lacking in both systematic reviews and RCTs.  
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### 21 22 **Other Reviews**

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24 A systematic review in colorectal surgery, identified after the last literature search, showed  
25 similar findings to the systematic reviews discussed above.<sup>(35)</sup> Mean length of primary  
26 hospital stay was statistically significantly reduced in ERAS patients; mean difference (MD) -  
27 2.44 (95% CI -3.06 to -1.83; 11 RCTs) but with significant statistical heterogeneity ( $I^2=88%$ ).  
28 There was no evidence to suggest increased rates of readmissions, complications and  
29 mortality. Some of the individual RCT results for primary length of stay did not appear to be  
30 consistent with results reported in other systematic reviews, and this may have impacted on  
31 the estimated reduction in length of primary hospital stay.<sup>(35)</sup>  
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35 Two reviews<sup>(36, 37)</sup> focusing on individual ERAS elements were found and details can be  
36 found in the full review (in press).  
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### 39 40 **Case studies**

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42 Ten of 14 UK NHS innovation sites provided adequate data for inclusion in this section.<sup>(38-40)</sup>  
43 Fifteen case studies of implementation of ERAS in NHS settings, and 11 NHS trusts (mostly  
44 in colorectal surgery) provided evidence relating to the implementation of an ERAS  
45 programme within their Trust.  
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49 There were variations in practice in terms of numbers and combinations of ERAS elements  
50 implemented; the most frequently implemented programme elements in the case studies  
51 were pre-admission information/counselling and early postoperative mobilisation. Available  
52 evidence did not address which enhanced recovery elements and combinations of elements  
53 were most effective. Substantial variation in what constitutes an enhanced recovery  
54 programme within and between different surgical specialities, and difficulties in implementing  
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3 certain ERAS components, suggest that the enhanced recovery pathway may be used as a  
4 framework and adapted to suit local situations. Evidence on compliance/adherence to  
5 enhanced recovery programmes was lacking.  
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9 Case studies identified the factors believed to act as barriers or facilitators to implementing  
10 an ERAS programme. Barriers to implementation included resistance to change from  
11 patients and staff, lack of funding or support from management,<sup>(38, 41-43)</sup> staff turnover,  
12 problems arising from poor documentation, the time required to complete documentation,  
13 and other practical issues.  
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18 Facilitators included the presence of a dedicated ERAS project lead/nurse to coordinate and  
19 sustain multidisciplinary working and continuity of the pathway, a multidisciplinary team  
20 approach, and continual education for staff and patients/patient representatives. One  
21 innovation site mentioned that it did not offer a seven day service for enhanced recovery due  
22 to staff resources. Patients operated on towards the end of the week may have to wait until  
23 after the weekend to be discharged if they need to be seen by any health care professionals  
24 or social services. The need to sustain multidisciplinary working means that, in the absence  
25 of 24/7 working for elective procedures, enhanced recovery programmes will tend to be front  
26 loaded into the start of the working week (typically Monday to Thursday). Recent evidence  
27 suggests a higher risk of death for patients who have elective surgical procedures carried out  
28 later in the working week and at the weekend,<sup>(44)</sup> the capacity to implement ERAS throughout  
29 the working week might ensure continuity of best care and help mitigate against such  
30 variation.  
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39 We included two published studies of patient experience of ERAS.<sup>(45, 46)</sup> Each study used  
40 qualitative research methods to analyse audiotaped material. The two studies provided  
41 limited evidence suggesting that patients who were willing to provide feedback took a  
42 positive view of their experience of treatment in an ERAS programme. The studies  
43 suggested that patients were willing to comment on their experience in a way that can help  
44 healthcare providers to identify areas for improvement.  
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### 50 **Cost-effectiveness**

51 Ten economic evaluations in adult populations undergoing various surgical procedures  
52 evaluated costs and outcomes over short time horizons (see Table 5).<sup>(47-56)</sup> All of the  
53 evaluations suggested that programmes that achieve a reduction in length of stay are cost  
54 saving, and are not to the detriment of patients in terms of complication rates, readmission  
55 and health-related quality-of-life. The quality of the clinical studies on which these  
56 evaluations were based was variable, but generally poor. The generalisability of the results of  
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3 these evaluations was limited by a lack of transparency in reporting, and the disparity in  
4 standard protocols and what had been evaluated across the settings made it unfeasible to  
5 select a cost-effective programme.  
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## 8 ***Discussion***

### 9 **Statement of Principal Findings**

10 Overall, the systematic reviews and additional RCTs suggest that length of hospital stay is  
11 reduced in ERAS patients compared to patients receiving conventional care. The evidence  
12 was based mainly on colorectal surgery and the applicability of findings to other surgical  
13 specialities remains less clear. Evidence for colorectal surgery suggests that enhanced  
14 recovery programmes may reduce hospital stays by 0.5 to 3.5 days compared with  
15 conventional care.  
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22 There were marked differences in length of stay across reviews and individual studies  
23 regardless of speciality. These differences may reflect differences in ERAS protocols and  
24 health care systems and/or outcome definitions. This raises questions regarding the  
25 magnitude of effect of the ERAS protocols on length of stay, which may be overstated in  
26 some reviews.  
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31 The evidence suggests that ERAS programmes do not compromise patient morbidity,  
32 mortality and readmission rates but outcome definitions varied across reviews and individual  
33 studies. Such differences make it difficult to determine the reliability and generalisability of  
34 the findings.  
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39 Equivocal findings were reported for quality of life and patient experience/satisfaction but the  
40 evidence was based on few studies, which utilised various methods to measure these  
41 outcomes. The limited evidence precludes conclusions on the effects of ERAS protocols on  
42 pain, mobilisation and reintervention.  
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47 The implementation evidence included resource use in terms of the professionals involved in  
48 delivery of enhanced recovery programmes, but details were very limited and did not add to  
49 the evidence synthesis. Most case studies were uncontrolled and represent experiences of a  
50 sample of centres that chose to report their data; their outcomes may not be representative  
51 of those achieved elsewhere in the UK NHS. Their main value as evidence is the light they  
52 shed on NHS clinicians' perceptions of requirements for successful implementation and  
53 barriers to implementation of ERAS.  
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3 The impact of surgical experience and surgical volume on clinical outcomes was not  
4 explored and any implications of differences in these areas remain unknown. As enhanced  
5 recovery invariably targets the fitter, more mobile patient, frailer patients may not receive  
6 parity of access to what may be considered optimal treatment and management. Managers  
7 and clinicians considering implementing such programmes should think about the likely  
8 implication on equity of access. Whether inequity is an unintended outcome of enhanced  
9 recovery, merits further investigation.  
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15 Our review of the cost effectiveness literature suggests that enhanced recovery programmes  
16 that achieve a reduction in length of stay may save costs without detrimental effects on  
17 complication rates, readmission and health-related quality of life. However, generalisability of  
18 the results of the economic evaluations is limited by a lack of transparency in reporting, use  
19 of different settings and populations and variable methodology in analyses. Data were  
20 lacking for resource use associated with the programmes evaluated and could not usefully  
21 inform the review of economic evaluations. In addition, the clinical effectiveness of some of  
22 the programmes considered in economic evaluations was not based on robust evidence.  
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### 28 **Strengths and weaknesses**

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31 The main strength of this study was our use of multiple approaches to acquire and  
32 synthesise evidence. The main limitations were poor methodological quality and poor  
33 reporting of the included studies, and the inherent difficulty of reviewing a complex  
34 intervention in different healthcare systems and surgical specialities. Current methods for  
35 synthesising such complex interventions are limited. The methodological limitations and are  
36 not discussed here as this was outside the scope of this project, but have been addressed in  
37 previous publications (eg. Noyes et al, 2013).<sup>(57)</sup> Another complication is that elements of  
38 early enhanced recovery programmes have become accepted practice within conventional  
39 care. This evolution makes combining studies over different periods and interpreting results  
40 of earlier studies in relation to the current context more difficult.  
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49 We found a large number of systematic reviews but there was substantial overlap in the  
50 included studies and evidence was not as abundant as the existence of multiple systematic  
51 reviews suggested. Most of the RCTs were small and not high quality. With the exception of  
52 one RCT, the remainder were single centre trials and therefore appear to have been  
53 undertaken to support implementation of an enhanced recovery programme in a specific  
54 setting rather than being planned as research studies. There were significant clinical and  
55 methodological differences between individual trials, and we therefore presented a narrative  
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3 synthesis. Relatively few trials were conducted in the UK and this may limit the  
4 generalisability of evidence to UK NHS settings.  
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8 Lack of evidence on important outcomes including pain and quality of life is also an issue for  
9 research in this field. Trials tended not to report on adherence to the planned enhanced  
10 recovery programme. Assessing adherence to interventions and the impact this has on  
11 health outcomes is an important issue which is often overlooked in studies, and is a limitation  
12 in the evidence base in this review.  
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16 An important feature of our review is the inclusion of evidence on the implementation of  
17 enhanced recovery programmes in the UK NHS. This evidence has not been synthesised  
18 previously and the original programme websites are archived, so future access is not  
19 assured. By summarising this evidence, we have ensured that the main findings continue to  
20 be publicly available. We sought evidence on the experience of health professionals and  
21 patients of a broad range of sources and study types. Important themes emerged from this  
22 evidence that may be of value for implementing and sustaining enhanced recovery  
23 programmes in UK NHS settings. Due to the rapid nature of the evidence synthesis, the list  
24 of sources searched to identify data on implementation and delivery of enhanced recovery  
25 programmes was not exhaustive and we acknowledge that relevant evidence may have been  
26 missed. Indeed, evidence from Scotland has been noted and eligible case studies have been  
27 identified from the NHS Scotland Quality Improvement Hub website. It should be noted that  
28 these are as limited as those included in the review.  
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38 However, case studies are susceptible to risk of bias. Use of a standard reporting format was  
39 a potential strength of the case studies but variation in what each site actually reported  
40 (particularly in terms of evidence of benefit from the introduction of enhanced recovery  
41 programmes) reduced the usefulness of the evidence.  
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46 We sought to incorporate published and unpublished evidence on patient experiences and  
47 views of enhanced recovery programmes. Evaluation of patient experience of care is  
48 increasingly important for the NHS, especially in view of unacceptable failures of care such  
49 as those highlighted in the Francis Report.<sup>(58)</sup> Though the evidence was generally positive for  
50 enhanced recovery, it was limited by a shortage of studies that used validated measures of  
51 patient experience and by study designs that could bias results in favour of enhanced  
52 recovery.  
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58 A further strength of this study was the consideration of cost-effectiveness evidence, but the  
59 nature of the evidence did not permit any analyses. There is a clear need to capture better  
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3 evaluated data on costs and benefits of enhanced recovery programmes from a clearly  
4 stated perspective.  
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### 7 **Implications for healthcare**

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10 Overall, there is consistent, albeit limited, evidence that enhanced recovery programmes can  
11 reduce length of patient hospital stay without increasing readmission rates. Data on re-  
12 intervention rates and patient-reported outcomes did not suggest significant differences  
13 between enhanced recovery and conventional care, but the evidence was very limited and  
14 based on small numbers of patients. The lack of evidence on patient outcomes, resource use  
15 and costs precludes firm conclusions on the overall value of enhanced recovery  
16 programmes.  
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23 ERAS does not appear to reduce complication or readmission rates; the only cost benefit  
24 may lie in a reduction in post-operative bed days. Optimal care is certainly the right thing to  
25 do, but the evidence does not identify which enhanced recovery programme elements and  
26 combinations of elements are most effective. As such, conclusions on which combinations  
27 provide greatest gains and how best to implement them cannot be made.  
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32 The extent to which managers and clinicians considering implementing enhanced recovery  
33 programmes can realise reductions and cost savings will therefore depend on length of stays  
34 achieved under their existing care pathway. Important themes emerged from the relevant  
35 evidence identified on implementation, including the role of ERAS facilitators and the need  
36 for full support from management. It appears that these components are essential for the  
37 successful implementation and sustained delivery of enhanced recovery programmes in NHS  
38 settings. Consideration of potential benefit also needs to take account of the costs of service  
39 redesign, the resource use associated with programmes of this nature, the potential for  
40 improvement in patient outcomes and the impact on equity of access.  
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### 49 **Implications for research**

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52 RCTs comparing an enhanced recovery programme with conventional care continue to be  
53 conducted and published, although mostly not in the UK. Given the available evidence,  
54 further single centre RCTs of this kind are not a priority. Rather, what is needed is improved  
55 collection and reporting of how enhanced recovery programmes are implemented, resourced  
56 and experienced in NHS settings. Also, exploration into the effect that varying levels of  
57 surgical volume and surgical experience, and different discharge protocols might have on the  
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3 success of an enhanced recovery pathway and subsequent outcomes. This will enhance our  
4 existing knowledge and understanding and provide evidence to support local decision-  
5 making about whether to adopt and how best to implement.  
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9 The two groups of implementation case studies included in our synthesis, although all were  
10 conducted in the UK, provide very limited information on how enhanced recovery  
11 programmes have actually been implemented in UK NHS settings. The standard reporting  
12 format originally proposed by The Enhanced Recovery Partnership Programme would  
13 enhance the value of future case studies if adhered to. Knowledge of how well the  
14 intervention has been implemented (fidelity) is essential for understanding how and why the  
15 intervention works and hence how outcomes can be further improved. Assessing fidelity may  
16 involve considering not only adherence to the requirements of the programme but also  
17 potential moderating factors, such as strategies used to assist delivery of the intervention,  
18 quality of delivery and participant responsiveness to new practices.<sup>(59)</sup> It would be helpful if  
19 future innovation programmes used standardised reporting. For multi-site programmes, a  
20 formal synthesis of findings from all participating sites should be undertaken as part of the  
21 evaluative process. This would ensure that the insights and contextual information which can  
22 inform the wider spread and adoption (or indeed discontinuation) would be systematically  
23 captured in a generalisable format.  
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33 Adherence/compliance to elements by staff and patients also requires further investigation.  
34 Rigorous data on patients' experiences of enhanced recovery programmes are lacking.  
35 Validated tools should be used and administered independently of those providing the  
36 service. Efforts should be made to obtain data from representative samples of patients  
37 receiving conventional care as well as those treated with enhanced recovery protocols, along  
38 with evidence on the experiences of their families/carers.  
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44 Evidence relating to the cost-effectiveness of enhanced recovery programmes in UK NHS  
45 settings is lacking. Whilst enhanced recovery programmes have the potential to deliver cost  
46 savings, improved measurement of costs and benefits is crucial to help decision-makers  
47 decide how best to make optimal use of limited resources.  
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14 manuscript is an honest, accurate, and transparent account of the study being reported; that  
15 no important aspects of the study have been omitted; and that any discrepancies from the  
16 study as planned (and, if relevant, registered) have been explained.  
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## References

1. Øvretveit J. Does Improving Quality Save Money? A Review of Evidence of Which Improvements to Quality Reduce Costs for Health Service Providers. London: The Health Foundation; 2009
2. Øvretveit J. Does Improving Care Coordination Save Money: A Review Of Research. London: The Health Foundation; 2011.
3. Kehlet H, Slim K. The future of fast-track surgery. *Br J Surg*. 2012 Aug;99(8):1025-6.
4. Sturm L, Cameron AL. Brief review: Fast-track surgery and enhanced recovery after surgery (ERAS) programs. Melbourne: Australian Safety and Efficacy Register of New Interventional Procedures - Surgical (ASERNIP-S); 2009.
5. Adamina M, Kehlet H, Tomlinson GA, Senagore AJ, Delaney CP. Enhanced recovery pathways optimize health outcomes and resource utilization: a meta-analysis of randomized controlled trials in colorectal surgery. *Surgery*. 2011;149(6):830-40.
6. Ahmed J, Khan S, Lim M, Chandrasekaran TV, MacFie J. Enhanced recovery after surgery protocols - compliance and variations in practice during routine colorectal surgery. *Colorectal Dis*. 2012;14(9):1045-51.
7. Coolsen MME, Wong-Lun-Hing EM, van Dam RM, van der Wilt AA, Slim K, Lassen K, et al. A systematic review of outcomes in patients undergoing liver surgery in an enhanced recovery after surgery pathways. *HPB surgery : a world journal of hepatic, pancreatic and biliary surgery*. 2012;Early view online.
8. Coolsen MME, van Dam RM, van der Wilt AA, Slim K, Lassen K, Dejong CHC. Systematic review and meta-analysis of enhanced recovery after pancreatic surgery with particular emphasis on pancreaticoduodenectomies. *World J Surg*. 2013;Published online 09 April 2013.
9. Eskicioglu C, Forbes SS, Aarts M-A, Okrainec A, McLeod RS. Enhanced Recovery after Surgery (ERAS) programs for patients having colorectal surgery: a meta-analysis of randomized trials. *J Gastrointest Surg*. 2009 Dec;13(12):2321-9.
10. Gouvas N, Tan E, Windsor A, Xynos E, Tekkis PP. Fast-track vs standard care in colorectal surgery: a meta-analysis update. *Int J Colorectal Dis*. [Comparative Study Meta-Analysis]. 2009 Oct;24(10):1119-31.
11. Hall TC, Dennison AR, Bilku DK, Metcalfe MS, Garcea G. Enhanced recovery programmes in hepatobiliary and pancreatic surgery: a systematic review. *Ann R Coll Surg Engl*. 2012;94:318-26.
12. Khan S, Wilson T, Ahmed J, Owais A, MacFie J. Quality of life and patient satisfaction with enhanced recovery protocols. *Colorectal Dis*. 2010;12(12):1175-82.
13. Lemmens L, van Zelm R, Borel Rinkes I, van Hillegersberg R, Kerckamp H. Clinical and organizational content of clinical pathways for digestive surgery: a systematic review. *Dig Surg*. 2009;26(2):91-9.
14. Rawlinson A, Kang P, Evans J, Khanna A. A systematic review of enhanced recovery protocols in colorectal surgery. *Ann R Coll Surg Engl*. [Review]. 2011;93(8):583-8.

15. Spanjersberg Willem R, Reurings J, Keus F, van Laarhoven Cornelis JHM. Fast track surgery versus conventional recovery strategies for colorectal surgery. *Cochrane Database of Systematic Reviews*. 2011(2).
16. Varadhan KK, Neal KR, Dejong CH, Fearon KC, Ljungqvist O, Lobo DN. The enhanced recovery after surgery (ERAS) pathway for patients undergoing major elective open colorectal surgery: a meta-analysis of randomized controlled trials. *Clin Nutr*. 2010;29(4):434-40.
17. Walter CJ, Collin J, Dumville JC, Drew PJ, Monson JR. Enhanced recovery in colorectal resections: a systematic review and meta-analysis. *Colorectal Dis*. [Meta-Analysis Research Support, Non-U.S. Gov't Review]. 2009 May;11(4):344-53.
18. Wind J, Polle SW, Fung Kon Jin PH, Dejong CH, von Meyenfeldt MF, Ubbink DT, et al. Systematic review of enhanced recovery programmes in colonic surgery. *Br J Surg*. [Review]. 2006 Jul;93(7):800-9.
19. Lv D, Wang X, Shi G. Perioperative enhanced recovery programmes for gynaecological cancer patients. *Cochrane Database of Systematic Reviews*. 2012(12).
20. Lv L, Shao Y-f, Zhou Y-b. The enhanced recovery after surgery (ERAS) pathway for patients undergoing colorectal surgery: an update of meta-analysis of randomized controlled trials. *Int J Colorectal Dis*. 2012;27:1549-54.
21. Chen Hu J, Xin Jiang L, Cai L, Tao Zheng H, Yuan Hu S, Bing Chen H, et al. Preliminary experience of fast-track surgery combined with laparoscopy-assisted radical distal gastrectomy for gastric cancer. *J Gastrointest Surg*. 2012 Oct;16(10):1830-9.
22. Kim JW, Kim WS, Cheong JH, Hyung WJ, Choi SH, Noh SH. Safety and efficacy of fast-track surgery in laparoscopic distal gastrectomy for gastric cancer: a randomized clinical trial. *World J Surg*. 2012 Dec;36(12):2879-87.
23. Garcia-Botello S, Canovas de Lucas R, Tornero C, Escamilla B, Espi-Macias A, Esclapez-Valero P, et al. Implementation of a perioperative multimodal rehabilitation protocol in elective colorectal surgery. A prospective randomised controlled study. *Cir Esp*. [Randomized Controlled Trial Research Support, Non-U.S. Gov't]. 2011 Mar;89(3):159-66.
24. Ionescu D, Iancu C, Ion D, Al-Hajjar N, Margarit S, Mocan L, et al. Implementing fast-track protocol for colorectal surgery: a prospective randomized clinical trial. *World J Surg*. [Comparative Study Randomized Controlled Trial]. 2009 Nov;33(11):2433-8.
25. Lee TG, Kang SB, Kim DW, Hong S, Heo SC, Park KJ. Comparison of early mobilization and diet rehabilitation program with conventional care after laparoscopic colon surgery: a prospective randomized controlled trial. *Dis Colon Rectum*. [Comparative Study Randomized Controlled Trial]. 2011 Jan;54(1):21-8.
26. Lemanu DP, Singh PP, Berridge K, Burr M, Birch C, Babor R, et al. Randomized clinical trial of enhanced recovery versus standard care after laparoscopic sleeve gastrectomy. *Br J Surg*. 2013 Mar;100(4):482-9.
27. Liu XX, Jiang ZW, Wang ZM, Li JS. Multimodal optimization of surgical care shows beneficial outcome in gastrectomy surgery. *JPEN J Parenter Enteral Nutr*. [Randomized Controlled Trial Research Support, Non-U.S. Gov't]. 2010 May-Jun;34(3):313-21.
28. Ren L, Zhu D, Wei Y, Pan X, Liang L, Xu J, et al. Enhanced Recovery After Surgery (ERAS) program attenuates stress and accelerates recovery in patients after radical resection for colorectal cancer: a prospective randomized controlled trial. *World J Surg*. [Comparative Study Randomized Controlled Trial Research Support, Non-U.S. Gov't]. 2012 Feb;36(2):407-14.

- 1  
2  
3 29. Wang D, Kong Y, Zhong B, Zhou X, Zhou Y. Fast-track surgery improves postoperative  
4 recovery in patients with gastric cancer: a randomized comparison with conventional postoperative  
5 care. *J Gastrointest Surg*. [Comparative Study; Randomized Controlled Trial]. 2010;14(4):620-7.  
6
- 7 30. Wang G, Jiang ZW, Xu J, Gong JF, Bao Y, Xie LF, et al. Fast-track rehabilitation program vs  
8 conventional care after colorectal resection: a randomized clinical trial. *World J Gastroenterol*.  
9 [Randomized Controlled Trial Research Support, Non-U.S. Gov't]. 2011 Feb 7;17(5):671-6.  
10
- 11 31. Wang Q, Suo J, Jiang J, Wang C, Zhao YQ, Cao X. Effectiveness of fast-track rehabilitation  
12 vs conventional care in laparoscopic colorectal resection for elderly patients: a randomized trial.  
13 *Colorectal Dis*. 2012 Aug;14(8):1009-13.  
14
- 15 32. Yang DJ, Zhang S, He WL, Chen HY, Cai SR, Chen CQ, et al. Fast track surgery accelerates  
16 the recovery of postoperative insulin sensitivity. *Chin Med J*. 2012 Sep;125(18):3261-5.  
17
- 18 33. Yang DJ, Zhang S, He WL, Huang WQ, Cai SR, Chen CQ, et al. Fast-track surgery  
19 accelerates the recovery of postoperative humoral immune function in elective operation for colorectal  
20 carcinoma: a randomized controlled clinical trial. *Chin Med J*. 2012 Apr 24;92(16):1112-5.  
21
- 22 34. Vlug MS, Wind J, Hollmann MW, Ubbink DT, Cense HA, Engel AF, et al. Laparoscopy in  
23 combination with fast track multimodal management is the best perioperative strategy in patients  
24 undergoing colonic surgery: a randomized clinical trial (LAFA-study). *Ann Surg*. [Comparative Study  
25 Multicenter Study Randomized Controlled Trial Research Support, Non-U.S. Gov't]. 2011  
26 Dec;254(6):868-75.  
27
- 28 35. Cheng-Le Z, Xing-Zhao Y, Xiao-Dong Z, Bi-Cheng C, Zhen Y. Enhanced recovery after  
29 surgery programs versus traditional care for colorectal surgery: A meta-analysis of randomized  
30 controlled trials. *Dis Colon Rectum*. 2013;56:667-78.  
31
- 32 36. Arsalani-Zadeh R, Elfadl D, Yassin N, MacFie J. Evidence-based review of enhancing  
33 postoperative recovery after breast surgery. *Br J Surg*. 2011 Feb;98(2):181-96.  
34
- 35 37. Hoffmann H, Kettelhack C. Fast-track surgery - conditions and challenges in postsurgical  
36 treatment: a review of elements of translational research in enhanced recovery after surgery. *Eur Surg*  
37 *Res*. 2012;49(1):24-34.  
38
- 39 38. Enhanced Recovery Partnership Programme Case Studies 2011: Gynaecology: Addenbrookes  
40 Hospital, Contract No.: Document Number].  
41
- 42 39. Enhanced Recovery Partnership Programme Case Studies 2011: Enhanced Recovery  
43 Programme: Yeovil District Hospital NHS Foundation Trust, Contract No.: Document Number].  
44
- 45 40. Enhanced Recovery Partnership Programme Case Studies 2011: Enhanced recovery for  
46 colorectal surgery: Yeovil District Hospital NHS Foundation Trust, Contract No.: Document  
47 Number].  
48
- 49 41. Enhanced Recovery Partnership Programme Case Studies 2011: Colorectal, Gynaecology,  
50 Urology, MSK: Medway NHS Foundation Trust, Contract No.: Document Number].  
51
- 52 42. Enhanced Recovery Partnership Programme Case Studies 2011: Colorectal surgery (all  
53 elective procedures) and most major emergencies from decision to treat surgically; Urology: radical  
54 Prostatectomy, Cystectomy, Nephrectomy; MSK: 1 Hip and knee replacement; Gynaecology:  
55 Hysterectomy (vaginal, abdominal and laparoscopic) moving to all majors: Royal Berkshire Hospital,  
56 Contract No.: Document Number].  
57
- 58 43. Enhanced Recovery Partnership Programme Case Studies 2011: Enhanced recovery after  
59 colorectal surgery: Royal Berkshire Hospital, Contract No.: Document Number].  
60

- 1  
2  
3 44. Aylin P, Alexandrescu R, Jen MH, Mayer EK, Bottle A. Day of week of procedure and 30 day  
4 mortality for elective surgery: retrospective analysis of hospital episode statistics. *BMJ*. [Article].  
5 2013 May;346:8.  
6  
7 45. Blazeby JM, Soulsby M, Winstone K, King PM, Bulley S, Kennedy RH. A qualitative  
8 evaluation of patients' experiences of an enhanced recovery programme for colorectal cancer.  
9 *Colorectal Dis*. 2010 Oct;12(10 Online):e236-42.  
10  
11 46. Taylor C, Burch J. Feedback on an enhanced recovery programme for colorectal surgery. *Br J*  
12 *Nurs*. 2011 Mar;20(5):286-90.  
13  
14 47. Reilly KA, Beard DJ, Barker KL, Dodd CA, Price AJ, Murray DW. Efficacy of an accelerated  
15 recovery protocol for Oxford unicompartmental knee arthroplasty: a randomised controlled trial.  
16 *Knee*. 2005;12(5):351-7.  
17  
18 48. Archibald LH, Ott MJ, Gale CM, Zhang J, Peters MS, Stroud GK. Enhanced recovery after  
19 colon surgery in a community hospital system. *Dis Colon Rectum*. 2011;54(7):840-5.  
20  
21 49. Sammour T, Zargar-Shoshtari K, Bhat A, Kahokehr A, Hill AG. A programme of Enhanced  
22 Recovery After Surgery (ERAS) is a cost-effective intervention in elective colonic surgery. *N Z Med*  
23 *J*. 2010;123(1319).  
24  
25 50. King PM, Blazeby JM, Ewings P, Longman RJ, Kipling RM, Franks PJ, et al. The influence  
26 of an enhanced recovery programme on clinical outcomes, costs and quality of life after surgery for  
27 colorectal cancer. *Colorectal Dis*. 2006;8(6):506-13.  
28  
29 51. Nielsen PR, Andreasen J, Asmussen M, Tønnesen H. Costs and quality of life for  
30 prehabilitation and early rehabilitation after surgery of the lumbar spine. *Journal [serial on the*  
31 *Internet]*. 2008 Date [cited Get economics? Reject]; 8: Available from:  
32 <http://www.biomedcentral.com/1472-6963/8/209>.  
33  
34 52. Jakobsen DH, Sonne E, Andreasen J, Kehlet H. Convalescence after colonic surgery with fast-  
35 track vs conventional care. *Colorectal Dis*. [Comparative Study]. 2006 Oct;8(8):683-7.  
36  
37 53. McBride N, Farrington F, Midford R. Implementing a school drug education programme:  
38 reflections on fidelity. *International Journal of Health Promotion and Education*. 2002;40(2):40-50.  
39  
40 54. Kariv Y, Delaney CP, Senagore AJ, Manilich EA, Hammel JP, Church JM, et al. Clinical  
41 outcomes and cost analysis of a fast track postoperative care pathway for ileal pouch-anal  
42 anastomosis. A case control study. *Dis Colon Rectum*. 2007;50(2):137-46.  
43  
44 55. Salhiyyah K, Elsobky S, Raja S, Attia R, Brazier J, Cooper GJ. A clinical and economic  
45 evaluation of fast-track recovery after cardiac surgery. *Heart Surgery Forum*. 2011;14(6):E330-4.  
46  
47 56. Yanatori M, Tomita S, Miura Y, Ueno Y. Feasibility of the fast-track recovery program after  
48 cardiac surgery in Japan. *General Thoracic and Cardiovascular Surgery*. 2007;55(11):445-9.  
49  
50 57. Noyes J, Gough D, Lewin S, Mayhew A, Michie S, Pantoja T, et al. A research and  
51 development agenda for systematic reviews that ask complex questions about complex interventions. *J*  
52 *Clin Epidemiol*. 2013 Nov;66(11):1262-70.  
53  
54 58. Report of the Mid Staffordshire NHS Foundation Trust Public Inquiry (Chaired by Robert  
55 Francis QC). London: The Stationery Office; 2013 Contract No.: Document Number].  
56  
57 59. Carroll C, Patterson M, Wood S, Booth A, Rick J, Balain S. A conceptual framework for  
58 implementation fidelity. *Implementation Science*. 2007;2(1):40.  
59  
60

1  
2  
3 60. Coolsen MME, van Dam RM, van der Wilt AA, Slim K, Lassen K, Dejong CHC. Systematic  
4 review and meta-analysis of enhanced recovery after pancreatic surgery with particular emphasis on  
5 pancreaticoduodenectomies: Supplementary Material. World J Surg. 2013;Published online 09 April  
6 2013.  
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Figure 1: Study flow diagram

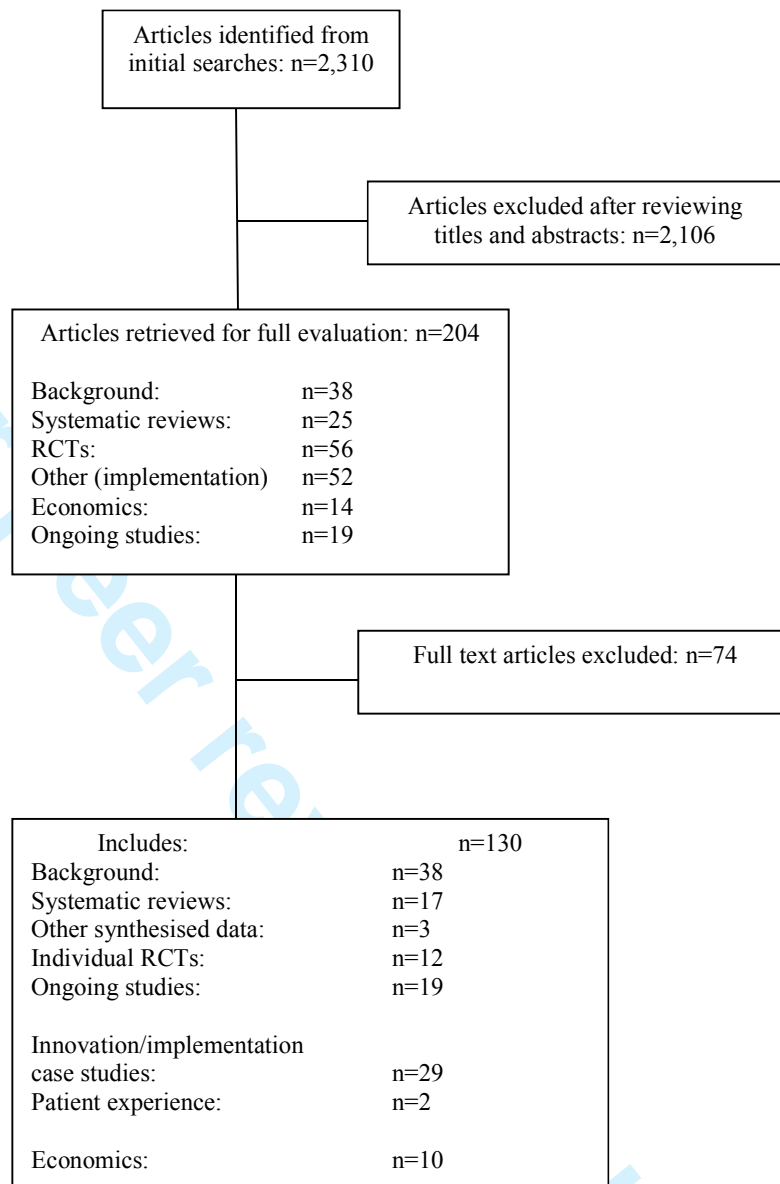


Table 1: Systematic review risk of bias assessment

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
<b>Colorectal/Colon surgery</b>							
Adamina (2011) <sup>(5)</sup>	✓	✓	UC	✓	UC	✓	✓
Ahmed (2012) <sup>(6)</sup>	✓	X	X	X	X	X	✓
Eskicioglu (2009) <sup>(9)</sup>	✓	✓	X	✓	✓	✓	✓
Gouvas (2009) <sup>(10)</sup>	✓	✓	X	✓	✓	✓	✓
Khan (2010) <sup>(12)</sup>	✓	✓	X	✓	X	✓	✓
Lv (2012a) <sup>(20)</sup>	✓	✓	X	X	✓	✓	✓
Rawlinson (2011) <sup>(14)</sup>	✓	X	X	✓	UC	X	UC
Spanjersberg (2011) <sup>(15)</sup>	✓	✓	✓	✓	✓	✓	✓
Varadhan (2010) <sup>(16)</sup>	✓	✓	X	✓	✓	✓	✓
Walter (2009) <sup>(17)</sup>	✓	✓	✓	✓	✓	✓	✓
Wind (2006) <sup>(18)</sup>	✓	✓	✓	✓	✓	✓	✓
<b>Gynaecological surgery</b>							
Lv (2012b) <sup>(19)</sup>	✓	X	X	X	X	✓	✓
<b>Liver/pancreatic surgery</b>							
Coolsen (2012) <sup>(7)</sup>	✓	✓	X	✓	X	✓	✓
Coolsen (2013) <sup>(8)</sup> Link to <sup>(60)</sup>	✓	✓	✓	✓	✓	✓	✓
Hall (2012) <sup>(11)</sup>	X	X	X	✓	X	✓	✓
<b>Various surgical specialities</b>							
Lemmens (2009) <sup>(13)</sup>	✓	X	X	✓	X	✓	✓
Sturm (2009) <sup>(4)</sup>	✓	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
<b>Bariatric surgery</b>									
Lemanu (2013) <sup>(26)</sup>	✓	✓	X	X	X	X	NA	UC	UC
<b>Colorectal/colon surgery</b>									
Garcia-Botello (2011) <sup>(23)</sup>	UC	X	UC	X	UC	X	NA	UC	✓
Ionescu (2009) <sup>(24)</sup>	✓	✓	X	X	UC	X	NA	UC	UC
Lee (2011) <sup>(25)</sup>	✓	✓	UC	X	UC	X	NA	UC	UC
Ren (2012) <sup>(28)</sup>	✓	✓	X	X	✓	X	NA	UC	UC
Wang (2011) <sup>(30)</sup>	UC	UC	UC	X	UC	X	NA	✓	✓
Wang (2012) <sup>(31)</sup>	UC	UC	X	X	✓	UC	UC	UC	UC
Yang (2012) <sup>(32, 33)</sup>	✓	UC	X	X	UC	X	NA	X	X
<b>Gastric surgery</b>									
Chen (2012) <sup>(21)</sup>	UC	UC	X	✓	✓	X	NA	UC	UC
Kim (2012) <sup>(22)</sup>	UC	UC	X	X	X	X	NA	UC	UC
Liu (2010) <sup>(27)</sup>	UC	X	X	X	X	X	NA	UC	UC
Wang (2010) <sup>(29)</sup>	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		
<b>Adamina (2011)</b> <sup>(5)</sup> 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)
<b>Ahmed (2012)</b> <sup>(6)</sup> 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%)
<b>Eskicioglu (2009)</b> <sup>(9)</sup> 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 <sup>2</sup> = 24%)
<b>Gouvas (2009)</b> <sup>(10)</sup> 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 <sup>2</sup> =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 <sup>2</sup> = 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 <sup>2</sup> =0%, 10 studies). Subgroup analysis showed that non-RCTs had significantly lower readmission rates in the control group.
<b>Khan (2010)</b> <sup>(12)</sup> 10 studies; 4 RCTs, 6 non-randomised comparative studies	Not applicable	Not applicable
<b>Lv (2012a)</b> <sup>(20)</sup> 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 <sup>2</sup> =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 <sup>2</sup> =0%).
<b>Rawlinson (2011)</b> <sup>(14)</sup> 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.
<b>Spanjersberg (2011)</b> <sup>(15)</sup> 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 <sup>2</sup> =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 <sup>2</sup> =59%, 4 RCTs) Subgroup analyses including the 2 RCTs involving limited number of ERAS elements did not significantly alter the findings.
<b>Varadhan (2010)</b> <sup>(16)</sup> 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 <sup>2</sup> = 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 <sup>2</sup> = 9%)
<b>Walter (2009)</b> <sup>(17)</sup> 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 <sup>2</sup> =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 <sup>2</sup> =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 <sup>2</sup> =0%, 2 CCTs). (p=0.05 which the authors consider significant).

Author & no. included studies	Length of hospital stay (days)	Readmission rates (N%)
<b>Wind (2006)<sup>(18)</sup></b> <i>6 studies; 3 RCTs, 3 CCTs</i>	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.
<b>Gynaecological surgery</b>		
<b>Lv (2012b)<sup>(19)</sup></b> <i>0 studies</i>	Not applicable	Not applicable
<b>Liver/pancreatic surgery</b>		
<b>Coolsen (2012)<sup>(7)</sup></b> <i>6 studies; 3 case-control, 2 RCTs (both arms ERAS elements; equivalent to prospective case series), one retrospective case series.</i>	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%
<b>Coolsen (2013)<sup>(8)</sup> Link to <sup>(60)</sup></b> <i>8 studies; 5 case-control (historical controls receiving traditional care); 2 retrospective case series; 1 prospective case series.</i>	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)
<b>Hall (2012)<sup>(11)</sup></b> <i>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.</i>	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 to 14.6% (4 studies); liver 0 to 13 % (5 studies)
<b>Various surgical specialities</b>		
<b>Lemmens (2009)<sup>(13)</sup></b> <i>13 studies; One RCT, 3 controlled clinical trials, 2 case-control, one retrospective case series, 6 pre- post-pathway studies</i>	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
<b>Sturm (2009)<sup>(4)</sup></b> <i>11 RCTs plus one systematic review</i>	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%)
<b>Bariatric surgery</b>		
Lemanu (2013) <sup>(26)</sup>	Median days (interquartile range) Length of index admission: ERAS 1 (1 to 2); control 2 (0), 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.
<b>Colorectal/colon surgery</b>		
Ionescu (2009) <sup>(24)</sup>	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) <sup>(25)</sup>	ERAS 6.43 (3.41); control 9.16 (2.67), p=0.001	ERAS 0 (0); control 0 (0)
Ren (2012) <sup>(28)</sup>	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) <sup>(30)</sup>	Mean (SD) ERAS 5.7 (1.6); control 6.6 (2.4), p<0.001	Not reported
Wang (2012) <sup>(31)</sup>	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) <sup>(32, 33)</sup>	Median days: ERAS 5.5 (5 to 6); control 7.0 (6 to 8), p<0.001	Not reported
Ionescu (2009) <sup>(24)</sup>	Mean (SD) ERAS 6.0 (1.0); control 11.7 (3.8), p<0.05	No hospital readmissions due to complications.
<b>Gastric surgery</b>		
Chen (2012) <sup>(21)</sup>	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) <sup>(22)</sup>	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) <sup>(27)</sup>	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) <sup>(29)</sup>	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
<p><b>Salihyyah et al (2011)<sup>(55)</sup></b></p> <p>UK</p> <p>Hospital setting</p> <p><u>Study Population</u> Cardiac surgery Inpatients</p> <p><u>Time horizon</u> 6 months</p>	<p><u>Intervention</u> Fast-track transfer post-surgery to an independent theatre recovery unit 1-2-1 nursing (n=84)</p> <p><u>Comparator</u> Transfer post-surgery to hospital intensive care unit (n=52)</p>	<p>Economic evaluation based on a single study</p> <p><u>Perspective</u> Hospital</p> <p><u>Primary outcomes</u> Length of stay; Duration of intubation</p> <p><u>Direct Costs</u> Total expenditure of unit divided by number of patients</p> <p><u>Productivity Costs</u> n/a</p>	<p><u>Results</u> The costs and benefits were not synthesised</p> <p>mean cost FT: £4182 (SD:2284) mean cost C: £4553 (SD:1355) (p&lt;0.001)</p> <p>total LOS NSD</p> <p>8 patients failed FT &amp; were transferred to ICU</p> <p>5 patients (4 FT &amp; 1 C) required readmission</p> <p><u>Uncertainty</u> One-way &amp; multi-way sensitivity analysis demonstrated robustness in result that FT costs less than C</p>
<p><b>Lin et al (2011)<sup>(52)</sup></b></p> <p>China</p> <p>Hospital setting</p> <p><u>Study Population</u> Liver resection Inpatients</p> <p><u>Time horizon</u> Not reported</p>	<p><u>Intervention</u> 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 &lt;24 hours, planned discharge 6 days post-surgery (n=56)</p> <p><u>Comparator</u> Conventional pathway (limited reporting) (n=61)</p>	<p>Economic evaluation based on a single study</p> <p><u>Perspective</u> Hospital</p> <p><u>Primary outcomes</u> Length of stay; Complications; Mortality; Readmission</p> <p><u>Direct Costs</u> Hospital charges: operation and anaesthesia; pharmacy; auxiliary examination; other</p> <p><u>Productivity Costs</u> n/a</p>	<p><u>Results</u> The costs and benefits were not synthesised</p> <p>mean charge pre-pathway RMB 26,626 mean charge post-pathway RMB 21,004 (p&lt;0.05)</p> <p>LOS reduced from 11 days to 7 days (p&lt;0.005) Complications, mortality &amp; readmissions NSD</p> <p><u>Uncertainty</u> n/a</p>
<p><b>Kariv et al (2006)<sup>(54)</sup></b></p> <p>USA</p> <p>Hospital setting</p> <p><u>Study Population</u> Patients undergoing open ileoanal pouch surgery</p> <p><u>Time horizon</u></p>	<p><u>Intervention</u> 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)</p>	<p>Economic evaluation based on a single study</p> <p><u>Perspective</u> Hospital</p> <p><u>Primary outcomes</u> Length of stay; Readmission; Reoperation</p> <p><u>Direct Costs</u> Total costs for each of the categories were presented: per case of hospitalisation; operating room; radiology;</p>	<p><u>Results</u> The costs and benefits were not synthesised</p> <p>total per case cost FT US\$ 5,692 total per case cost C US\$ 6672 diff US\$980 (p=0.001)</p> <p>median postoperative los FT = 4 days C= 5 days (p=0.012) NSD in readmission outcomes</p> <p><u>Uncertainty</u></p>

Study Details	Study Comparators	Main Analytical Approaches, primary outcomes, and costs	Incremental cost-effectiveness (ICER) estimates and Decision Uncertainty
30 days	<u>Comparator</u> 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  <u>Productivity Costs</u> n/a	n/a
<b>Yanatori et al (2007)</b> <sup>(56)</sup>  Japan  Hospital setting  <u>Study Population</u> Cardiovascular surgery (cardiac arrest requiring cardiopulmonary bypass)  <u>Time horizon</u> 2 years	<u>Intervention</u> Admitted 4 days prior to surgery, preoperative education by nurses, surgeons and rehab staff; discharge at day 7 post surgery  <u>Comparator</u> Conventional protocol – details not reported	Economic evaluation based on a single study  <u>Perspective</u> Healthcare provider/hospital  <u>Primary outcomes</u> Length of stay; Complications  <u>Direct Costs</u> Only total costs were presented  <u>Productivity Costs</u> n/a	<u>Results</u> 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)  <u>Uncertainty</u> n/a
<b>Larsen et al (2009)</b> <sup>(53)</sup>  Denmark  Hospital setting  <u>Study Population</u> All patients for elective primary total hip/knee arthroplasty or unicompartmental knee arthroplasty  <u>Time horizon</u> One year	<u>Intervention</u> 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)  <u>Comparator</u> Patients receive info on day of admission; patients randomly among wards, various nurses in charge of care; and various occupational and physiotherapists 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  <u>Perspective</u> Societal  <u>Primary outcomes</u> Length of stay; Adverse events (first 3months)  <u>Health-related quality-of-life</u> QALYS (EQ-5D) (baseline to 3 months)  <u>Direct Costs</u> 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  <u>Productivity Costs</u> Average wage rate for age-specific groups	<u>Results</u> 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  <u>Uncertainty</u> Bootstrapping, uni and multivariate
<b>Sammour et al (2010)</b> <sup>(49)</sup>	<u>Intervention</u>	Economic evaluation based on a single study	<u>Results</u>

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

Study Details	Study Comparators	Main Analytical Approaches, primary outcomes, and costs	Incremental cost-effectiveness (ICER) estimates and Decision Uncertainty
<p><u>Study Population</u> Lumbar fusion patients with degenerative lumbar disease</p> <p><u>Time horizon</u> 6 months</p>	<p>post-op mobilisation (n=28)</p> <p><u>Comparator</u> Standard care, not including components above (n=32)</p>	<p><u>Primary outcome</u> Measured using 15D-score (self-reported at inclusion, day of surgery, day of discharge, and 1, 3 and 6 months post-op)</p> <p><u>Direct Costs</u> 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.</p> <p><u>Productivity costs</u> Based on return to work rates &amp; Danish average daily wage</p>	<p>Intervention productivity costs were 8,021 Euros compared with 9,152 for standard care</p> <p>NS difference in HR quality of life scores</p> <p><u>Uncertainty</u> Optimistic and pessimistic scenarios varying individually pre-op costs, post-op hospital costs, direct costs, and productivity costs</p>
<p><b>Reilly et al(2005)<sup>(47)</sup></b></p> <p>UK</p> <p>Hospital setting</p> <p><u>Study Population</u> Patients undergoing unicompartmental knee arthroplasty</p> <p><u>Time horizon</u> Unclear</p>	<p><u>Intervention</u> Accelerated discharge: aim to discharge day after surgery (n=20)</p> <p><u>Comparator</u> Standard discharge: approx. 5 days post-surgery (n=21)</p>	<p>Economic evaluation based on a single study</p> <p><u>Perspective</u> Hospital</p> <p><u>Primary outcome</u> Oxford Knee Assessment</p> <p><u>Direct Costs</u> Fixed costs (surgical staff, anaesthetics, prosthesis, pharmacy), outpatient appointment, specialist registrar time.</p> <p><u>Productivity costs</u> n/a</p>	<p><u>Results</u> The costs and benefits were not synthesised</p> <p>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)</p> <p>Total costs for intervention per patient £3,391 compared with £4,634 for standard care</p> <p><u>Uncertainty</u> n/a</p>
<p><b>Archibald<sup>(48)</sup></b></p> <p>USA</p> <p>Hospital setting</p> <p><u>Study Population</u> Colorectal surgery patients</p> <p><u>Time horizon</u> unclear</p>	<p><u>Intervention</u> 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 &amp; 770 not enrolled)</p> <p><u>Comparator</u> Standard care historical baseline (n=1673)</p>	<p>Economic evaluation based on a study comparing two time periods, where ERAS was available in one and not in the other.</p> <p><u>Primary outcome</u> Length of stay ; POD; Readmission</p> <p><u>Direct Costs</u> Hospital costs (total direct and indirect costs identified via hospital billing system)</p> <p><u>Productivity costs</u> n/a</p>	<p><u>Results</u> The costs and benefits were not synthesised</p> <p>Mean LOS for the intervention was 8.4 days compared with 6.9 days for the comparator (p&lt;0.0001)</p> <p>Mean POD for the intervention was 7.6 days compared with 6.3 days (p&lt;0.0001)</p> <p>Mean hospital cost for the intervention population was US\$18,741 compared with US\$16,978 for the comparator.</p> <p><u>Uncertainty</u> n/a</p>

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For peer review only



## 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.

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3 • **Implementation and patient experience**

4 Evidence from case studies relating to the experiences of patients and clinical  
5 teams in implementing and delivering enhanced recovery programmes in UK  
6 settings will be identified from the following sources:  
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10 • Association of Surgeons of Great Britain and Ireland  
11 • British Association of Day Surgery  
12 • British Orthopedic Association  
13 • British Association of Urology Surgeons  
14 • British Association Breast Surgeons  
15 • Department of Health Enhanced Recovery Partnership Programme  
16 • Enhanced Recovery Partnership Programme Innovation sites  
17 • ERAS (UK)  
18 • NHS Evidence  
19 • NHS Institute for Innovation and Improvement  
20 • NHS Improvement - Enhanced Recovery  
21 • NHS Cancer Action Team  
22 • NICE  
23 • Royal College of Anaesthetists  
24 • Royal College of Obstetricians and Gynaecologists  
25 • Royal College of Surgeons  
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28 Relevant individuals will also be identified and contacted for additional  
29 evidence, including Regional Leads at the NHS Institute for Innovation and  
30 Improvement, and ERAS (UK) society members.  
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33 **Inclusion/exclusion criteria**

34 *Participants*

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

43 Reviews and studies of enhanced recovery programmes, as defined in the  
44 original articles, will be considered for inclusion. Eligible interventions could  
45 include enhanced recovery combined with other techniques to reduce the  
46 impact of any type of elective surgery.  
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49 Reviews and studies will then be assessed to identify which ones encompass  
50 the main components of the approach, as stated by the Enhanced Recovery  
51 Partnership Programme; there will be no restriction on the number of  
52 components, or individual elements within each component, needed for a  
53 study to be eligible for inclusion. The essential elements include providing  
54 support and information to ensure the patient is in the best possible condition  
55 for surgery (pre-operative), ensuring the patient has the best possible  
56 management during surgery (intra-operative), ensuring the patient  
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3 experiences the best post-operative rehabilitation (post-operative). See also  
4 Appendix 2 for example protocol.  
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#### 6 *Comparator*

7 Usual/standard care without a multimodal enhanced recovery programme, as  
8 defined in the included studies.  
9

#### 10 *Outcomes*

11 All health and cost-related outcomes will be considered for inclusion; eligible  
12 studies must report at least one outcome. We will then distinguish between  
13 clinical outcomes (mobilisation, mortality and morbidity, pain, readmission  
14 rates, re-intervention rates, length of hospital stay), patient outcomes (eg.  
15 patient experience and satisfaction, quality of life), and resource use in acute  
16 and, where available, primary care settings (eg. workforce utilisation and  
17 costs, including involvement of an Enhanced Programme Facilitator and  
18 resource implications post-discharge).  
19

20  
21 Patient experience must be assessed using validated questionnaires and  
22 surveys (eg. 2011 National Inpatient Survey, Picker Institute Europe & Care  
23 Quality Commission).  
24

#### 25 *Study design*

26  
27 Systematic reviews of primary studies and economic evaluations will be  
28 included if they evaluate enhanced recovery programmes in patients  
29 undergoing elective surgery. Other synthesised evidence, such as reviews of  
30 reviews, will be eligible for inclusion, but will be assessed separately.  
31

32  
33 Also eligible for inclusion will be individual RCTs not included in the above  
34 reviews, and UK NHS cost analysis studies identified from HEED. Case  
35 studies, impact assessments, or surveys of patient experience documenting  
36 the experience of implementing enhanced recovery in a UK setting will also  
37 be considered.  
38

39  
40 No language restrictions will be applied. Where feasible, foreign language  
41 papers will be translated and included in the synthesis. Where this is not  
42 feasible, the number of articles will be reported.  
43

#### 44 *Selection*

##### 45 • ***Clinical and cost effectiveness and implementation***

46 Search results will be stored in a reference management database (Endnote).  
47 Two researchers will independently screen all titles and abstracts obtained  
48 through the searches for potentially relevant articles. Full manuscripts of  
49 potentially relevant articles will be ordered and two researchers will  
50 independently assess the relevance of each article using the criteria above.  
51 Disagreements between reviewers will be resolved by discussion or by  
52 recourse to a third reviewer if necessary.  
53

#### 54 *Data extraction*

55  
56 Data will be extracted into review software (EPPI Reviewer 4.0). Data  
57 extraction forms will be piloted on a small selection of studies and adjusted as  
58  
59  
60

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)  <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:

- **Cost-effectiveness**

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

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

- **Patient experience**

Patient details	Results
	<p data-bbox="565 323 797 354"><u>Patient outcome:</u></p> <p data-bbox="565 390 1256 457"><b>Responses to standard questions from the 2010 National Inpatient Survey</b></p> <p data-bbox="565 459 1247 527">Were you involved as much as you wanted to be in decisions about your care and treatment?</p> <p data-bbox="565 529 1317 596">How much information about your condition or treatment was given to you?</p> <p data-bbox="565 598 1292 665">Did you feel you were involved in decisions about your discharge from hospital?</p> <p data-bbox="565 667 1292 768">Did hospital staff tell you who to contact if you were worried about your condition or treatment after you left hospital?</p>

### **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

1  
2  
3 NHS highlighting any potential limiting factors that might affect this. We will  
4 highlight any evidence as to which components of enhanced recovery  
5 programmes are most essential for achieving improvements in clinical and  
6 patient outcomes, and resource use.  
7

8  
9 • **Implementation**

10 Based on the evidence in the systematic reviews and from UK case studies,  
11 we will consider the time taken to implement; any workforce implications;  
12 requirements for training; equipment etc.  
13

14 Using evidence from the studies we will critically describe the key factors  
15 associated with successful (and unsuccessful) adoption, implementation and  
16 sustainability of enhanced recovery programmes in NHS acute hospital  
17 settings. We will also highlight any factors that are associated with minimising  
18 the postoperative burden of enhanced recovery programmes on general  
19 practice.  
20

21  
22 • **Patient experience**

23 We will summarise what is currently known about patient experience and will  
24 attempt to assess any implications for health equity using the approach  
25 developed by the SUPPORT Collaboration (Oxman, 2010).  
26

- 27  
28 • Which groups or settings are likely to be disadvantaged in relation to  
29 enhanced recovery being considered?  
30  
31 • Are there plausible reasons for anticipating differences in the relative  
32 effectiveness of enhanced recovery for disadvantaged groups or settings?  
33  
34 • Are there likely to be different baseline conditions across groups or  
35 settings such that the absolute effectiveness of enhanced recovery would  
36 be different for disadvantaged groups or settings?  
37  
38 • Are there important considerations that should be made when  
39 implementing enhanced recovery to ensure that inequities are reduced, if  
40 possible, and that they are not increased?  
41  
42

43  
44 **Dissemination**

45 The proposed research will seek to establish whether initiatives to reduce  
46 length of stay in acute hospital settings such as enhanced recovery  
47 programmes are 'the right thing to do' and more crucially shed light on 'how to  
48 do the right things right'. At the outset, a detailed dissemination strategy will  
49 be produced to ensure that key individuals, NHS Trusts and organisations  
50 with an interest in enhanced recovery programmes are made aware of the  
51 research and its eventual findings.  
52

53 The selection of specific dissemination activities will be informed by the key  
54 messages generated by the research, and will take account of the needs and  
55 preferences of the audiences to be targeted. In developing plans, the project  
56 team will draw upon the expertise of the Centre for Reviews and  
57  
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3 Dissemination, recent guidance (CRD, 2009) and lessons from recent  
4 research that has explored how best to disseminate (Wilson, 2010a, 2010b).  
5

6  
7 Dissemination activities will include the production and distribution of a short  
8 non-technical evidence briefing targeted at the end users (key individuals,  
9 NHS Trusts and organisations with an interest in enhanced recovery  
10 programmes), submission of papers for peer-reviewed publication and  
11 submission of abstracts to conferences. The results will also be made  
12 available on the NIHR HS&DR and CRD websites.  
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The project will take 9 months to complete. The key milestones are as follows:

	<b>Oct</b>	<b>Nov</b>	<b>Dec</b>	<b>Jan</b>	<b>Feb</b>	<b>Mar</b>	<b>Apr</b>	<b>May</b>	<b>June</b>	<b>July</b>
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

## References

2011 National Inpatient Survey, Picker Institute Europe & Care Quality Commission. Available at: [www.cqc.org.uk/Inpatientsurvey2011](http://www.cqc.org.uk/Inpatientsurvey2011).

Appleby J, Ham C, Imison C, Jennings M. *Improving NHS productivity*. London: The King's Fund; July 2010 [cited 2011 January 24]; Available from: [http://www.kingsfund.org.uk/publications/improving\\_nhs.html](http://www.kingsfund.org.uk/publications/improving_nhs.html)

Carroll C, Patterson M, Wood S, Booth A, Rick J, Balain S: A conceptual framework for implementation fidelity. *Implementation Science* 2007; **2**:40.

Crombie IK. *The pocket guide to critical appraisal: a handbook for health care professionals*. London: BMJ, 1996.

Department of Health (2011) *Enhanced Recovery Partnership Programme*. London: DH.

Ham C (2009). *Health in a Cold Climate*. London: The Nuffield Trust.

Kehlet H & Dahl JB. *Anaesthesia, surgery, and challenges in postoperative recovery*. *Lancet* 2003; **362**: 1921-1928.

Lewis R, Collins R, Flynn A, Emmans Dean M, Myers L, Wilson P, & Eastwood A. *A Systematic Review of Cancer Waiting Time Audits*. Report no 27. Centre for Reviews and Dissemination; 2005.

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](https://doi.org/10.1371/journal.pmed1000097). doi:10.1371/journal.pmed1000097

Oxman, A. D., Lavis, J. N. Lewin, S., & Fretheim, A. (2010) *SUPPORT Tools for evidence-informed health Policymaking (STP)*. Report no 4-2010. Oslo: Norwegian Knowledge Centre for the Health Services.

Sammour T et al. *A programme of Enhanced Recovery After Surgery (ERAS) is a cost-effective intervention in elective colonic surgery*. *New Zealand Medical Journal*. 2010;123(1319):61-70.

Sturm L, Cameron AL, Safety A, Surgical ERoNIP-, Surgeons RACo. *Brief Review: Fast-track Surgery and Enhanced Recovery After Surgery (ERAS) Programs: ASERNIP-S*; 2009. Available from: [http://books.google.co.uk/books?id=bl\\_XSAAACAAJ](http://books.google.co.uk/books?id=bl_XSAAACAAJ)

*Systematic reviews: CRD's guidance for undertaking reviews in healthcare*. 3rd ed. York: Centre for Reviews and Dissemination; 2009.

Wainwright T, Middleton R. *An orthopaedic enhanced recovery pathway*. *Current Anaesthesia & Critical Care* (2010).

**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

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2  
3 **Appendix 2 – Enhanced Recovery After Surgery Protocol (example)**  
4 ERAS Society 2012  
5

6 **Preoperative**  
7

- 8 • Pre-admission counselling
- 9 • Fluid and carbohydrate loading
- 10 • No prolonged fasting
- 11 • No/selective bowel preparation
- 12 • Antibiotic prophylaxis
- 13 • Thromboprophylaxis
- 14 • No pre-medication

15  
16  
17 **Intraoperative**  
18

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

24  
25  
26 **Postoperative**  
27

- 28 • Mid-thoracic epidural anaesthesia/analgesia
  - 29 • No nasogastric tubes
  - 30 • Prevention of nausea and vomiting
  - 31 • Avoidance of salt and water overload
  - 32 • Early removal of catheter
  - 33 • Early oral nutrition
  - 34 • Non-opioid oral analgesia/NSAIDs
  - 35 • Early mobilisation
  - 36 • Stimulation of gut motility
  - 37 • Audit of compliance and outcomes
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# PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
<b>TITLE</b>			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
<b>ABSTRACT</b>			
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
<b>INTRODUCTION</b>			
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
<b>METHODS</b>			
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

Page 1 of 2

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
<b>RESULTS</b>			
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
<b>DISCUSSION</b>			
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
<b>FUNDING</b>			
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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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

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doi:10.1371/journal.pmed1000097

For more information, visit: [www.prisma-statement.org](http://www.prisma-statement.org).

Page 2 of 2

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# BMJ Open

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

Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2014-005015.R1
Article Type:	Research
Date Submitted by the Author:	12-Jun-2014
Complete List of Authors:	Paton, Fiona; University of York, Centre for Reviews and Dissemination Chambers, Duncan; The University of York, Centre for Reviews and Dissemination Wilson, Paul; University of York, Centre for Reviews and Dissemination Eastwood, Alison; University of York, Centre for Reviews and Dissemination Craig, Dawn; University of York, Centre for Reviews and Dissemination Fox, Dave; University of York, Centre for Reviews and Dissemination Jayne, David; Leeds Teaching Hospitals, McGinnes, Erika; Leeds Teaching Hospitals,
<b>Primary Subject Heading</b>:	Surgery
Secondary Subject Heading:	Health services research
Keywords:	enhanced recovery, fast track, length of hospital stay

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Manuscripts

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3 **Effectiveness and implementation of enhanced recovery after surgery programmes: a**  
4 **rapid evidence synthesis**  
5

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7 Fiona Paton, Duncan Chambers, Paul Wilson, Alison Eastwood, Dawn Craig, Dave Fox,  
8 David Jayne, Erika McGinnes  
9

10 Centre for Reviews and Dissemination, University of York F Paton, D Chambers, P Wilson, A  
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12 Leeds Teaching Hospitals NHS Trust, Leeds D Jayne, E McGinnes  
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52 reflect those of the NIHR Health Services and Delivery Research programme or the  
53 Department of Health.  
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3 Abstract  
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### 6 **Objectives**

7 To assess the evidence on the impact of enhanced recovery programmes for patients  
8 undergoing elective surgery in acute hospital settings in the UK.  
9  
10

### 11 **Design**

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

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

35 Seventeen systematic reviews and 12 additional RCTs were included. Ten relevant  
36 economic evaluations were included. No cost analysis studies were identified. Most of the  
37 evidence focused on colorectal surgery. Fourteen innovation case studies and 15  
38 implementation case studies undertaken in NHS settings described factors critical to the  
39 success of an enhanced recovery programme.  
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44 Evidence for colorectal surgery suggests that enhanced recovery programmes may reduce  
45 hospital stays by 0.5 to 3.5 days compared with conventional care. There were no significant  
46 differences in reported readmission rates. Other surgical specialties showed greater variation  
47 in reductions in length of stay reflecting the limited evidence identified.  
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52 Findings relating to other outcomes were hampered by a lack of robust evidence and poor  
53 reporting.  
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### 56 **Conclusions**

57 There is consistent, albeit limited, evidence that enhanced recovery programmes can reduce  
58 length of patient hospital stay without increasing readmission rates. The extent to which  
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3 managers and clinicians considering implementing enhanced recovery programmes in UK  
4 settings can realise savings will depend on length of stay achieved under their existing care  
5 pathway.  
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12 Strengths and limitations of the study  
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16 • Enhanced recovery programmes have been adopted with enthusiasm by the NHS as  
17 a means to achieving productivity gains and cost-savings. This evolution makes  
18 combining studies over different periods and interpreting results of earlier studies in  
19 relation to the current context more difficult.  
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24 • The evidence base to support such widespread implementation suggests possible  
25 benefits in terms of reduced length of hospital stay, fewer postoperative  
26 complications, reduced readmissions and improved patient outcomes.  
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- 29  
30 • Although there is a reasonable volume of evidence evaluating enhanced recovery  
31 programmes in colorectal surgery, robust evidence is sparse. Optimal care is  
32 certainly the right thing to do, but the evidence does not identify which enhanced  
33 recovery programme elements and combinations of elements are most effective.  
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37 • Findings relating to other outcomes, costs of enhanced recovery programmes,  
38 experience in using the programmes, and patient experience were limited by  
39 generally poor quality evidence and poor reporting. As such, conclusions on which  
40 combinations provide greatest gains and how best to implement them cannot be  
41 made.  
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## 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.<sup>(1, 2)</sup> 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<sup>(3)</sup> and is now spreading<sup>(3)</sup> 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<sup>(4)</sup> 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<sup>(5-21)</sup> and 12 additional RCTs<sup>(22-34)</sup> 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.<sup>(35)</sup> 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)<sup>(19)</sup> to 3.75 days (95% CI 5.11 to 2.40 days).<sup>(18)</sup> Evidence from individual RCTs in colorectal surgery also suggest reduced length of hospital 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.

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3 Deaths were rare and no significant differences between treatment groups were found in the  
4 systematic reviews and additional RCTs, regardless of surgical speciality. Morbidity was  
5 defined differently across systematic reviews and RCTs; rates between treatment groups  
6 were sometimes inconsistent, but generally indicated no statistically significant differences.  
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10 Mobilisation rates were inconsistent across systematic reviews, but most reported no  
11 significant differences in time to mobilisation between treatment groups. Mobilisation was  
12 rarely reported as an outcome in the additional RCTs.  
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16 Where systematic reviews and additional RCTs assessed quality of life and patient  
17 experience/satisfaction, equivocal findings were reported. Evidence on reintervention rates,  
18 pain and resource use was lacking in both systematic reviews and RCTs.  
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### 21 22 **Other Reviews**

23  
24 A systematic review in colorectal surgery, identified after the last literature search, showed  
25 similar findings to the systematic reviews discussed above.<sup>(36)</sup> Mean length of primary  
26 hospital stay was statistically significantly reduced in ERAS patients; mean difference (MD) -  
27 2.44 (95% CI -3.06 to -1.83; 11 RCTs) but with significant statistical heterogeneity ( $I^2=88%$ ).  
28 There was no evidence to suggest increased rates of readmissions, complications and  
29 mortality. Some of the individual RCT results for primary length of stay did not appear to be  
30 consistent with results reported in other systematic reviews, and this may have impacted on  
31 the estimated reduction in length of primary hospital stay.<sup>(36)</sup>  
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38 Two reviews<sup>(37, 38)</sup> focusing on individual ERAS elements were found and details can be  
39 found in the full review (in press).  
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### 42 43 **Case studies**

44 Ten of 14 UK NHS innovation sites provided adequate data for inclusion in this section.<sup>(39-41)</sup>  
45 Fifteen case studies of implementation of ERAS in NHS settings, and 11 NHS trusts (mostly  
46 in colorectal surgery) provided evidence relating to the implementation of an ERAS  
47 programme within their Trust.  
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51 There were variations in practice in terms of numbers and combinations of ERAS elements  
52 implemented; the most frequently implemented programme elements in the case studies  
53 were pre-admission information/counselling and early postoperative mobilisation. Available  
54 evidence did not address which enhanced recovery elements and combinations of elements  
55 were most effective. Substantial variation in what constitutes an enhanced recovery  
56 programme within and between different surgical specialities, and difficulties in implementing  
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3 certain ERAS components, suggest that the enhanced recovery pathway may be used as a  
4 framework and adapted to suit local situations. Evidence on compliance/adherence to  
5 enhanced recovery programmes was lacking.  
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9 Case studies identified the factors believed to act as barriers or facilitators to implementing  
10 an ERAS programme. Barriers to implementation included resistance to change from  
11 patients and staff, lack of funding or support from management,<sup>(39, 42-44)</sup> staff turnover,  
12 problems arising from poor documentation, the time required to complete documentation,  
13 and other practical issues.  
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18 Facilitators included the presence of a dedicated ERAS project lead/nurse to coordinate and  
19 sustain multidisciplinary working and continuity of the pathway, a multidisciplinary team  
20 approach, and continual education for staff and patients/patient representatives. One  
21 innovation site mentioned that it did not offer a seven day service for enhanced recovery due  
22 to staff resources. Patients operated on towards the end of the week may have to wait until  
23 after the weekend to be discharged if they need to be seen by any health care professionals  
24 or social services. The need to sustain multidisciplinary working means that, in the absence  
25 of 24/7 working for elective procedures, enhanced recovery programmes will tend to be front  
26 loaded into the start of the working week (typically Monday to Thursday). Recent evidence  
27 suggests a higher risk of death for patients who have elective surgical procedures carried out  
28 later in the working week and at the weekend,<sup>(45)</sup> the capacity to implement ERAS throughout  
29 the working week might ensure continuity of best care and help mitigate against such  
30 variation.  
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39 We included two published studies of patient experience of ERAS.<sup>(46, 47)</sup> Each study used  
40 qualitative research methods to analyse audiotaped material. The two studies provided  
41 limited evidence suggesting that patients who were willing to provide feedback took a  
42 positive view of their experience of treatment in an ERAS programme. The studies  
43 suggested that patients were willing to comment on their experience in a way that can help  
44 healthcare providers to identify areas for improvement.  
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### 50 **Cost-effectiveness**

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

### 9 **Statement of Principal Findings**

10 Overall, the systematic reviews and additional RCTs suggest that length of hospital stay is  
11 reduced in ERAS patients compared to patients receiving conventional care. The evidence  
12 was based mainly on colorectal surgery and the applicability of findings to other surgical  
13 specialities remains less clear. Evidence for colorectal surgery suggests that enhanced  
14 recovery programmes may reduce hospital stays by 0.5 to 3.5 days compared with  
15 conventional care.  
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22 There were marked differences in length of stay across reviews and individual studies  
23 regardless of speciality. These differences may reflect differences in ERAS protocols and  
24 health care systems and/or outcome definitions. This raises questions regarding the  
25 magnitude of effect of the ERAS protocols on length of stay, which may be overstated in  
26 some reviews.  
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31 The evidence suggests that ERAS programmes do not compromise patient morbidity,  
32 mortality and readmission rates but outcome definitions varied across reviews and individual  
33 studies. Such differences make it difficult to determine the reliability and generalisability of  
34 the findings.  
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39 Equivocal findings were reported for quality of life and patient experience/satisfaction but the  
40 evidence was based on few studies, which utilised various methods to measure these  
41 outcomes. The limited evidence precludes conclusions on the effects of ERAS protocols on  
42 pain, mobilisation and reintervention.  
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47 The implementation evidence included resource use in terms of the professionals involved in  
48 delivery of enhanced recovery programmes, but details were very limited and did not add to  
49 the evidence synthesis. Most case studies were uncontrolled and represent experiences of a  
50 sample of centres that chose to report their data; their outcomes may not be representative  
51 of those achieved elsewhere in the UK NHS. Their main value as evidence is the light they  
52 shed on NHS clinicians' perceptions of requirements for successful implementation and  
53 barriers to implementation of ERAS.  
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3 The impact of surgical experience and surgical volume on clinical outcomes was not  
4 explored and any implications of differences in these areas remain unknown. As enhanced  
5 recovery invariably targets the fitter, more mobile patient, frailer patients may not receive  
6 parity of access to what may be considered optimal treatment and management. Managers  
7 and clinicians considering implementing such programmes should think about the likely  
8 implication on equity of access. Whether inequity is an unintended outcome of enhanced  
9 recovery, merits further investigation.  
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15 Our review of the cost effectiveness literature suggests that enhanced recovery programmes  
16 that achieve a reduction in length of stay may save costs without detrimental effects on  
17 complication rates, readmission and health-related quality of life. However, generalisability of  
18 the results of the economic evaluations is limited by a lack of transparency in reporting, use  
19 of different settings and populations and variable methodology in analyses. Data were  
20 lacking for resource use associated with the programmes evaluated and could not usefully  
21 inform the review of economic evaluations. In addition, the clinical effectiveness of some of  
22 the programmes considered in economic evaluations was not based on robust evidence.  
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### 28 **Strengths and weaknesses**

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31 The main strength of this study was our use of multiple approaches to acquire and  
32 synthesise evidence. The main limitations were poor methodological quality and poor  
33 reporting of the included studies, and the inherent difficulty of reviewing a complex  
34 intervention in different healthcare systems and surgical specialities. Current methods for  
35 synthesising such complex interventions are limited. The methodological limitations and are  
36 not discussed here as this was outside the scope of this project, but have been addressed in  
37 previous publications (eg. Noyes et al, 2013).<sup>(58)</sup> Another complication is that elements of  
38 early enhanced recovery programmes have become accepted practice within conventional  
39 care. This evolution makes combining studies over different periods and interpreting results  
40 of earlier studies in relation to the current context more difficult.  
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49 We found a large number of systematic reviews but there was substantial overlap in the  
50 included studies and evidence was not as abundant as the existence of multiple systematic  
51 reviews suggested. Most of the RCTs were small and not high quality. With the exception of  
52 one RCT, the remainder were single centre trials and therefore appear to have been  
53 undertaken to support implementation of an enhanced recovery programme in a specific  
54 setting rather than being planned as research studies. There were significant clinical and  
55 methodological differences between individual trials, and we therefore presented a narrative  
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3 synthesis. Relatively few trials were conducted in the UK and this may limit the  
4 generalisability of evidence to UK NHS settings.  
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8 Lack of evidence on important outcomes including pain and quality of life is also an issue for  
9 research in this field. Trials tended not to report on adherence to the planned enhanced  
10 recovery programme. Assessing adherence to interventions and the impact this has on  
11 health outcomes is an important issue which is often overlooked in studies, and is a limitation  
12 in the evidence base in this review.  
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17 Three additional systematic reviews of effectiveness were brought to our attention during  
18 manuscript submission. One systematic review incorporates RCTs in colorectal surgery  
19 (Greco, 2013),<sup>(59)</sup> one incorporates RCTs and cohort studies in abdominal surgery (Neville,  
20 2014)<sup>(59)</sup> and one includes RCTs and quasi-RCTs across various surgical specialities  
21 (Nicholson, 2014).<sup>(59)</sup> The trials included in Greco (2013)<sup>(59)</sup> and Nicholson (2014)<sup>(59)</sup> overlap  
22 with those included in this review and the findings are consistent. The inclusion of these two  
23 reviews would therefore not have significantly altered the findings from this review. Neville  
24 (2014)<sup>(59)</sup> provides some additional data on patient-reported outcomes, including some  
25 evidence on post-discharge functional status. However, these outcomes were not frequently  
26 reported, and the additional evidence was mainly from study designs that would not have  
27 met the inclusion criteria for this review.  
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35 An important feature of our review is the inclusion of evidence on the implementation of  
36 enhanced recovery programmes in the UK NHS. This evidence has not been synthesised  
37 previously and the original programme websites are archived, so future access is not  
38 assured. By summarising this evidence, we have ensured that the main findings continue to  
39 be publicly available. We sought evidence on the experience of health professionals and  
40 patients of a broad range of sources and study types. Important themes emerged from this  
41 evidence that may be of value for implementing and sustaining enhanced recovery  
42 programmes in UK NHS settings. Due to the rapid nature of the evidence synthesis, the list  
43 of sources searched to identify data on implementation and delivery of enhanced recovery  
44 programmes was not exhaustive and we acknowledge that relevant evidence may have been  
45 missed. Indeed, evidence from Scotland has been noted and eligible case studies have been  
46 identified from the NHS Scotland Quality Improvement Hub website. It should be noted that  
47 these are as limited as those included in the review. A qualitative study was brought to our  
48 attention at peer review; the study was published after our final search date. Pearsall et al  
49 (2014)<sup>(60)</sup> conducted a qualitative study to explore the barriers and enablers in implementing  
50 an enhanced recovery after surgery programme in a University hospital in Canada. The  
51 themes identified are consistent with those reported in this review.  
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4 However, case studies are susceptible to risk of bias. Use of a standard reporting format was  
5 a potential strength of the case studies but variation in what each site actually reported  
6 (particularly in terms of evidence of benefit from the introduction of enhanced recovery  
7 programmes) reduced the usefulness of the evidence.  
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11 We sought to incorporate published and unpublished evidence on patient experiences and  
12 views of enhanced recovery programmes. Evaluation of patient experience of care is  
13 increasingly important for the NHS, especially in view of unacceptable failures of care such  
14 as those highlighted in the Francis Report.<sup>(61)</sup> Though the evidence was generally positive for  
15 enhanced recovery, it was limited by a shortage of studies that used validated measures of  
16 patient experience and by study designs that could bias results in favour of enhanced  
17 recovery.  
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24 A further strength of this study was the consideration of cost-effectiveness evidence, but the  
25 nature of the evidence did not permit any analyses. There is a clear need to capture better  
26 evaluated data on costs and benefits of enhanced recovery programmes from a clearly  
27 stated perspective. A systematic review of economic evaluations (Lee, 2014)<sup>(59)</sup> was brought  
28 to our attention during manuscript publication. The review confirmed the need for well-  
29 designed trials to determine the cost-effectiveness of enhanced recovery programmes from  
30 both the institutional and societal perspectives.  
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### 36 **Implications for healthcare**

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38 Overall, there is consistent, albeit limited, evidence that enhanced recovery programmes can  
39 reduce length of patient hospital stay without increasing readmission rates. Data on re-  
40 intervention rates and patient-reported outcomes did not suggest significant differences  
41 between enhanced recovery and conventional care, but the evidence was very limited and  
42 based on small numbers of patients. The lack of evidence on patient outcomes, resource use  
43 and costs precludes firm conclusions on the overall value of enhanced recovery  
44 programmes.  
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51 ERAS does not appear to reduce complication or readmission rates; the only cost benefit  
52 may lie in a reduction in post-operative bed days. Optimal care is certainly the right thing to  
53 do, but the evidence does not identify which enhanced recovery programme elements and  
54 combinations of elements are most effective. As such, conclusions on which combinations  
55 provide greatest gains and how best to implement them cannot be made.  
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3 The extent to which managers and clinicians considering implementing enhanced recovery  
4 programmes can realise reductions and cost savings will therefore depend on length of stays  
5 achieved under their existing care pathway. Important themes emerged from the relevant  
6 evidence identified on implementation, including the role of ERAS facilitators and the need  
7 for full support from management. It appears that these components are essential for the  
8 successful implementation and sustained delivery of enhanced recovery programmes in NHS  
9 settings. Consideration of potential benefit also needs to take account of the costs of service  
10 redesign, the resource use associated with programmes of this nature, the potential for  
11 improvement in patient outcomes and the impact on equity of access.  
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### 20 **Implications for research**

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22 RCTs comparing an enhanced recovery programme with conventional care continue to be  
23 conducted and published, although mostly not in the UK. Given the available evidence,  
24 further single centre RCTs of this kind are not a priority. Rather, what is needed is improved  
25 collection and reporting of how enhanced recovery programmes are implemented, resourced  
26 and experienced in NHS settings. Also, exploration into the effect that varying levels of  
27 surgical volume and surgical experience, and different discharge protocols might have on the  
28 success of an enhanced recovery pathway and subsequent outcomes. This will enhance our  
29 existing knowledge and understanding and provide evidence to support local decision-  
30 making about whether to adopt and how best to implement.  
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38 The two groups of implementation case studies included in our synthesis, although all were  
39 conducted in the UK, provide very limited information on how enhanced recovery  
40 programmes have actually been implemented in UK NHS settings. The standard reporting  
41 format originally proposed by The Enhanced Recovery Partnership Programme would  
42 enhance the value of future case studies if adhered to. Knowledge of how well the  
43 intervention has been implemented (fidelity) is essential for understanding how and why the  
44 intervention works and hence how outcomes can be further improved. Assessing fidelity may  
45 involve considering not only adherence to the requirements of the programme but also  
46 potential moderating factors, such as strategies used to assist delivery of the intervention,  
47 quality of delivery and participant responsiveness to new practices.<sup>(62)</sup> It would be helpful if  
48 future innovation programmes used standardised reporting. For multi-site programmes, a  
49 formal synthesis of findings from all participating sites should be undertaken as part of the  
50 evaluative process. This would ensure that the insights and contextual information which can  
51 inform the wider spread and adoption (or indeed discontinuation) would be systematically  
52 captured in a generalisable format.  
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4 Adherence/compliance to elements by staff and patients also requires further investigation.  
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6 Rigorous data on patients' experiences of enhanced recovery programmes are lacking.  
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8 Validated tools should be used and administered independently of those providing the  
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10 service. Efforts should be made to obtain data from representative samples of patients  
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12 receiving conventional care as well as those treated with enhanced recovery protocols, along  
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14 with evidence on the experiences of their families/carers.

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

1. Øvretveit J. Does Improving Quality Save Money? A Review of Evidence of Which Improvements to Quality Reduce Costs for Health Service Providers. London: The Health Foundation, 2009.
2. Øvretveit J. Does Improving Care Coordination Save Money: A Review Of Research. London: The Health Foundation, 2011.
3. Kehlet H, Slim K. The future of fast-track surgery. *Br J Surg*. 2012 Aug;99(8):1025-6.
4. Enhanced Recovery Partnership Programme. Delivering enhanced recovery – Helping patients to get better sooner after surgery. London: Department of Health, 2010 March 31st. Report No.
5. Sturm L, Cameron AL. Brief review: Fast-track surgery and enhanced recovery after surgery (ERAS) programs. Melbourne: Australian Safety and Efficacy Register of New Interventional Procedures - Surgical (ASERNIP-S), 2009 Contract No.: 3.
6. Adamina M, Kehlet H, Tomlinson GA, **et al**. Enhanced recovery pathways optimize health outcomes and resource utilization: a meta-analysis of randomized controlled trials in colorectal surgery. *Surgery*. 2011;149(6):830-40.
7. Ahmed J, Khan S, Lim M, **et al**. Enhanced recovery after surgery protocols - compliance and variations in practice during routine colorectal surgery. *Colorectal Dis*. 2012;14(9):1045-51.
8. Coolsen MME, Wong-Lun-Hing EM, van Dam RM, **et al**. A systematic review of outcomes in patients undergoing liver surgery in an enhanced recovery after surgery pathways. *HPB surgery : a world journal of hepatic, pancreatic and biliary surgery*. 2012;Early view online.
9. Coolsen MME, van Dam RM, van der Wilt AA, **et al**. Systematic review and meta-analysis of enhanced recovery after pancreatic surgery with particular emphasis on pancreaticoduodenectomies. *World J Surg*. 2013;Published online 09 April 2013.
10. Eskicioglu C, Forbes SS, Aarts M-A, **et al**. Enhanced Recovery after Surgery (ERAS) programs for patients having colorectal surgery: a meta-analysis of randomized trials. *J Gastrointest Surg*. 2009 Dec;13(12):2321-9.
11. Gouvas N, Tan E, Windsor A, **et al**. Fast-track vs standard care in colorectal surgery: a meta-analysis update. *Int J Colorectal Dis*. 2009 Oct;24(10):1119-31.
12. Hall TC, Dennison AR, Bilku DK, **et al**. Enhanced recovery programmes in hepatobiliary and pancreatic surgery: a systematic review. *Ann R Coll Surg Engl*. 2012;94:318-26.
13. Khan S, Wilson T, Ahmed J, **et al**. Quality of life and patient satisfaction with enhanced recovery protocols. *Colorectal Dis*. 2010;12(12):1175-82.
14. Lemmens L, van Zelm R, Borel Rinkes I, **et al**. Clinical and organizational content of clinical pathways for digestive surgery: a systematic review. *Dig Surg*. 2009;26(2):91-9.
15. Rawlinson A, Kang P, Evans J, **et al**. A systematic review of enhanced recovery protocols in colorectal surgery. *Ann R Coll Surg Engl*. 2011;93(8):583-8.

16. Spanjersberg Willem R, Reurings J, **et al**. Fast track surgery versus conventional recovery strategies for colorectal surgery. *Cochrane Database of Systematic Reviews*. 2011 (2).
17. Varadhan KK, Neal KR, Dejong CH, **et al**. The enhanced recovery after surgery (ERAS) pathway for patients undergoing major elective open colorectal surgery: a meta-analysis of randomized controlled trials. *Clin Nutr*. 2010;29(4):434-40.
18. Walter CJ, Collin J, Dumville JC, **et al**. Enhanced recovery in colorectal resections: a systematic review and meta-analysis. *Colorectal Dis*. 2009 May;11(4):344-53.
19. Wind J, Polle SW, Fung Kon Jin PH, **et al**. Systematic review of enhanced recovery programmes in colonic surgery. *Br J Surg*. 2006 Jul;93(7):800-9.
20. Lv D, Wang X, Shi G. Perioperative enhanced recovery programmes for gynaecological cancer patients. *Cochrane Database of Systematic Reviews*. 2012 (12).
21. Lv L, Shao Y-f, Zhou Y-b. The enhanced recovery after surgery (ERAS) pathway for patients undergoing colorectal surgery: an update of meta-analysis of randomized controlled trials. *Int J Colorectal Dis*. 2012;27:1549-54.
22. Chen Hu J, Xin Jiang L, Cai L, **et al**. Preliminary experience of fast-track surgery combined with laparoscopy-assisted radical distal gastrectomy for gastric cancer. *J Gastrointest Surg*. 2012 Oct;16(10):1830-9.
23. Kim JW, Kim WS, Cheong JH, **et al**. Safety and efficacy of fast-track surgery in laparoscopic distal gastrectomy for gastric cancer: a randomized clinical trial. *World J Surg*. 2012 Dec;36(12):2879-87.
24. Garcia-Botello S, Canovas de Lucas R, **et al**. Implementation of a perioperative multimodal rehabilitation protocol in elective colorectal surgery. A prospective randomised controlled study. *Cir Esp*. 2011 Mar;89(3):159-66.
25. Ionescu D, Iancu C, Ion D, **et al**. Implementing fast-track protocol for colorectal surgery: a prospective randomized clinical trial. *World J Surg*. 2009 Nov;33(11):2433-8.
26. Lee TG, Kang SB, Kim DW, **et al**. Comparison of early mobilization and diet rehabilitation program with conventional care after laparoscopic colon surgery: a prospective randomized controlled trial. *Dis Colon Rectum*. 2011 Jan;54(1):21-8.
27. Lemanu DP, Singh PP, Berridge K, **et al**. Randomized clinical trial of enhanced recovery versus standard care after laparoscopic sleeve gastrectomy. *Br J Surg*. 2013 Mar;100(4):482-9.
28. Liu XX, Jiang ZW, Wang ZM, **et al**. Multimodal optimization of surgical care shows beneficial outcome in gastrectomy surgery. *JPEN J Parenter Enteral Nutr*. 2010 May-Jun;34(3):313-21.
29. Ren L, Zhu D, Wei Y, **et al**. Enhanced Recovery After Surgery (ERAS) program attenuates stress and accelerates recovery in patients after radical resection for colorectal cancer: a prospective randomized controlled trial. *World J Surg*. 2012 Feb;36(2):407-14.
30. Wang D, Kong Y, Zhong B, **et al**. Fast-track surgery improves postoperative recovery in patients with gastric cancer: a randomized comparison with conventional postoperative care. *J Gastrointest Surg*. 2010;14(4):620-7.

- 1  
2  
3 31. Wang G, Jiang ZW, Xu J, **et al.** Fast-track rehabilitation program vs conventional  
4 care after colorectal resection: a randomized clinical trial. *World J Gastroenterol.* 2011 Feb  
5 7;17(5):671-6.  
6  
7 32. Wang Q, Suo J, Jiang J, **et al.** Effectiveness of fast-track rehabilitation vs  
8 conventional care in laparoscopic colorectal resection for elderly patients: a randomized trial.  
9 *Colorectal Dis.* 2012 Aug;14(8):1009-13.  
10  
11 33. Yang DJ, Zhang S, He WL, **et al.** Fast track surgery accelerates the recovery of  
12 postoperative insulin sensitivity. *Chin Med J.* 2012 Sep;125(18):3261-5.  
13  
14 34. Yang DJ, Zhang S, He WL, **et al.** Fast-track surgery accelerates the recovery of  
15 postoperative humoral immune function in elective operation for colorectal carcinoma: a  
16 randomized controlled clinical trial. *Chin Med J.* 2012 Apr 24;92(16):1112-5.  
17  
18 35. Vlug MS, Wind J, Hollmann MW, **et al.** Laparoscopy in combination with fast track  
19 multimodal management is the best perioperative strategy in patients undergoing colonic  
20 surgery: a randomized clinical trial (LAFA-study). *Ann Surg.* 2011 Dec;254(6):868-75.  
21  
22 36. Cheng-Le Z, Xing-Zhao YX-D, Z., **et al.** Enhanced recovery after surgery programs  
23 versus traditional care for colorectal surgery: A meta-analysis of randomized controlled trials.  
24 *Dis Colon Rectum.* 2013;56:667-78.  
25  
26 37. Arsalani-Zadeh R, Elfadl D, Yassin N, **et al.** Evidence-based review of enhancing  
27 postoperative recovery after breast surgery. *Br J Surg.* 2011 Feb;98(2):181-96.  
28  
29 38. Hoffmann H, Kettelhack C. Fast-track surgery - conditions and challenges in  
30 postsurgical treatment: a review of elements of translational research in enhanced recovery  
31 after surgery. *Eur Surg Res.* 2012;49(1):24-34.  
32  
33 39. Enhanced Recovery Partnership Programme Case Studies 2011: Gynaecology.  
34 Addenbrookes Hospital.  
35  
36 40. Enhanced Recovery Partnership Programme Case Studies 2011: Enhanced  
37 Recovery Programme. Yeovil District Hospital NHS Foundation Trust.  
38  
39 41. Enhanced Recovery Partnership Programme Case Studies 2011: Enhanced recovery  
40 for colorectal surgery. Yeovil District Hospital NHS Foundation Trust.  
41  
42 42. Enhanced Recovery Partnership Programme Case Studies 2011: Colorectal,  
43 Gynaecology, Urology, MSK. Medway NHS Foundation Trust.  
44  
45 43. Enhanced Recovery Partnership Programme Case Studies 2011: Colorectal surgery  
46 (all elective procedures) and most major emergencies from decision to treat surgically;  
47 Urology: radical Prostatectomy, Cystectomy, Nephrectomy; MSK: 1 Hip and knee  
48 replacement; Gynaecology: Hysterectomy (vaginal, abdominal and laparoscopic) moving to  
49 all majors. Royal Berkshire Hospital.  
50  
51 44. Enhanced Recovery Partnership Programme Case Studies 2011: Enhanced recovery  
52 after colorectal surgery. Royal Berkshire Hospital.  
53  
54 45. Aylin P, Alexandrescu R, Jen MH, **et al.** Day of week of procedure and 30 day  
55 mortality for elective surgery: retrospective analysis of hospital episode statistics. *BMJ.* 2013  
56 May;346:8.  
57  
58 46. Blazeby JM, Soulsby M, Winstone K, **et al.** A qualitative evaluation of patients'  
59 experiences of an enhanced recovery programme for colorectal cancer. *Colorectal Dis.* 2010  
60 Oct;12(10 Online):e236-42.

- 1  
2  
3 47. Taylor C, Burch J. Feedback on an enhanced recovery programme for colorectal  
4 surgery. *Br J Nurs*. 2011 Mar;20(5):286-90.
- 5  
6 48. Reilly KA, Beard DJ, Barker KL, **et al**. Efficacy of an accelerated recovery protocol  
7 for Oxford unicompartmental knee arthroplasty: a randomised controlled trial. *Knee*.  
8 2005;12(5):351-7.
- 9  
10 49. Archibald LH, Ott MJ, Gale CM, **et al**. Enhanced recovery after colon surgery in a  
11 community hospital system. *Dis Colon Rectum*. 2011;54(7):840-5.
- 12  
13 50. Sammour T, Zargar-Shoshtari K, Bhat A, **et al**. A programme of Enhanced Recovery  
14 After Surgery (ERAS) is a cost-effective intervention in elective colonic surgery. *N Z Med J*.  
15 2010;123(1319).
- 16  
17 51. King PM, Blazeby JM, Ewings P, **et al**. The influence of an enhanced recovery  
18 programme on clinical outcomes, costs and quality of life after surgery for colorectal cancer.  
19 *Colorectal Dis*. 2006;8(6):506-13.
- 20  
21 52. Nielsen PR, Andreassen J, Asmussen M, **et al**. Costs and quality of life for  
22 prehabilitation and early rehabilitation after surgery of the lumbar spine. *BMC Health Serv*  
23 *Res* [Internet]. 2008; 8:[209 p.]. Available from: [http://www.biomedcentral.com/1472-](http://www.biomedcentral.com/1472-6963/8/209)  
24 [6963/8/209](http://www.biomedcentral.com/1472-6963/8/209).
- 25  
26 53. Jakobsen DH, Sonne E, Andreassen J, **et al**. Convalescence after colonic surgery  
27 with fast-track vs conventional care. *Colorectal Dis*. 2006 Oct;8(8):683-7.
- 28  
29 54. McBride N, Farrington F, Midford R. Implementing a school drug education  
30 programme: reflections on fidelity. *International Journal of Health Promotion and Education*.  
31 2002;40(2):40-50.
- 32  
33 55. Kariv Y, Delaney CP, Senagore AJ, **et al**. Clinical outcomes and cost analysis of a  
34 fast track postoperative care pathway for ileal pouch-anal anastomosis. A case control study.  
35 *Dis Colon Rectum*. 2007;50(2):137-46.
- 36  
37 56. Salhiyyah K, Elsobky S, Raja S, **et al**. A clinical and economic evaluation of fast-  
38 track recovery after cardiac surgery. *Heart Surgery Forum*. 2011;14(6):E330-4.
- 39  
40 57. Yanatori M, Tomita S, Miura Y, **et al**. Feasibility of the fast-track recovery program  
41 after cardiac surgery in Japan. *General Thoracic and Cardiovascular Surgery*.  
42 2007;55(11):445-9.
- 43  
44 58. Noyes J, Gough D, Lewin S, **et al**. A research and development agenda for  
45 systematic reviews that ask complex questions about complex interventions. *J Clin*  
46 *Epidemiol*. 2013 Nov;66(11):1262-70.
- 47  
48 59. Eiselt J, Racek J, Trefil L, **et al**. Ferric saccharate infusion enhances lipid  
49 peroxidation in hemodialysis (hd) patients [abstract]. *Nephrol Dial Transplant* [Internet]. 2001;  
50 16(6):[A141 p.]. Available from:  
51 <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/203/CN-00445203/frame.html>.
- 52  
53 60. Pearsall EA, Meghji Z, Pitzul KB, **et al**. A Qualitative Study to Understand the  
54 Barriers and Enablers in Implementing an Enhanced Recovery After Surgery Program. *Ann*  
55 *Surg*. 2014 Mar 18.
- 56  
57 61. Report of the Mid Staffordshire NHS Foundation Trust Public Inquiry (Chaired by  
58 Robert Francis QC). London: The Stationery Office, 2013.
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52  
53  
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55  
56  
57  
58  
59  
60

62. Carroll C, Patterson M, Wood S, **et al.** A conceptual framework for implementation fidelity. *Implementation Science*. 2007;2(1):40.

63. Coolsen MME, van Dam RM, van der Wilt AA, **et al.** Systematic review and meta-analysis of enhanced recovery after pancreatic surgery with particular emphasis on pancreaticoduodenectomies: Supplementary Material. *World J Surg*. 2013;Published online 09 April 2013.

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15 and contributed to the methods section of the review. DJ and EMcG provided advice  
16 throughout the rapid synthesis and commented on the draft review.  
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25 in the submitted work in the previous three years; no other relationships or activities that  
26 could appear to have influenced the submitted work.  
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33 manuscript is an honest, accurate, and transparent account of the study being reported; that  
34 no important aspects of the study have been omitted; and that any discrepancies from the  
35 study as planned (and, if relevant, registered) have been explained.  
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39 **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
<b>Colorectal/Colon surgery</b>							
Adamina (2011) <sup>(6)</sup>	✓	✓	UC	✓	UC	✓	✓
Ahmed (2012) <sup>(7)</sup>	✓	X	X	X	X	X	✓
Eskicioglu (2009) <sup>(10)</sup>	✓	✓	X	✓	✓	✓	✓
Gouvas (2009) <sup>(11)</sup>	✓	✓	X	✓	✓	✓	✓
Khan (2010) <sup>(13)</sup>	✓	✓	X	✓	X	✓	✓
Lv (2012a) <sup>(21)</sup>	✓	✓	X	X	✓	✓	✓
Rawlinson (2011) <sup>(15)</sup>	✓	X	X	✓	UC	X	UC
Spanjersberg (2011) <sup>(16)</sup>	✓	✓	✓	✓	✓	✓	✓
Varadhan (2010) <sup>(17)</sup>	✓	✓	X	✓	✓	✓	✓
Walter (2009) <sup>(18)</sup>	✓	✓	✓	✓	✓	✓	✓
Wind (2006) <sup>(19)</sup>	✓	✓	✓	✓	✓	✓	✓
<b>Gynaecological surgery</b>							
Lv (2012b) <sup>(20)</sup>	✓	X	X	X	X	✓	✓
<b>Liver/pancreatic surgery</b>							
Coolsen (2012) <sup>(8)</sup>	✓	✓	X	✓	X	✓	✓
Coolsen (2013) <sup>(9)</sup> Link to <sup>(63)</sup>	✓	✓	✓	✓	✓	✓	✓
Hall (2012) <sup>(12)</sup>	X	X	X	✓	X	✓	✓
<b>Various surgical specialities</b>							
Lemmens (2009) <sup>(14)</sup>	✓	X	X	✓	X	✓	✓
Sturm (2009) <sup>(5)</sup>	✓	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
<b>Bariatric surgery</b>									
Lemanu (2013) <sup>(27)</sup>	✓	✓	X	X	X	X	NA	UC	UC
<b>Colorectal/colon surgery</b>									
Garcia-Botello (2011) <sup>(24)</sup>	UC	X	UC	X	UC	X	NA	UC	✓
Ionescu (2009) <sup>(25)</sup>	✓	✓	X	X	UC	X	NA	UC	UC
Lee (2011) <sup>(26)</sup>	✓	✓	UC	X	UC	X	NA	UC	UC
Ren (2012) <sup>(29)</sup>	✓	✓	X	X	✓	X	NA	UC	UC
Wang (2011) <sup>(31)</sup>	UC	UC	UC	X	UC	X	NA	✓	✓
Wang (2012) <sup>(32)</sup>	UC	UC	X	X	✓	UC	UC	UC	UC
Yang (2012) <sup>(33, 34)</sup>	✓	UC	X	X	UC	X	NA	X	X
<b>Gastric surgery</b>									
Chen (2012) <sup>(22)</sup>	UC	UC	X	✓	✓	X	NA	UC	UC
Kim (2012) <sup>(23)</sup>	UC	UC	X	X	X	X	NA	UC	UC
Liu (2010) <sup>(28)</sup>	UC	X	X	X	X	X	NA	UC	UC
Wang (2010) <sup>(30)</sup>	UC	UC	X	X	UC	X	NA	X	X

UC: unclear reporting; NA: not applicable

### Figure legend:

Figure 1: Study flow diagram

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3 **Effectiveness and implementation of enhanced recovery after surgery programmes: a**  
4 **rapid evidence synthesis**  
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7 Fiona Paton, Duncan Chambers, Paul Wilson, Alison Eastwood, Dawn Craig, Dave Fox,  
8 David Jayne, Erika McGinnes  
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10 Centre for Reviews and Dissemination, University of York F Paton, D Chambers, P Wilson,  
11 A Eastwood, D Craig, D Fox  
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24 submitted work; no financial relationships with any organisations that might have an interest  
25 in the submitted work in the previous three years; no other relationships or activities that  
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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: ~~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.
- Although 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.<sup>(1,2)</sup> 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<sup>(3)</sup> 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



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3 clinical and cost effectiveness of enhanced recovery programmes, and the implementation,  
4 delivery and impact of such programmes in secondary care settings in the UK.  
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### 7 **Methods**

8 Eight databases, including DARE, NHS EED and MEDLINE were searched to from 1990 to  
9 March 2013 without language restrictions. The PROSPERO database was searched to  
10 identify ongoing systematic reviews. Relevant reports and guidelines were screened for  
11 further studies. Reference lists of retrieved articles, reviews and evaluations were scanned,  
12 and relevant individuals contacted for additional evidence.  
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17 Systematic reviews, RCTs not included in the systematic reviews, economic evaluations,  
18 and UK NHS cost analysis studies were included if they evaluated the impact of enhanced  
19 recovery programmes (encompassing different combinations of the main preoperative,  
20 intraoperative and postoperative pathway elements described by the Enhanced Recovery Partnership  
21 Programme<sup>(4)</sup> on health or cost-related outcomes. Eligible studies included patients  
22 undergoing elective surgery in an acute hospital in the UK NHS or a comparable healthcare  
23 system. Comparators were only relevant to clinical and cost-effectiveness evaluations, and  
24 included conventional (usual/standard) care without a structured multimodal enhanced  
25 recovery patient pathway (as defined in the included studies). Case studies, impact  
26 assessments and surveys of patient experience that documented the experience of  
27 implementing enhanced recovery in a UK setting were also eligible.  
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36 Quality assessment of systematic reviews, RCTs and economic evaluations was based on  
37 existing CRD critical appraisal methods (<http://www.crd.york.ac.uk/crdweb/HomePage.asp>;  
38 CRD, 2009). Cost analysis studies, studies of patient experience, and case studies of  
39 implementation were not formally quality assessed.  
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43 All stages of the review process were performed by one researcher and checked by a  
44 second. Disagreements between reviewers were resolved by discussion or by recourse to a  
45 third reviewer where necessary.  
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49 The type and range of evidence precluded meta-analysis and we therefore performed a  
50 narrative synthesis, differentiating clinical outcomes (eg. mobilisation, mortality and  
51 morbidity, and length of hospital stay), patient-reported outcomes (eg. patient experience  
52 and satisfaction), resource use in secondary care (eg. workforce utilisation and costs), and  
53 implementation case studies.  
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## Results

Seventeen systematic reviews<sup>(5-21)</sup> and 12 additional RCTs<sup>(22-34)</sup> 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.<sup>(35)</sup> 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)<sup>(19)</sup> to 3.75 days (95% CI 5.11 to 2.40 days).<sup>(18)</sup> ([Walter 2009](#)) Evidence from individual RCTs in colorectal surgery also suggest reduced length of hospital 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

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3 formally explored, but may have reflected differences in ERAS protocols and surgical  
4 populations.  
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7 Deaths were rare and no significant differences between treatment groups were found in the  
8 systematic reviews and additional RCTs, regardless of surgical speciality. Morbidity was  
9 defined differently across systematic reviews and RCTs; rates between treatment groups  
10 were sometimes inconsistent, but generally indicated no statistically significant differences.  
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14 Mobilisation rates were inconsistent across systematic reviews, but most reported no  
15 significant differences in time to mobilisation between treatment groups. Mobilisation was  
16 rarely reported as an outcome in the additional RCTs.  
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20 Where systematic reviews and additional RCTs assessed quality of life and patient  
21 experience/satisfaction, equivocal findings were reported. Evidence on reintervention rates,  
22 pain and resource use was lacking in both systematic reviews and RCTs.  
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### 27 **Other Reviews**

28 A systematic review in colorectal surgery, identified after the last literature search, showed  
29 similar findings to the systematic reviews discussed above.<sup>(36)</sup> Mean length of primary  
30 hospital stay was statistically significantly reduced in ERAS patients; mean difference (MD) -  
31 2.44 (95% CI -3.06 to -1.83; 11 RCTs) but with significant statistical heterogeneity ( $I^2=88\%$ ).  
32 There was no evidence to suggest increased rates of readmissions, complications and  
33 mortality. Some of the individual RCT results for primary length of stay did not appear to be  
34 consistent with results reported in other systematic reviews, and this may have impacted on  
35 the estimated reduction in length of primary hospital stay.<sup>(36)</sup>  
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42 Two reviews<sup>(37, 38)</sup> focusing on individual ERAS elements were found and details can be  
43 found in the full review (in press).  
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### 47 **Case studies**

48 Ten of 14 UK NHS innovation sites provided adequate data for inclusion in this section.<sup>(39-41)</sup>  
49 Fifteen case studies of implementation of ERAS in NHS settings, and 11 NHS trusts (mostly  
50 in colorectal surgery) provided evidence relating to the implementation of an ERAS  
51 programme within their Trust.  
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55 There were variations in practice in terms of numbers and combinations of ERAS elements  
56 implemented; the most frequently implemented programme elements in the case studies  
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3 were pre-admission information/counselling and early postoperative mobilisation. Available  
4 evidence did not address which enhanced recovery elements and combinations of elements  
5 were most effective. Substantial variation in what constitutes an enhanced recovery  
6 programme within and between different surgical specialities, and difficulties in implementing  
7 certain ERAS components, suggest that the enhanced recovery pathway may be used as a  
8 framework and adapted to suit local situations. Evidence on compliance/adherence to  
9 enhanced recovery programmes was lacking.  
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15 Case studies identified the factors believed to act as barriers or facilitators to implementing  
16 an ERAS programme. Barriers to implementation included resistance to change from  
17 patients and staff, lack of funding or support from management,<sup>(39, 42-44)</sup> staff turnover,  
18 problems arising from poor documentation, the time required to complete documentation,  
19 and other practical issues.  
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24 Facilitators included the presence of a dedicated ERAS project lead/nurse to coordinate and  
25 sustain multidisciplinary working and continuity of the pathway, a multidisciplinary team  
26 approach, and continual education for staff and patients/patient representatives. One  
27 innovation site mentioned that it did not offer a seven day service for enhanced recovery due  
28 to staff resources. Patients operated on towards the end of the week may have to wait until  
29 after the weekend to be discharged if they need to be seen by any health care professionals  
30 or social services. The need to sustain multidisciplinary working means that, in the absence  
31 of 24/7 working for elective procedures, enhanced recovery programmes will tend to be front  
32 loaded into the start of the working week (typically Monday to Thursday). Recent evidence  
33 suggests a higher risk of death for patients who have elective surgical procedures carried  
34 out later in the working week and at the weekend,<sup>(45)</sup> the capacity to implement ERAS  
35 throughout the working week might ensure continuity of best care and help mitigate against  
36 such variation.  
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45 We included two published studies of patient experience of ERAS.<sup>(46, 47)</sup> Each study used  
46 qualitative research methods to analyse audiotaped material. The two studies provided  
47 limited evidence suggesting that patients who were willing to provide feedback took a  
48 positive view of their experience of treatment in an ERAS programme. The studies  
49 suggested that patients were willing to comment on their experience in a way that can help  
50 healthcare providers to identify areas for improvement.  
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### 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](#)).<sup>(48-57)</sup> 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.

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3 The implementation evidence included resource use in terms of the professionals involved in  
4 delivery of enhanced recovery programmes, but details were very limited and did not add to  
5 the evidence synthesis. Most case studies were uncontrolled and represent experiences of a  
6 sample of centres that chose to report their data; their outcomes may not be representative  
7 of those achieved elsewhere in the UK NHS. Their main value as evidence is the light they  
8 shed on NHS clinicians' perceptions of requirements for successful implementation and  
9 barriers to implementation of ERAS.  
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15 The impact of surgical experience and surgical volume on clinical outcomes was not  
16 explored and any implications of differences in these areas remain unknown. As enhanced  
17 recovery invariably targets the fitter, more mobile patient, frailer patients may not receive  
18 parity of access to what may be considered optimal treatment and management. Managers  
19 and clinicians considering implementing such programmes should think about the likely  
20 implication on equity of access. Whether inequity is an unintended outcome of enhanced  
21 recovery, merits further investigation.  
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28 Our review of the cost effectiveness literature suggests that enhanced recovery programmes  
29 that achieve a reduction in length of stay may save costs without detrimental effects on  
30 complication rates, readmission and health-related quality of life. However, generalisability of  
31 the results of the economic evaluations is limited by a lack of transparency in reporting, use  
32 of different settings and populations and variable methodology in analyses. Data were  
33 lacking for resource use associated with the programmes evaluated and could not usefully  
34 inform the review of economic evaluations. In addition, the clinical effectiveness of some of  
35 the programmes considered in economic evaluations was not based on robust evidence.  
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### 41 **Strengths and weaknesses**

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44 The main strength of this study was our use of multiple approaches to acquire and  
45 synthesise evidence. The main limitations were poor methodological quality and poor  
46 reporting of the included studies, and the inherent difficulty of reviewing a complex  
47 intervention in different healthcare systems and surgical specialities. Current methods for  
48 synthesising such complex interventions are limited. The methodological limitations and are  
49 not discussed here as this was outside the scope of this project, but have been addressed in  
50 previous publications (eg. Noyes et al, 2013).<sup>(58)</sup> Another complication is that elements of  
51 early enhanced recovery programmes have become accepted practice within conventional  
52 care. This evolution makes combining studies over different periods and interpreting results  
53 of earlier studies in relation to the current context more difficult.  
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4 We found a large number of systematic reviews but there was substantial overlap in the  
5 included studies and evidence was not as abundant as the existence of multiple systematic  
6 reviews suggested. Most of the RCTs were small and not high quality. With the exception of  
7 one RCT, the remainder were single centre trials and therefore appear to have been  
8 undertaken to support implementation of an enhanced recovery programme in a specific  
9 setting rather than being planned as research studies. There were significant clinical and  
10 methodological differences between individual trials, and we therefore presented a narrative  
11 synthesis. Relatively few trials were conducted in the UK and this may limit the  
12 generalisability of evidence to UK NHS settings.  
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20 Lack of evidence on important outcomes including pain and quality of life is also an issue for  
21 research in this field. Trials tended not to report on adherence to the planned enhanced  
22 recovery programme. Assessing adherence to interventions and the impact this has on  
23 health outcomes is an important issue which is often overlooked in studies, and is a  
24 limitation in the evidence base in this review.  
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29 Three additional systematic reviews of effectiveness were brought to our attention during  
30 manuscript submission. One systematic review incorporates RCTs in colorectal surgery  
31 (Greco, 2013)<sup>(59)</sup> - one incorporates RCTs and cohort studies in abdominal surgery (Neville,  
32 2014)<sup>(59)</sup> and one includes RCTs and quasi-RCTs across various surgical specialities  
33 (Nicholson, 2014)<sup>(59)</sup> The trials included in Greco (2013)<sup>(59)</sup> and Nicholson (2014)<sup>(59)</sup> overlap  
34 with those included in this review and the findings are consistent. The inclusion of these two  
35 reviews would therefore not have significantly altered the findings from this review. Neville  
36 (2014)<sup>(59)</sup> provides some additional data on patient-reported outcomes, including some  
37 evidence on post-discharge functional status. However, these outcomes were not frequently  
38 reported, and the additional evidence was mainly from study designs that would not have  
39 met the inclusion criteria for this review.  
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48 An important feature of our review is the inclusion of evidence on the implementation of  
49 enhanced recovery programmes in the UK NHS. This evidence has not been synthesised  
50 previously and the original programme websites are archived, so future access is not  
51 assured. By summarising this evidence, we have ensured that the main findings continue to  
52 be publicly available. We sought evidence on the experience of health professionals and  
53 patients of a broad range of sources and study types. Important themes emerged from this  
54 evidence that may be of value for implementing and sustaining enhanced recovery  
55 programmes in UK NHS settings. Due to the rapid nature of the evidence synthesis, the list  
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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 \(2014\)<sup>\(60\)</sup> 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.<sup>(61)</sup> 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 \(Lee, 2014\)<sup>\(59\)</sup> 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



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3 based on small numbers of patients. The lack of evidence on patient outcomes, resource  
4 use and costs precludes firm conclusions on the overall value of enhanced recovery  
5 programmes.  
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9 ERAS does not appear to reduce complication or readmission rates; the only cost benefit  
10 may lie in a reduction in post-operative bed days. Optimal care is certainly the right thing to  
11 do, but the evidence does not identify which enhanced recovery programme elements and  
12 combinations of elements are most effective. As such, conclusions on which combinations  
13 provide greatest gains and how best to implement them cannot be made.  
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18 The extent to which managers and clinicians considering implementing enhanced recovery  
19 programmes can realise reductions and cost savings will therefore depend on length of stays  
20 achieved under their existing care pathway. Important themes emerged from the relevant  
21 evidence identified on implementation, including the role of ERAS facilitators and the need  
22 for full support from management. It appears that these components are essential for the  
23 successful implementation and sustained delivery of enhanced recovery programmes in  
24 NHS settings. Consideration of potential benefit also needs to take account of the costs of  
25 service redesign, the resource use associated with programmes of this nature, the potential  
26 for improvement in patient outcomes and the impact on equity of access.  
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### 33 **Implications for research**

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36 RCTs comparing an enhanced recovery programme with conventional care continue to be  
37 conducted and published, although mostly not in the UK. Given the available evidence,  
38 further single centre RCTs of this kind are not a priority. Rather, what is needed is improved  
39 collection and reporting of how enhanced recovery programmes are implemented, resourced  
40 and experienced in NHS settings. Also, exploration into the effect that varying levels of  
41 surgical volume and surgical experience, and different discharge protocols might have on  
42 the success of an enhanced recovery pathway and subsequent outcomes. This will enhance  
43 our existing knowledge and understanding and provide evidence to support local decision-  
44 making about whether to adopt and how best to implement.  
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52 The two groups of implementation case studies included in our synthesis, although all were  
53 conducted in the UK, provide very limited information on how enhanced recovery  
54 programmes have actually been implemented in UK NHS settings. The standard reporting  
55 format originally proposed by The Enhanced Recovery Partnership Programme would  
56 enhance the value of future case studies if adhered to. Knowledge of how well the  
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3 intervention has been implemented (fidelity) is essential for understanding how and why the  
4 intervention works and hence how outcomes can be further improved. Assessing fidelity may  
5 involve considering not only adherence to the requirements of the programme but also  
6 potential moderating factors, such as strategies used to assist delivery of the intervention,  
7 quality of delivery and participant responsiveness to new practices.<sup>(62)</sup> It would be helpful if  
8 future innovation programmes used standardised reporting. For multi-site programmes, a  
9 formal synthesis of findings from all participating sites should be undertaken as part of the  
10 evaluative process. This would ensure that the insights and contextual information which can  
11 inform the wider spread and adoption (or indeed discontinuation) would be systematically  
12 captured in a generalisable format.  
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19 Adherence/compliance to elements by staff and patients also requires further investigation.  
20 Rigorous data on patients' experiences of enhanced recovery programmes are lacking.  
21 Validated tools should be used and administered independently of those providing the  
22 service. Efforts should be made to obtain data from representative samples of patients  
23 receiving conventional care as well as those treated with enhanced recovery protocols,  
24 along with evidence on the experiences of their families/carers.  
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30 Evidence relating to the cost-effectiveness of enhanced recovery programmes in UK NHS  
31 settings is lacking. Whilst enhanced recovery programmes have the potential to deliver cost  
32 savings, improved measurement of costs and benefits is crucial to help decision-makers  
33 decide how best to make optimal use of limited resources.  
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## References

1. Øvretveit J. Does Improving Quality Save Money? A Review of Evidence of Which Improvements to Quality Reduce Costs for Health Service Providers. London: The Health Foundation, 2009.
2. Øvretveit J. Does Improving Care Coordination Save Money: A Review Of Research. London: The Health Foundation, 2011.
3. Kehlet H, Slim K. The future of fast-track surgery. *Br J Surg*. 2012 Aug;99(8):1025-6.
4. Enhanced Recovery Partnership Programme. Delivering enhanced recovery – Helping patients to get better sooner after surgery. London: Department of Health, 2010 March 31st.
5. Sturm L, Cameron AL. Brief review: Fast-track surgery and enhanced recovery after surgery (ERAS) programs. Melbourne: Australian Safety and Efficacy Register of New Interventional Procedures - Surgical (ASERNIP-S), 2009 Contract No.: 3.
6. Adamina M, Kehlet H, Tomlinson GA, Senagore AJ, Delaney CP. Enhanced recovery pathways optimize health outcomes and resource utilization: a meta-analysis of randomized controlled trials in colorectal surgery. *Surgery*. 2011;149(6):830-40.
7. Ahmed J, Khan S, Lim M, Chandrasekaran TV, MacFie J. Enhanced recovery after surgery protocols - compliance and variations in practice during routine colorectal surgery. *Colorectal Dis*. 2012;14(9):1045-51.
8. Coolsen MME, Wong-Lun-Hing EM, van Dam RM, van der Wilt AA, Slim K, Lassen K, et al. A systematic review of outcomes in patients undergoing liver surgery in an enhanced recovery after surgery pathways. *HPB surgery : a world journal of hepatic, pancreatic and biliary surgery*. 2012;Early view online.
9. Coolsen MME, van Dam RM, van der Wilt AA, Slim K, Lassen K, Dejong CHC. Systematic review and meta-analysis of enhanced recovery after pancreatic surgery with particular emphasis on pancreaticoduodenectomies. *World J Surg*. 2013;Published online 09 April 2013.
10. Eskicioglu C, Forbes SS, Aarts M-A, Okrainec A, McLeod RS. Enhanced Recovery after Surgery (ERAS) programs for patients having colorectal surgery: a meta-analysis of randomized trials. *J Gastrointest Surg*. 2009 Dec;13(12):2321-9.
11. Gouvas N, Tan E, Windsor A, Xynos E, Tekkis PP. Fast-track vs standard care in colorectal surgery: a meta-analysis update. *Int J Colorectal Dis*. 2009 Oct;24(10):1119-31.
12. Hall TC, Dennison AR, Bilku DK, Metcalfe MS, Garcea G. Enhanced recovery programmes in hepatobiliary and pancreatic surgery: a systematic review. *Ann R Coll Surg Engl*. 2012;94:318-26.
13. Khan S, Wilson T, Ahmed J, Owais A, MacFie J. Quality of life and patient satisfaction with enhanced recovery protocols. *Colorectal Dis*. 2010;12(12):1175-82.
14. Lemmens L, van Zelm R, Borel Rinkes I, van Hillegersberg R, Kerckamp H. Clinical and organizational content of clinical pathways for digestive surgery: a systematic review. *Dig Surg*. 2009;26(2):91-9.

15. Rawlinson A, Kang P, Evans J, Khanna A. A systematic review of enhanced recovery protocols in colorectal surgery. *Ann R Coll Surg Engl.* 2011;93(8):583-8.
16. Spanjersberg Willem R, Reurings J, Keus F, van Laarhoven Cornelis JHM. Fast track surgery versus conventional recovery strategies for colorectal surgery. *Cochrane Database of Systematic Reviews.* 2011 (2).
17. Varadhan KK, Neal KR, Dejong CH, Fearon KC, Ljungqvist O, Lobo DN. The enhanced recovery after surgery (ERAS) pathway for patients undergoing major elective open colorectal surgery: a meta-analysis of randomized controlled trials. *Clin Nutr.* 2010;29(4):434-40.
18. Walter CJ, Collin J, Dumville JC, Drew PJ, Monson JR. Enhanced recovery in colorectal resections: a systematic review and meta-analysis. *Colorectal Dis.* 2009 May;11(4):344-53.
19. Wind J, Polle SW, Fung Kon Jin PH, Dejong CH, von Meyenfeldt MF, Ubbink DT, et al. Systematic review of enhanced recovery programmes in colonic surgery. *Br J Surg.* 2006 Jul;93(7):800-9.
20. Lv D, Wang X, Shi G. Perioperative enhanced recovery programmes for gynaecological cancer patients. *Cochrane Database of Systematic Reviews.* 2012 (12).
21. Lv L, Shao Y-f, Zhou Y-b. The enhanced recovery after surgery (ERAS) pathway for patients undergoing colorectal surgery: an update of meta-analysis of randomized controlled trials. *Int J Colorectal Dis.* 2012;27:1549-54.
22. Chen Hu J, Xin Jiang L, Cai L, Tao Zheng H, Yuan Hu S, Bing Chen H, et al. Preliminary experience of fast-track surgery combined with laparoscopy-assisted radical distal gastrectomy for gastric cancer. *J Gastrointest Surg.* 2012 Oct;16(10):1830-9.
23. Kim JW, Kim WS, Cheong JH, Hyung WJ, Choi SH, Noh SH. Safety and efficacy of fast-track surgery in laparoscopic distal gastrectomy for gastric cancer: a randomized clinical trial. *World J Surg.* 2012 Dec;36(12):2879-87.
24. Garcia-Botello S, Canovas de Lucas R, Tornero C, Escamilla B, Espi-Macias A, Esclapez-Valero P, et al. Implementation of a perioperative multimodal rehabilitation protocol in elective colorectal surgery. A prospective randomised controlled study. *Cir Esp.* 2011 Mar;89(3):159-66. PubMed PMID: 21345423.
25. Ionescu D, Iancu C, Ion D, Al-Hajjar N, Margarit S, Mocan L, et al. Implementing fast-track protocol for colorectal surgery: a prospective randomized clinical trial. *World J Surg.* 2009 Nov;33(11):2433-8.
26. Lee TG, Kang SB, Kim DW, Hong S, Heo SC, Park KJ. Comparison of early mobilization and diet rehabilitation program with conventional care after laparoscopic colon surgery: a prospective randomized controlled trial. *Dis Colon Rectum.* 2011 Jan;54(1):21-8.
27. Lemanu DP, Singh PP, Berridge K, Burr M, Birch C, Babor R, et al. Randomized clinical trial of enhanced recovery versus standard care after laparoscopic sleeve gastrectomy. *Br J Surg.* 2013 Mar;100(4):482-9.
28. Liu XX, Jiang ZW, Wang ZM, Li JS. Multimodal optimization of surgical care shows beneficial outcome in gastrectomy surgery. *JPEN J Parenter Enteral Nutr.* 2010 May-Jun;34(3):313-21.

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2  
3 29. Ren L, Zhu D, Wei Y, Pan X, Liang L, Xu J, et al. Enhanced Recovery After Surgery  
4 (ERAS) program attenuates stress and accelerates recovery in patients after radical  
5 resection for colorectal cancer: a prospective randomized controlled trial. *World J Surg.* 2012  
6 Feb;36(2):407-14.  
7
- 8 30. Wang D, Kong Y, Zhong B, Zhou X, Zhou Y. Fast-track surgery improves  
9 postoperative recovery in patients with gastric cancer: a randomized comparison with  
10 conventional postoperative care. *J Gastrointest Surg.* 2010;14(4):620-7.  
11
- 12 31. Wang G, Jiang ZW, Xu J, Gong JF, Bao Y, Xie LF, et al. Fast-track rehabilitation  
13 program vs conventional care after colorectal resection: a randomized clinical trial. *World J*  
14 *Gastroenterol.* 2011 Feb 7;17(5):671-6.  
15
- 16 32. Wang Q, Suo J, Jiang J, Wang C, Zhao YQ, Cao X. Effectiveness of fast-track  
17 rehabilitation vs conventional care in laparoscopic colorectal resection for elderly patients: a  
18 randomized trial. *Colorectal Dis.* 2012 Aug;14(8):1009-13.  
19
- 20 33. Yang DJ, Zhang S, He WL, Chen HY, Cai SR, Chen CQ, et al. Fast track surgery  
21 accelerates the recovery of postoperative insulin sensitivity. *Chin Med J.* 2012  
22 Sep;125(18):3261-5.  
23
- 24 34. Yang DJ, Zhang S, He WL, Huang WQ, Cai SR, Chen CQ, et al. Fast-track surgery  
25 accelerates the recovery of postoperative humoral immune function in elective operation for  
26 colorectal carcinoma: a randomized controlled clinical trial. *Chin Med J.* 2012 Apr  
27 24;92(16):1112-5.  
28
- 29 35. Vlug MS, Wind J, Hollmann MW, Ubbink DT, Cense HA, Engel AF, et al.  
30 Laparoscopy in combination with fast track multimodal management is the best perioperative  
31 strategy in patients undergoing colonic surgery: a randomized clinical trial (LAFA-study). *Ann*  
32 *Surg.* 2011 Dec;254(6):868-75.  
33
- 34 36. Cheng-Le Z, Xing-Zhao YX-D, Z., Bi-Cheng C, Zhen Y. Enhanced recovery after  
35 surgery programs versus traditional care for colorectal surgery: A meta-analysis of  
36 randomized controlled trials. *Dis Colon Rectum.* 2013;56:667-78.  
37
- 38 37. Aرسالani-Zadeh R, Elfadl D, Yassin N, MacFie J. Evidence-based review of  
39 enhancing postoperative recovery after breast surgery. *Br J Surg.* 2011 Feb;98(2):181-96.  
40
- 41 38. Hoffmann H, Kettelhack C. Fast-track surgery - conditions and challenges in  
42 postsurgical treatment: a review of elements of translational research in enhanced recovery  
43 after surgery. *Eur Surg Res.* 2012;49(1):24-34.  
44
- 45 39. Enhanced Recovery Partnership Programme Case Studies 2011: Gynaecology.  
46 Addenbrookes Hospital.  
47
- 48 40. Enhanced Recovery Partnership Programme Case Studies 2011: Enhanced  
49 Recovery Programme. Yeovil District Hospital NHS Foundation Trust.  
50
- 51 41. Enhanced Recovery Partnership Programme Case Studies 2011: Enhanced  
52 recovery for colorectal surgery. Yeovil District Hospital NHS Foundation Trust.  
53
- 54 42. Enhanced Recovery Partnership Programme Case Studies 2011: Colorectal,  
55 Gynaecology, Urology, MSK. Medway NHS Foundation Trust.  
56  
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3 43. Enhanced Recovery Partnership Programme Case Studies 2011: Colorectal surgery  
4 (all elective procedures) and most major emergencies from decision to treat surgically;  
5 Urology: radical Prostatectomy, Cystectomy, Nephrectomy; MSK: 1 Hip and knee  
6 replacement; Gynaecology: Hysterectomy (vaginal, abdominal and laparoscopic) moving to  
7 all majors. Royal Berkshire Hospital.  
8
- 9 44. Enhanced Recovery Partnership Programme Case Studies 2011: Enhanced  
10 recovery after colorectal surgery. Royal Berkshire Hospital.  
11
- 12 45. Aylin P, Alexandrescu R, Jen MH, Mayer EK, Bottle A. Day of week of procedure and  
13 30 day mortality for elective surgery: retrospective analysis of hospital episode statistics.  
14 BMJ. 2013 May;346:8.  
15
- 16 46. Blazeby JM, Soulsby M, Winstone K, King PM, Bulley S, Kennedy RH. A qualitative  
17 evaluation of patients' experiences of an enhanced recovery programme for colorectal  
18 cancer. Colorectal Dis. 2010 Oct;12(10 Online):e236-42.  
19
- 20 47. Taylor C, Burch J. Feedback on an enhanced recovery programme for colorectal  
21 surgery. Br J Nurs. 2011 Mar;20(5):286-90. PubMed PMID: MEDLINE:21471876.  
22
- 23 48. Reilly KA, Beard DJ, Barker KL, Dodd CA, Price AJ, Murray DW. Efficacy of an  
24 accelerated recovery protocol for Oxford unicompartmental knee arthroplasty: a randomised  
25 controlled trial. Knee. 2005;12(5):351-7.  
26
- 27 49. Archibald LH, Ott MJ, Gale CM, Zhang J, Peters MS, Stroud GK. Enhanced recovery  
28 after colon surgery in a community hospital system. Dis Colon Rectum. 2011;54(7):840-5.  
29
- 30 50. Sammour T, Zargar-Shoshtari K, Bhat A, Kahokehr A, Hill AG. A programme of  
31 Enhanced Recovery After Surgery (ERAS) is a cost-effective intervention in elective colonic  
32 surgery. N Z Med J. 2010;123(1319).  
33
- 34 51. King PM, Blazeby JM, Ewings P, Longman RJ, Kipling RM, Franks PJ, et al. The  
35 influence of an enhanced recovery programme on clinical outcomes, costs and quality of life  
36 after surgery for colorectal cancer. Colorectal Dis. 2006;8(6):506-13.  
37
- 38 52. Nielsen PR, Andreasen J, Asmussen M, Tønnesen H. Costs and quality of life for  
39 prehabilitation and early rehabilitation after surgery of the lumbar spine. BMC Health Serv  
40 Res Available from: <http://www.biomedcentral.com/1472-6963/8/209>.  
41
- 42 53. Jakobsen DH, Sonne E, Andreasen J, Kehlet H. Convalescence after colonic surgery  
43 with fast-track vs conventional care. Colorectal Dis. 2006 Oct;8(8):683-7.  
44
- 45 54. McBride N, Farrington F, Midford R. Implementing a school drug education  
46 programme: reflections on fidelity. International Journal of Health Promotion and Education.  
47 2002;40(2):40-50.  
48
- 49 55. Kariv Y, Delaney CP, Senagore AJ, Manilich EA, Hammel JP, Church JM, et al.  
50 Clinical outcomes and cost analysis of a fast track postoperative care pathway for ileal  
51 pouch-anal anastomosis. A case control study. Dis Colon Rectum. 2007;50(2):137-46.  
52
- 53 56. Salhiyyah K, Elsobky S, Raja S, Attia R, Brazier J, Cooper GJ. A clinical and  
54 economic evaluation of fast-track recovery after cardiac surgery. Heart Surgery Forum.  
55 2011;14(6):E330-4.  
56  
57  
58  
59  
60

- 1  
2  
3 57. Yanatori M, Tomita S, Miura Y, Ueno Y. Feasibility of the fast-track recovery program  
4 after cardiac surgery in Japan. *General Thoracic and Cardiovascular Surgery*.  
5 2007;55(11):445-9.  
6
- 7 58. Noyes J, Gough D, Lewin S, Mayhew A, Michie S, Pantoja T, et al. A research and  
8 development agenda for systematic reviews that ask complex questions about complex  
9 interventions. *J Clin Epidemiol*. 2013 Nov;66(11):1262-70.  
10
- 11 59. Eiselt J, Racek J, Trefil L, Opatrny Jr K. Ferric saccharate infusion enhances lipid  
12 peroxidation in hemodialysis (hd) patients [abstract]. *Nephrol Dial Transplant* [Internet]. 2001  
13 Available from: <http://onlinelibrary.wiley.com/doi/10.1093/ndt/16.10.1971>  
14 <http://onlinelibrary.wiley.com/doi/10.1093/ndt/16.10.1971>  
15 <http://onlinelibrary.wiley.com/doi/10.1093/ndt/16.10.1971>  
16
- 17 60. Pearsall EA, Meghji Z, Pitzul KB, Aarts MA, McKenzie M, McLeod RS, et al. A  
18 Qualitative Study to Understand the Barriers and Enablers in Implementing an Enhanced  
19 Recovery After Surgery Program. *Ann Surg*. 2014 Mar 18.  
20
- 21 61. Report of the Mid Staffordshire NHS Foundation Trust Public Inquiry (Chaired by  
22 Robert Francis QC). London: The Stationery Office, 2013.  
23
- 24 62. Carroll C, Patterson M, Wood S, Booth A, Rick J, Balain S. A conceptual framework  
25 for implementation fidelity. *Implementation Science*. 2007;2(1):40.  
26
- 27 63. Coolsen MME, van Dam RM, van der Wilt AA, Slim K, Lassen K, Dejong CHC.  
28 Systematic review and meta-analysis of enhanced recovery after pancreatic surgery with  
29 particular emphasis on pancreaticoduodenectomies: Supplementary Material. *World J Surg*.  
30 2013;Published online 09 April 2013.  
31  
32  
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Figure 1: Study flow diagram

For peer review only



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
<b>Colorectal/Colon surgery</b>							
Adamina (2011) <sup>(6)</sup>	✓	✓	UC	✓	UC	✓	✓
Ahmed (2012) <sup>(7)</sup>	✓	X	X	X	X	X	✓
Eskicioglu (2009) <sup>(10)</sup>	✓	✓	X	✓	✓	✓	✓
Gouvas (2009) <sup>(11)</sup>	✓	✓	X	✓	✓	✓	✓
Khan (2010) <sup>(13)</sup>	✓	✓	X	✓	X	✓	✓
Lv (2012a) <sup>(21)</sup>	✓	✓	X	X	✓	✓	✓
Rawlinson (2011) <sup>(15)</sup>	✓	X	X	✓	UC	X	UC
Spanjersberg (2011) <sup>(16)</sup>	✓	✓	✓	✓	✓	✓	✓
Varadhan (2010) <sup>(17)</sup>	✓	✓	X	✓	✓	✓	✓
Walter (2009) <sup>(18)</sup>	✓	✓	✓	✓	✓	✓	✓
Wind (2006) <sup>(19)</sup>	✓	✓	✓	✓	✓	✓	✓
<b>Gynaecological surgery</b>							
Lv (2012b) <sup>(20)</sup>	✓	X	X	X	X	✓	✓
<b>Liver/pancreatic surgery</b>							
Coolsen (2012) <sup>(8)</sup>	✓	✓	X	✓	X	✓	✓
Coolsen (2013) <sup>(9)</sup> Link to <sup>(63)</sup>	✓	✓	✓	✓	✓	✓	✓
Hall (2012) <sup>(12)</sup>	X	X	X	✓	X	✓	✓
<b>Various surgical specialities</b>							
Lemmens (2009) <sup>(14)</sup>	✓	X	X	✓	X	✓	✓
Sturm (2009) <sup>(5)</sup>	✓	X	X	✓	UC	✓	✓

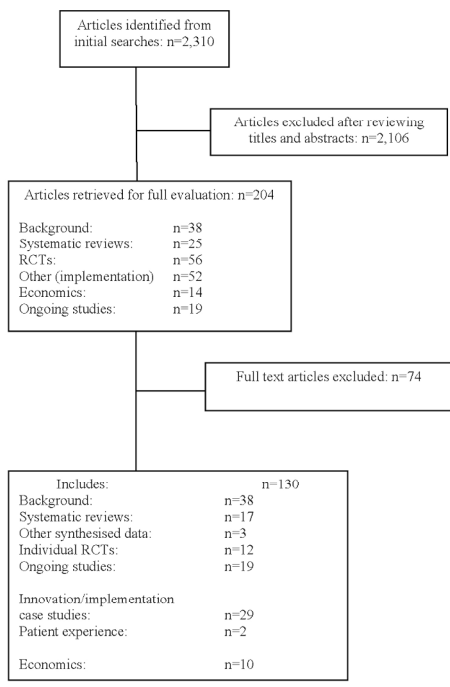
UC=unclear reporting

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
<b>Bariatric surgery</b>									
Lemanu (2013) <sup>(27)</sup>	✓	✓	X	X	X	X	NA	UC	UC
<b>Colorectal/colon surgery</b>									
Garcia-Botello (2011) <sup>(24)</sup>	UC	X	UC	X	UC	X	NA	UC	✓
Ionescu (2009) <sup>(25)</sup>	✓	✓	X	X	UC	X	NA	UC	UC
Lee (2011) <sup>(26)</sup>	✓	✓	UC	X	UC	X	NA	UC	UC
Ren (2012) <sup>(28)</sup>	✓	✓	X	X	✓	X	NA	UC	UC
Wang (2011) <sup>(31)</sup>	UC	UC	UC	X	UC	X	NA	✓	✓
Wang (2012) <sup>(32)</sup>	UC	UC	X	X	✓	UC	UC	UC	UC
Yang (2012) <sup>(33, 34)</sup>	✓	UC	X	X	UC	X	NA	X	X
<b>Gastric surgery</b>									
Chen (2012) <sup>(22)</sup>	UC	UC	X	✓	✓	X	NA	UC	UC
Kim (2012) <sup>(23)</sup>	UC	UC	X	X	X	X	NA	UC	UC
Liu (2010) <sup>(28)</sup>	UC	X	X	X	X	X	NA	UC	UC
Wang (2010) <sup>(30)</sup>	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		
<b>Adamina (2011)<sup>(8)</sup></b> 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)
<b>Ahmed (2012)<sup>(7)</sup></b> 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%)
<b>Eskicioglu (2009)<sup>(10)</sup></b> 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; $I^2=24\%$ )
<b>Gouvas (2009)<sup>(11)</sup></b> 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.
<b>Khan (2010)<sup>(13)</sup></b> 10 studies; 4 RCTs, 6 non-randomised comparative studies	Not applicable	Not applicable
<b>Lv (2012a)<sup>(21)</sup></b> 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, $I^2=0\%$ ).
<b>Rawlinson (2011)<sup>(19)</sup></b> 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.
<b>Spanjersberg (2011)<sup>(16)</sup></b> 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.
<b>Varadhan (2010)<sup>(12)</sup></b> 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; $I^2=9\%$ )
<b>Walter (2009)<sup>(18)</sup></b> 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/%)
<b>Wind (2006)<sup>(19)</sup></b> 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.
<b>Gynaecological surgery</b>		
<b>Lv (2012b)<sup>(20)</sup></b> 0 studies	Not applicable	Not applicable
<b>Liver/pancreatic surgery</b>		
<b>Coolsen (2012)<sup>(8)</sup></b> 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%
<b>Coolsen (2013)<sup>(9)</sup> Link to <sup>(63)</sup></b> 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)
<b>Hall (2012)<sup>(12)</sup></b> 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 to 14.6% (4 studies); liver 0 to 13 % (5 studies)
<b>Various surgical specialities</b>		
<b>Lemmens (2009)<sup>(14)</sup></b> 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
<b>Sturm (2009)<sup>(5)</sup></b> 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/%)
<b>Bariatric surgery</b>		
Lemanu (2013) <sup>(27)</sup>	Median days (interquartile range) Length of index admission: ERAS 1 (1 to 2); control 2 (0), 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.
<b>Colorectal/colon surgery</b>		
Ionescu (2009) <sup>(25)</sup>	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) <sup>(26)</sup>	ERAS 6.43 (3.41); control 9.16 (2.67), p=0.001	ERAS 0 (0); control 0 (0)
Ren (2012) <sup>(29)</sup>	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) <sup>(31)</sup>	Mean (SD) ERAS 5.7 (1.6); control 6.6 (2.4), p<0.001	Not reported
Wang (2012) <sup>(32)</sup>	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) <sup>(33, 34)</sup>	Median days: ERAS 5.5 (5 to 6); control 7.0 (6 to 8), p<0.001	Not reported
Ionescu (2009) <sup>(25)</sup>	Mean (SD) ERAS 6.0 (1.0); control 11.7 (3.8), p<0.05	No hospital readmissions due to complications.
<b>Gastric surgery</b>		
Chen (2012) <sup>(22)</sup>	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) <sup>(23)</sup>	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) <sup>(28)</sup>	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) <sup>(30)</sup>	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
<p><b>Salihyiah <i>et al</i> (2011)<sup>(55)</sup></b></p> <p>UK</p> <p>Hospital setting</p> <p><u>Study Population</u> Cardiac surgery Inpatients</p> <p><u>Time horizon</u> 6 months</p>	<p><u>Intervention</u> Fast-track transfer post-surgery to an independent theatre recovery unit 1-2-1 nursing (n=84)</p> <p><u>Comparator</u> Transfer post-surgery to hospital intensive care unit (n=52)</p>	<p>Economic evaluation based on a single study</p> <p><u>Perspective</u> Hospital</p> <p><u>Primary outcomes</u> Length of stay; Duration of intubation</p> <p><u>Direct Costs</u> Total expenditure of unit divided by number of patients</p> <p><u>Productivity Costs</u> n/a</p>	<p><u>Results</u> The costs and benefits were not synthesised</p> <p>mean cost FT: £4182 (SD:2284) mean cost C: £4553 (SD:1355) (p&lt;0.001)</p> <p>total LOS NSD</p> <p>8 patients failed FT &amp; were transferred to ICU</p> <p>5 patients (4 FT &amp; 1 C) required readmission</p> <p><u>Uncertainty</u> One-way &amp; multi-way sensitivity analysis demonstrated robustness in result that FT costs less than C</p>
<p><b>Lin <i>et al</i> (2011)<sup>(53)</sup></b></p> <p>China</p> <p>Hospital setting</p> <p><u>Study Population</u> Liver resection Inpatients</p> <p><u>Time horizon</u> Not reported</p>	<p><u>Intervention</u> 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 &lt;24 hours, planned discharge 6 days post-surgery (n=56)</p> <p><u>Comparator</u> Conventional pathway (limited reporting) (n=61)</p>	<p>Economic evaluation based on a single study</p> <p><u>Perspective</u> Hospital</p> <p><u>Primary outcomes</u> Length of stay; Complications; Mortality; Readmission</p> <p><u>Direct Costs</u> Hospital charges: operation and anaesthesia; pharmacy; auxiliary examination; other</p> <p><u>Productivity Costs</u> n/a</p>	<p><u>Results</u> The costs and benefits were not synthesised</p> <p>mean charge pre-pathway RMB 26,626 mean charge post-pathway RMB 21,004 (p&lt;0.05)</p> <p>LOS reduced from 11 days to 7 days (p&lt;0.005) Complications, mortality &amp; readmissions NSD</p> <p><u>Uncertainty</u> n/a</p>
<p><b>Kariv <i>et al</i> (2006)<sup>(56)</sup></b></p> <p>USA</p> <p>Hospital setting</p> <p><u>Study Population</u> Patients undergoing open ileoanal pouch surgery</p>	<p><u>Intervention</u> 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</p>	<p>Economic evaluation based on a single study</p> <p><u>Perspective</u> Hospital</p> <p><u>Primary outcomes</u> Length of stay; Readmission; Reoperation</p> <p><u>Direct Costs</u> Total costs for each of the categories were presented:</p>	<p><u>Results</u> The costs and benefits were not synthesised</p> <p>total per case cost FT US\$ 5,692 total per case cost C US\$ 6672 diff US\$980 (p=0.001)</p> <p>median postoperative los FT = 4 days C= 5 days (p=0.012) NSD in readmission outcomes</p>

Study Details	Study Comparators	Main Analytical Approaches, primary outcomes, and costs	Incremental cost-effectiveness (ICER) estimates and Decision Uncertainty
<p><u>Time horizon</u> 30 days</p>	<p>days (n=97)</p> <p><u>Comparator</u> 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)</p>	<p>per case of hospitalisation; operating room; radiology; anaesthesia; pharmacy; laboratory; ICU; and nursing care</p> <p><u>Productivity Costs</u> n/a</p>	<p><u>Uncertainty</u> n/a</p>
<p><b>Yanatori <i>et al</i> (2007)<sup>[57]</sup></b></p> <p>Japan</p> <p>Hospital setting</p> <p><u>Study Population</u> Cardiovascular surgery (cardiac arrest requiring cardiopulmonary bypass)</p> <p><u>Time horizon</u> 2 years</p>	<p><u>Intervention</u> Admitted 4 days prior to surgery, preoperative education by nurses, surgeons and rehab staff; discharge at day 7 post surgery</p> <p><u>Comparator</u> Conventional protocol – details not reported</p>	<p>Economic evaluation based on a single study</p> <p><u>Perspective</u> Healthcare provider/hospital</p> <p><u>Primary outcomes</u> Length of stay; Complications</p> <p><u>Direct Costs</u> Only total costs were presented</p> <p><u>Productivity Costs</u> n/a</p>	<p><u>Results</u> The costs and benefits were not synthesised</p> <p>Total mean cost for FT YEN 712,545 Total mean cost for C YEN 383,268 (p=0.038)</p> <p>Mean post-op LOS FT=15(12.4) C=36.7(6) (p=0.01)</p> <p><u>Uncertainty</u> n/a</p>
<p><b>Larsen <i>et al</i> (2009)<sup>[54]</sup></b></p> <p>Denmark</p> <p>Hospital setting</p> <p><u>Study Population</u> All patients for elective primary total hip/knee arthroplasty or unicompartmental knee arthroplasty</p> <p><u>Time horizon</u> One year</p>	<p><u>Intervention</u> 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)</p> <p><u>Comparator</u> Patients receive info on day of admission; patients randomly among wards, various nurses in charge of care; and various occupational and physiotherapists 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)</p>	<p>Economic evaluation based on a single study</p> <p><u>Perspective</u> Societal</p> <p><u>Primary outcomes</u> Length of stay; Adverse events (first 3months)</p> <p><u>Health-related quality-of-life</u> QALYS (EQ-5D) (baseline to 3 months)</p> <p><u>Direct Costs</u> 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</p> <p><u>Productivity Costs</u> Average wage rate for age-specific groups</p>	<p><u>Results</u> Accelerated intervention was both more effective and less costly than the comparator</p> <p>Average total cost for I DKK90,227 (+/- 47,475)</p> <p>Average total cost for C DKK71,344 (+/- 39,958)</p> <p>Average QALYs was 0.83 for the intervention and 0.78 in the comparator.</p> <p>Average QALY gain for hip patients I v C = 0.08 (CI: 0.02 to 0.05) (p=0.006)</p> <p>Average QALY gain for knee patients was NS</p> <p><u>Uncertainty</u> Bootstrapping, uni and multivariate</p>



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

Study Details	Study Comparators	Main Analytical Approaches, primary outcomes, and costs	Incremental cost-effectiveness (ICER) estimates and Decision Uncertainty
<p>Hospital setting</p> <p><u>Study Population</u> Lumbar fusion patients with degenerative lumbar disease</p> <p><u>Time horizon</u> 6 months</p>	<p>operation technique, better pain reduction, early nutrition and aggressive post-op mobilisation (n=28)</p> <p><u>Comparator</u> Standard care, not including components above (n=32)</p>	<p>Societal</p> <p><u>Primary outcome</u> Measured using 15D-score (self-reported at inclusion, day of surgery, day of discharge, and 1, 3 and 6 months post-op)</p> <p><u>Direct Costs</u> 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.</p> <p><u>Productivity costs</u> Based on return to work rates &amp; Danish average daily wage</p>	<p>Intervention direct cost 1,174 Euros per patient compared with 1,668 for standard care</p> <p>Intervention productivity costs were 8,021 Euros compared with 9,152 for standard care</p> <p>NS difference in HR quality of life scores</p> <p><u>Uncertainty</u> Optimistic and pessimistic scenarios varying individually pre-op costs, post-op hospital costs, direct costs, and productivity costs</p>
<p><b>Reilly et al(2005)<sup>(48)</sup></b></p> <p>UK</p> <p>Hospital setting</p> <p><u>Study Population</u> Patients undergoing unicompartmental knee arthroplasty</p> <p><u>Time horizon</u> Unclear</p>	<p><u>Intervention</u> Accelerated discharge: aim to discharge day after surgery (n=20)</p> <p><u>Comparator</u> Standard discharge: approx. 5 days post-surgery (n=21)</p>	<p>Economic evaluation based on a single study</p> <p><u>Perspective</u> Hospital</p> <p><u>Primary outcome</u> Oxford Knee Assessment</p> <p><u>Direct Costs</u> Fixed costs (surgical staff, anaesthetics, prosthesis, pharmacy), outpatient appointment, specialist registrar time.</p> <p><u>Productivity costs</u> n/a</p>	<p><u>Results</u> The costs and benefits were not synthesised</p> <p>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)</p> <p>Total costs for intervention per patient £3,391 compared with £4,634 for standard care</p> <p><u>Uncertainty</u> n/a</p>
<p><b>Archibald<sup>(49)</sup></b></p> <p>USA</p> <p>Hospital setting</p> <p><u>Study Population</u> Colorectal surgery patients</p> <p><u>Time horizon</u> unclear</p>	<p><u>Intervention</u> 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 &amp; 770 not enrolled)</p> <p><u>Comparator</u> Standard care historical baseline (n=1673)</p>	<p>Economic evaluation based on a study comparing two time periods, where ERAS was available in one and not in the other.</p> <p><u>Primary outcome</u> Length of stay ; POD; Readmission</p> <p><u>Direct Costs</u> Hospital costs (total direct and indirect costs identified via hospital billing system)</p> <p><u>Productivity costs</u> n/a</p>	<p><u>Results</u> The costs and benefits were not synthesised</p> <p>Mean LOS for the intervention was 8.4 days compared with 6.9 days for the comparator (p&lt;0.0001); Mean POD for the intervention was 7.6 days compared with 6.3 days (p&lt;0.0001)</p> <p>Mean hospital cost for the intervention population was US\$18,741 compared with US\$16,978 for the comparator.</p> <p><u>Uncertainty</u> n/a</p>

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# PRISMA 2009 Checklist

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Section/topic	#	Checklist item	Reported on page #
<b>TITLE</b>			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
<b>ABSTRACT</b>			
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
<b>INTRODUCTION</b>			
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
<b>METHODS</b>			
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

Page 1 of 2

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
<b>RESULTS</b>			
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
<b>DISCUSSION</b>			
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
<b>FUNDING</b>			
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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# BMJ Open

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

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Date Submitted by the Author:	01-Jul-2014
Complete List of Authors:	Paton, Fiona; University of York, Centre for Reviews and Dissemination Chambers, Duncan; The University of York, Centre for Reviews and Dissemination Wilson, Paul; University of York, Centre for Reviews and Dissemination Eastwood, Alison; University of York, Centre for Reviews and Dissemination Craig, Dawn; University of York, Centre for Reviews and Dissemination Fox, Dave; University of York, Centre for Reviews and Dissemination Jayne, David; Leeds Teaching Hospitals, McGinnes, Erika; Leeds Teaching Hospitals,
<b>Primary Subject Heading</b>:	Surgery
Secondary Subject Heading:	Health services research
Keywords:	enhanced recovery, fast track, length of hospital stay

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3 **Effectiveness and implementation of enhanced recovery after surgery programmes: a**  
4 **rapid evidence synthesis**  
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7 Fiona Paton, Duncan Chambers, Paul Wilson, Alison Eastwood, Dawn Craig, Dave Fox,  
8 David Jayne, Erika McGinnes  
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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.
- Although 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.<sup>(1,2)</sup> 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<sup>(3)</sup> 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

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3 clinical and cost effectiveness of enhanced recovery programmes, and the implementation,  
4 delivery and impact of such programmes in secondary care settings in the UK.  
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### 7 **Methods**

8 Eight databases, including DARE, NHS EED and MEDLINE were searched to from 1990 to  
9 March 2013 without language restrictions. The PROSPERO database was searched to  
10 identify ongoing systematic reviews. Relevant reports and guidelines were screened for  
11 further studies. Reference lists of retrieved articles, reviews and evaluations were scanned,  
12 and relevant individuals contacted for additional evidence.  
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18 Systematic reviews, RCTs not included in the systematic reviews, economic evaluations,  
19 and UK NHS cost analysis studies were included if they evaluated the impact of enhanced  
20 recovery programmes (encompassing different combinations of the main preoperative,  
21 intraoperative and postoperative pathway elements described by the Enhanced Recovery Partnership  
22 Programme<sup>(4)</sup> on health or cost-related outcomes. Eligible studies included patients  
23 undergoing elective surgery in an acute hospital in the UK NHS or a comparable healthcare  
24 system. Comparators were only relevant to clinical and cost-effectiveness evaluations, and  
25 included conventional (usual/standard) care without a structured multimodal enhanced  
26 recovery patient pathway (as defined in the included studies). Case studies, impact  
27 assessments and surveys of patient experience that documented the experience of  
28 implementing enhanced recovery in a UK setting were also eligible.  
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36 Quality assessment of systematic reviews, RCTs and economic evaluations was based on  
37 existing CRD critical appraisal methods (<http://www.crd.york.ac.uk/crdweb/HomePage.asp>;  
38 CRD, 2009). Cost analysis studies, studies of patient experience, and case studies of  
39 implementation were not formally quality assessed.  
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44 All stages of the review process were performed by one researcher and checked by a  
45 second. Disagreements between reviewers were resolved by discussion or by recourse to a  
46 third reviewer where necessary.  
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50 The type and range of evidence precluded meta-analysis and we therefore performed a  
51 narrative synthesis, differentiating clinical outcomes (eg. mobilisation, mortality and  
52 morbidity, and length of hospital stay), patient-reported outcomes (eg. patient experience  
53 and satisfaction), resource use in secondary care (eg. workforce utilisation and costs), and  
54 implementation case studies.  
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## Results

Seventeen systematic reviews<sup>(5-21)</sup> and 12 additional RCTs<sup>(22-34)</sup> 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.<sup>(35)</sup> 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.<sup>(7)</sup> Ahmed (2012)<sup>(7)</sup> 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)<sup>(19)</sup> to 3.75 days (95% CI 5.11 to 2.40 days).<sup>(18)</sup> Evidence from individual RCTs in colorectal

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3 surgery also suggest reduced length of hospital stay following an ERAS programme (mean  
4 length of stay 4.15 days to 6.43 days) compared to conventional care (mean length of stay  
5 6.6 days to 11.7 days). There were no significant differences in reported readmission rates,  
6 but it was unclear how readmissions were defined and measured in the reviews and RCTs.  
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10 Other surgical specialties showed greater variation in reported reductions in length of stay,  
11 but this is likely to reflect the greater uncertainty due to the more limited evidence base for  
12 these specialties. Statistical heterogeneity varied between reviews and was often not  
13 formally explored, but may have reflected differences in ERAS protocols, lack of compliance  
14 with important ERAS elements, and differences in surgical populations and procedures.  
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19 Deaths were rare and no significant differences between treatment groups were found in the  
20 systematic reviews and additional RCTs, regardless of surgical speciality. Morbidity was  
21 defined differently across systematic reviews and RCTs; rates between treatment groups  
22 were sometimes inconsistent, but generally indicated no statistically significant differences.  
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27 Mobilisation rates were inconsistent across systematic reviews, but most reported no  
28 significant differences in time to mobilisation between treatment groups. Mobilisation was  
29 rarely reported as an outcome in the additional RCTs.  
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33 Where systematic reviews and additional RCTs assessed quality of life and patient  
34 experience/satisfaction, equivocal findings were reported. Evidence on reintervention rates,  
35 pain and resource use was lacking in both systematic reviews and RCTs.  
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### 39 **Other Reviews**

40 A systematic review in colorectal surgery, identified after the last literature search, showed  
41 similar findings to the systematic reviews discussed above.<sup>(36)</sup> Mean length of primary  
42 hospital stay was statistically significantly reduced in ERAS patients; mean difference (MD) -  
43 2.44 (95% CI -3.06 to -1.83; 11 RCTs) but with significant statistical heterogeneity ( $I^2=88%$ ).  
44 There was no evidence to suggest increased rates of readmissions, complications and  
45 mortality. Some of the individual RCT results for primary length of stay did not appear to be  
46 consistent with results reported in other systematic reviews, and this may have impacted on  
47 the estimated reduction in length of primary hospital stay.<sup>(36)</sup>  
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55 Two reviews<sup>(37, 38)</sup> focusing on individual ERAS elements were identified, both of which  
56 highlighted the lack of evidence on the full ERAS pathway and the lack of compliance with  
57 ERAS protocols. Details can be found in the full review (in press).  
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### **Case studies**

Ten of 14 UK NHS innovation sites provided adequate data for inclusion in this section.<sup>(39-41)</sup> 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,<sup>(39, 42-44)</sup> 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,<sup>(45)</sup> the capacity to implement ERAS throughout the working week might ensure continuity of best care and help mitigate against such variation.

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3 We included two published studies of patient experience of ERAS.<sup>(46, 47)</sup> Each study used  
4 qualitative research methods to analyse audiotaped material. The two studies provided  
5 limited evidence suggesting that patients who were willing to provide feedback took a  
6 positive view of their experience of treatment in an ERAS programme. The studies  
7 suggested that patients were willing to comment on their experience in a way that can help  
8 healthcare providers to identify areas for improvement.  
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### 12 **Cost-effectiveness**

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

#### 31 **Statement of Principal Findings**

32 Overall, the systematic reviews and additional RCTs suggest that length of hospital stay is  
33 reduced in ERAS patients compared to patients receiving conventional care. The evidence  
34 was based mainly on colorectal surgery and the applicability of findings to other surgical  
35 specialities remains less clear. Evidence for colorectal surgery suggests that enhanced  
36 recovery programmes may reduce hospital stays by 0.5 to 3.5 days compared with  
37 conventional care.  
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44 There were marked differences in length of stay across reviews and individual studies  
45 regardless of speciality. These differences may reflect differences in ERAS protocols,  
46 compliance to ERAS programmes, health care systems and procedures, and/or outcome  
47 definitions. This raises questions regarding the magnitude of effect of the ERAS protocols on  
48 length of stay, which may be overstated in some reviews.  
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53 The evidence suggests that ERAS programmes do not compromise patient morbidity,  
54 mortality and readmission rates but outcome definitions varied across reviews and individual  
55 studies. Such differences make it difficult to determine the reliability and generalisability of  
56 the findings.  
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4 Equivocal findings were reported for quality of life and patient experience/satisfaction but the  
5 evidence was based on few studies, which utilised various methods to measure these  
6 outcomes. The limited evidence precludes conclusions on the effects of ERAS protocols on  
7 pain, mobilisation and reintervention.  
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12 The implementation evidence included resource use in terms of the professionals involved in  
13 delivery of enhanced recovery programmes, but details were very limited and did not add to  
14 the evidence synthesis. Most case studies were uncontrolled and represent experiences of a  
15 sample of centres that chose to report their data; their outcomes may not be representative  
16 of those achieved elsewhere in the UK NHS. Their main value as evidence is the light they  
17 shed on NHS clinicians' perceptions of requirements for successful implementation and  
18 barriers to implementation of ERAS.  
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24 The impact of surgical experience and surgical volume on clinical outcomes was not  
25 explored and any implications of differences in these areas remain unknown. As enhanced  
26 recovery invariably targets the fitter, more mobile patient, frailer patients may not receive  
27 parity of access to what may be considered optimal treatment and management. Managers  
28 and clinicians considering implementing such programmes should think about the likely  
29 implication on equity of access. Whether inequity is an unintended outcome of enhanced  
30 recovery, merits further investigation.  
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37 Our review of the cost effectiveness literature suggests that enhanced recovery programmes  
38 that achieve a reduction in length of stay may save costs without detrimental effects on  
39 complication rates, readmission and health-related quality of life. However, generalisability of  
40 the results of the economic evaluations is limited by a lack of transparency in reporting, use  
41 of different settings and populations and variable methodology in analyses. Data were  
42 lacking for resource use associated with the programmes evaluated and could not usefully  
43 inform the review of economic evaluations. In addition, the clinical effectiveness of some of  
44 the programmes considered in economic evaluations was not based on robust evidence.  
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### 50 **Strengths and weaknesses**

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53 The main strength of this study was our use of multiple approaches to acquire and  
54 synthesise evidence. The main limitations were poor methodological quality and poor  
55 reporting of the included studies, and the inherent difficulty of reviewing a complex  
56 intervention in different healthcare systems and surgical specialities. Current methods for  
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3 synthesising such complex interventions are limited. The methodological limitations and are  
4 not discussed here as this was outside the scope of this project, but have been addressed in  
5 previous publications (eg. Noyes et al, 2013).<sup>(58)</sup> Another complication is that elements of  
6 early enhanced recovery programmes have become accepted practice within conventional  
7 care. This evolution makes combining studies over different periods and interpreting results  
8 of earlier studies in relation to the current context more difficult.  
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13 We found a large number of systematic reviews but there was substantial overlap in the  
14 included studies and evidence was not as abundant as the existence of multiple systematic  
15 reviews suggested. Most of the RCTs were small and not high quality. With the exception of  
16 one RCT, the remainder were single centre trials and therefore appear to have been  
17 undertaken to support implementation of an enhanced recovery programme in a specific  
18 setting rather than being planned as research studies. There were significant clinical and  
19 methodological differences between individual trials, and we therefore presented a narrative  
20 synthesis. Relatively few trials were conducted in the UK and this may limit the  
21 generalisability of evidence to UK NHS settings.  
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29 Lack of evidence on important outcomes including pain and quality of life is also an issue for  
30 research in this field. Trials tended not to report on adherence to the planned enhanced  
31 recovery programme. Assessing adherence to interventions and the impact this has on  
32 health outcomes is an important issue which is often overlooked in studies, and is a  
33 limitation in the evidence base in this review.  
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38 Three additional systematic reviews of effectiveness were brought to our attention during  
39 manuscript submission. One systematic review incorporates RCTs in colorectal surgery  
40 (Greco, 2013),<sup>(59)</sup> one incorporates RCTs and cohort studies in abdominal surgery (Neville,  
41 2014)<sup>(59)</sup> and one includes RCTs and quasi-RCTs across various surgical specialities  
42 (Nicholson, 2014).<sup>(59)</sup> The trials included in Greco (2013)<sup>(59)</sup> and Nicholson (2014)<sup>(59)</sup> overlap  
43 with those included in this review and the findings are consistent. The inclusion of these two  
44 reviews would therefore not have significantly altered the findings from this review. Neville  
45 (2014)<sup>(59)</sup> provides some additional data on patient-reported outcomes, including some  
46 evidence on post-discharge functional status. However, these outcomes were not frequently  
47 reported, and the additional evidence was mainly from study designs that would not have  
48 met the inclusion criteria for this review.  
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56 An important feature of our review is the inclusion of evidence on the implementation of  
57 enhanced recovery programmes in the UK NHS. This evidence has not been synthesised  
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3 previously and the original programme websites are archived, so future access is not  
4 assured. By summarising this evidence, we have ensured that the main findings continue to  
5 be publicly available. We sought evidence on the experience of health professionals and  
6 patients of a broad range of sources and study types. Important themes emerged from this  
7 evidence that may be of value for implementing and sustaining enhanced recovery  
8 programmes in UK NHS settings. Due to the rapid nature of the evidence synthesis, the list  
9 of sources searched to identify data on implementation and delivery of enhanced recovery  
10 programmes was not exhaustive and we acknowledge that relevant evidence may have  
11 been missed. Indeed, evidence from Scotland has been noted and eligible case studies  
12 have been identified from the NHS Scotland Quality Improvement Hub website. It should be  
13 noted that these are as limited as those included in the review. A qualitative study was  
14 brought to our attention at peer review; the study was published after our final search date.  
15 Pearsall et al (2014)<sup>(60)</sup> conducted a qualitative study to explore the barriers and enablers in  
16 implementing an enhanced recovery after surgery programme in a University hospital in  
17 Canada. The themes identified are consistent with those reported in this review.  
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27 However, case studies are susceptible to risk of bias. Use of a standard reporting format  
28 was a potential strength of the case studies but variation in what each site actually reported  
29 (particularly in terms of evidence of benefit from the introduction of enhanced recovery  
30 programmes) reduced the usefulness of the evidence.  
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35 We sought to incorporate published and unpublished evidence on patient experiences and  
36 views of enhanced recovery programmes. Evaluation of patient experience of care is  
37 increasingly important for the NHS, especially in view of unacceptable failures of care such  
38 as those highlighted in the Francis Report.<sup>(61)</sup> Though the evidence was generally positive for  
39 enhanced recovery, it was limited by a shortage of studies that used validated measures of  
40 patient experience and by study designs that could bias results in favour of enhanced  
41 recovery.  
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47 A further strength of this study was the consideration of cost-effectiveness evidence, but the  
48 nature of the evidence did not permit any analyses. There is a clear need to capture better  
49 evaluated data on costs and benefits of enhanced recovery programmes from a clearly  
50 stated perspective. A systematic review of economic evaluations (Lee, 2014)<sup>(62)</sup> was brought  
51 to our attention during manuscript publication. The review confirmed the need for well-  
52 designed research to determine the cost-effectiveness of enhanced recovery programmes  
53 from both the institutional and societal perspectives.  
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### 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.

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4 The two groups of implementation case studies included in our synthesis, although all were  
5 conducted in the UK, provide very limited information on how enhanced recovery  
6 programmes have actually been implemented in UK NHS settings. The standard reporting  
7 format originally proposed by The Enhanced Recovery Partnership Programme would  
8 enhance the value of future case studies if adhered to. Knowledge of how well the  
9 intervention has been implemented (fidelity) is essential for understanding how and why the  
10 intervention works and hence how outcomes can be further improved. Assessing fidelity may  
11 involve considering not only adherence to the requirements of the programme but also  
12 potential moderating factors, such as strategies used to assist delivery of the intervention,  
13 quality of delivery and participant responsiveness to new practices.<sup>(63)</sup> It would be helpful if  
14 future innovation programmes used standardised reporting. For multi-site programmes, a  
15 formal synthesis of findings from all participating sites should be undertaken as part of the  
16 evaluative process. This would ensure that the insights and contextual information which can  
17 inform the wider spread and adoption (or indeed discontinuation) would be systematically  
18 captured in a generalisable format.  
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29 Adherence/compliance to elements by staff and patients also requires further investigation.  
30 Rigorous data on patients' experiences of enhanced recovery programmes are lacking.  
31 Validated tools should be used and administered independently of those providing the  
32 service. Efforts should be made to obtain data from representative samples of patients  
33 receiving conventional care as well as those treated with enhanced recovery protocols,  
34 along with evidence on the experiences of their families/carers.  
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40 Evidence relating to the cost-effectiveness of enhanced recovery programmes in UK NHS  
41 settings is lacking. Whilst enhanced recovery programmes have the potential to deliver cost  
42 savings, improved measurement of costs and benefits is crucial to help decision-makers  
43 decide how best to make optimal use of limited resources.  
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49 **Word Count: 4,179**  
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6

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9  
10

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13 the final review write-up. D Chambers and FP were involved in all stages of the rapid  
14 synthesis including production of the final review write-up. DF conducted literature searches  
15 and contributed to the methods section of the review. DJ and EMcG provided advice  
16 throughout the rapid synthesis and commented on the draft review.  
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23 [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) and declare: no support from any organisation for the  
24 submitted work; no financial relationships with any organisations that might have an interest  
25 in the submitted work in the previous three years; no other relationships or activities that  
26 could appear to have influenced the submitted work.  
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32 **Transparency declaration:** The lead author (the manuscript's guarantor) affirms that this  
33 manuscript is an honest, accurate, and transparent account of the study being reported; that  
34 no important aspects of the study have been omitted; and that any discrepancies from the  
35 study as planned (and, if relevant, registered) have been explained.  
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39 **Data sharing:** No additional data available.  
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## References

1. Øvretveit J. Does Improving Quality Save Money? A Review of Evidence of Which Improvements to Quality Reduce Costs for Health Service Providers. London: The Health Foundation, 2009.
2. Øvretveit J. Does Improving Care Coordination Save Money: A Review Of Research. London: The Health Foundation, 2011.
3. Kehlet H, Slim K. The future of fast-track surgery. *Br J Surg*. 2012 Aug;99(8):1025-6.
4. Enhanced Recovery Partnership Programme. Delivering enhanced recovery – Helping patients to get better sooner after surgery. London: Department of Health, 2010 March 31st.
5. Sturm L, Cameron AL. Brief review: Fast-track surgery and enhanced recovery after surgery (ERAS) programs. Melbourne: Australian Safety and Efficacy Register of New Interventional Procedures - Surgical (ASERNIP-S), 2009 Contract No.: 3.
6. Adamina M, Kehlet H, Tomlinson GA, et al. Enhanced recovery pathways optimize health outcomes and resource utilization: a meta-analysis of randomized controlled trials in colorectal surgery. *Surgery*. 2011;149(6):830-40. PubMed PMID: DARE-12011003749. Pubmed Central PMCID: Get SR
7. Ahmed J, Khan S, Lim M, Chandrasekaran TV, et al. Enhanced recovery after surgery protocols - compliance and variations in practice during routine colorectal surgery. *Colorectal Dis*. 2012;14(9):1045-51.
8. Coolsen MME, Wong-Lun-Hing EM, van Dam RM, et al. A systematic review of outcomes in patients undergoing liver surgery in an enhanced recovery after surgery pathways. *HPB surgery : a world journal of hepatic, pancreatic and biliary surgery*. 2012;Early view online.
9. Coolsen MME, van Dam RM, van der Wilt AA, et al. Systematic review and meta-analysis of enhanced recovery after pancreatic surgery with particular emphasis on pancreaticoduodenectomies. *World J Surg*. 2013;Published online 09 April 2013.
10. Eskicioglu C, Forbes SS, Aarts M-A, et al. Enhanced Recovery after Surgery (ERAS) programs for patients having colorectal surgery: a meta-analysis of randomized trials. *J Gastrointest Surg*. 2009 Dec;13(12):2321-9.
11. Gouvas N, Tan E, Windsor A, et al. Fast-track vs standard care in colorectal surgery: a meta-analysis update. *Int J Colorectal Dis*. 2009 Oct;24(10):1119-31.
12. Hall TC, Dennison AR, Bilku DK, et al. Enhanced recovery programmes in hepatobiliary and pancreatic surgery: a systematic review. *Ann R Coll Surg Engl*. 2012;94:318-26.
13. Khan S, Wilson T, Ahmed J, et al. Quality of life and patient satisfaction with enhanced recovery protocols. *Colorectal Dis*. 2010;12(12):1175-82.
14. Lemmens L, van Zelm R, Borel Rinkes I, et al. Clinical and organizational content of clinical pathways for digestive surgery: a systematic review. *Dig Surg*. 2009;26(2):91-9.

15. Rawlinson A, Kang P, Evans J, et al. A systematic review of enhanced recovery protocols in colorectal surgery. *Ann R Coll Surg Engl.* 2011;93(8):583-8.
16. Spanjersberg Willem R, Reurings J, Keus F, et al. Fast track surgery versus conventional recovery strategies for colorectal surgery. *Cochrane Database of Systematic Reviews.* 2011 (2).
17. Varadhan KK, Neal KR, Dejong CH, et al. The enhanced recovery after surgery (ERAS) pathway for patients undergoing major elective open colorectal surgery: a meta-analysis of randomized controlled trials. *Clin Nutr.* 2010;29(4):434-40.
18. Walter CJ, Collin J, Dumville JC, et al. Enhanced recovery in colorectal resections: a systematic review and meta-analysis. *Colorectal Dis.* 2009 May;11(4):344-53.
19. Wind J, Polle SW, Fung Kon Jin PH, et al. Systematic review of enhanced recovery programmes in colonic surgery. *Br J Surg.* 2006 Jul;93(7):800-9.
20. Lv D, Wang X, Shi G. Perioperative enhanced recovery programmes for gynaecological cancer patients. *Cochrane Database of Systematic Reviews.* 2012 (12).
21. Lv L, Shao Y-f, Zhou Y-b. The enhanced recovery after surgery (ERAS) pathway for patients undergoing colorectal surgery: an update of meta-analysis of randomized controlled trials. *Int J Colorectal Dis.* 2012;27:1549-54.
22. Chen Hu J, Xin Jiang L, Cai L, T et al. Preliminary experience of fast-track surgery combined with laparoscopy-assisted radical distal gastrectomy for gastric cancer. *J Gastrointest Surg.* 2012 Oct;16(10):1830-9.
23. Kim JW, Kim WS, Cheong JH, et al. Safety and efficacy of fast-track surgery in laparoscopic distal gastrectomy for gastric cancer: a randomized clinical trial. *World J Surg.* 2012 Dec;36(12):2879-87.
24. Garcia-Botello S, Canovas de Lucas R, et al. Implementation of a perioperative multimodal rehabilitation protocol in elective colorectal surgery. A prospective randomised controlled study. *Cir Esp.* 2011 Mar;89(3):159-66.
25. Ionescu D, Iancu C, Ion D, et al. Implementing fast-track protocol for colorectal surgery: a prospective randomized clinical trial. *World J Surg.* 2009 Nov;33(11):2433-8.
26. Lee TG, Kang SB, Kim DW, et al. Comparison of early mobilization and diet rehabilitation program with conventional care after laparoscopic colon surgery: a prospective randomized controlled trial. *Dis Colon Rectum.* 2011 Jan;54(1):21-8.
27. Lemanu DP, Singh PP, Berridge K, et al. Randomized clinical trial of enhanced recovery versus standard care after laparoscopic sleeve gastrectomy. *Br J Surg.* 2013 Mar;100(4):482-9.
28. Liu XX, Jiang ZW, Wang ZM, et al. Multimodal optimization of surgical care shows beneficial outcome in gastrectomy surgery. *JPEN J Parenter Enteral Nutr.* 2010 May-Jun;34(3):313-21.
29. Ren L, Zhu D, Wei Y, Pan X, et al. Enhanced Recovery After Surgery (ERAS) program attenuates stress and accelerates recovery in patients after radical resection for colorectal cancer: a prospective randomized controlled trial. *World J Surg.* 2012 Feb;36(2):407-14.



- 1  
2  
3 30. Wang D, Kong Y, Zhong B, et al. Fast-track surgery improves postoperative recovery  
4 in patients with gastric cancer: a randomized comparison with conventional postoperative  
5 care. *J Gastrointest Surg*. 2010;14(4):620-7.  
6
- 7 31. Wang G, Jiang ZW, Xu J, et al. Fast-track rehabilitation program vs conventional  
8 care after colorectal resection: a randomized clinical trial. *World J Gastroenterol*. 2011 Feb  
9 7;17(5):671-6.  
10
- 11 32. Wang Q, Suo J, Jiang J, et al. Effectiveness of fast-track rehabilitation vs  
12 conventional care in laparoscopic colorectal resection for elderly patients: a randomized trial.  
13 *Colorectal Dis*. 2012 Aug;14(8):1009-13.  
14
- 15 33. Yang DJ, Zhang S, He WL, et al. Fast track surgery accelerates the recovery of  
16 postoperative insulin sensitivity. *Chin Med J*. 2012 Sep;125(18):3261-5.  
17
- 18 34. Yang DJ, Zhang S, He WL, et al. Fast-track surgery accelerates the recovery of  
19 postoperative humoral immune function in elective operation for colorectal carcinoma: a  
20 randomized controlled clinical trial. *Chin Med J*. 2012 Apr 24;92(16):1112-5.  
21
- 22 35. Vlug MS, Wind J, Hollmann MW, et al. Laparoscopy in combination with fast track  
23 multimodal management is the best perioperative strategy in patients undergoing colonic  
24 surgery: a randomized clinical trial (LAFAs-study). *Ann Surg*. 2011 Dec;254(6):868-75.  
25
- 26 36. Cheng-Le Z, Xing-Zhao Y, Xiao-Dong Z, et al. Enhanced recovery after surgery  
27 programs versus traditional care for colorectal surgery: A meta-analysis of randomized  
28 controlled trials. *Dis Colon Rectum*. 2013;56:667-78.  
29
- 30 37. Arsalani-Zadeh R, Elfadl D, Yassin N, MacFie J. Evidence-based review of  
31 enhancing postoperative recovery after breast surgery. *Br J Surg*. 2011 Feb;98(2):181-96.  
32
- 33 38. Hoffmann H, Kettelhack C. Fast-track surgery - conditions and challenges in  
34 postsurgical treatment: a review of elements of translational research in enhanced recovery  
35 after surgery. *Eur Surg Res*. 2012;49(1):24-34.  
36
- 37 39. Lin CH, Wang FC, Lin SC, et al. Antipsychotic combination using low-dose  
38 antipsychotics is as efficacious and safe as, but cheaper, than optimal-dose monotherapy in  
39 the treatment of schizophrenia: A randomized, double-blind study. *Int Clin Psychopharmacol*.  
40 2013;28(5):267-74.  
41
- 42 40. Werner D, Locke C. Experiences of chronic stress one year after the Gulf oil spill.  
43 *International Journal of Emergency Mental Health*. 2012;14(4):239-45.  
44
- 45 41. Advenier, Kapsambelis. Psychiatric diagnosis in the age of industrial medicine.  
46 French . References. *Topique*. 2013.  
47
- 48 42. Christodoulou NG, Christodoulou GN. Financial crises: Impact on mental health and  
49 suggested responses. *Psychother Psychosom*. 2013;82(5):279-84.  
50
- 51 43. Morrissey JP, Domino ME, Cuddeback GS. Assessing the effectiveness of recovery-  
52 oriented ACT in reducing state psychiatric hospital use. *Psychiatr Serv*. 2013;64(4):303-11.  
53
- 54 44. Kirk Jr TA, Di Leo P, Rehmer P, et al. A case and care management program to  
55 reduce use of acute care by clients with substance use disorders. *Psychiatr Serv*.  
56 2013;64(5):491-3.  
57  
58  
59  
60

- 1  
2  
3 45. Aylin P, Alexandrescu R, Jen MH, et al. Day of week of procedure and 30 day  
4 mortality for elective surgery: retrospective analysis of hospital episode statistics. *BMJ*. 2013  
5 May;346:8.  
6  
7 46. Blazeby JM, Soulsby M, Winstone K, et al. A qualitative evaluation of patients'  
8 experiences of an enhanced recovery programme for colorectal cancer. *Colorectal Dis*. 2010  
9 Oct;12(10 Online):e236-42.  
10  
11 47. Taylor C, Burch J. Feedback on an enhanced recovery programme for colorectal  
12 surgery. *Br J Nurs*. 2011 2011 Mar;20(5):286-90.  
13  
14 48. Reilly KA, Beard DJ, Barker KL, et al. Efficacy of an accelerated recovery protocol for  
15 Oxford unicompartmental knee arthroplasty: a randomised controlled trial. *Knee*.  
16 2005;12(5):351-7.  
17  
18 49. Archibald LH, Ott MJ, Gale CM, et al. Enhanced recovery after colon surgery in a  
19 community hospital system. *Dis Colon Rectum*. 2011;54(7):840-5.  
20  
21 50. Sammour T, Zargar-Shoshtari K, Bhat A, et al. A programme of Enhanced Recovery  
22 After Surgery (ERAS) is a cost-effective intervention in elective colonic surgery. *N Z Med J*.  
23 2010;123(1319).  
24  
25 51. King PM, Blazeby JM, Ewings P, et al. The influence of an enhanced recovery  
26 programme on clinical outcomes, costs and quality of life after surgery for colorectal cancer.  
27 *Colorectal Dis*. 2006;8(6):506-13.  
28  
29 52. Nielsen PR, Andreasen J, Asmussen M, et al. Costs and quality of life for  
30 prehabilitation and early rehabilitation after surgery of the lumbar spine. *BMC Health Serv*  
31 *Res [Internet]*. 2008 26/06/13; 8:[209 p.]. Available from:  
32 <http://www.biomedcentral.com/1472-6963/8/209>.  
33  
34 53. Jakobsen DH, Sonne E, Andreasen J, et al. Convalescence after colonic surgery with  
35 fast-track vs conventional care. *Colorectal Dis*. 2006 Oct;8(8):683-7.  
36  
37 54. McBride N, Farrington F, Midford R. Implementing a school drug education  
38 programme: reflections on fidelity. *International Journal of Health Promotion and Education*.  
39 2002;40(2):40-50.  
40  
41 55. Kariv Y, Delaney CP, Senagore AJ, et al. Clinical outcomes and cost analysis of a  
42 fast track postoperative care pathway for ileal pouch-anal anastomosis. A case control study.  
43 *Dis Colon Rectum*. 2007;50(2):137-46.  
44  
45 56. Salhiyyah K, Elsobky S, Raja S, et al. A clinical and economic evaluation of fast-track  
46 recovery after cardiac surgery. *Heart Surgery Forum*. 2011;14(6):E330-4.  
47  
48 57. Yanatori M, Tomita S, Miura Y, et al. Feasibility of the fast-track recovery program  
49 after cardiac surgery in Japan. *General Thoracic and Cardiovascular Surgery*.  
50 2007;55(11):445-9.  
51  
52 58. Noyes J, Gough D, Lewin S, et al. A research and development agenda for  
53 systematic reviews that ask complex questions about complex interventions. *J Clin*  
54 *Epidemiol*. 2013 Nov;66(11):1262-70.  
55  
56 59. Eiselt J, Racek J, Trefil L, et al. Ferric saccharate infusion enhances lipid  
57 peroxidation in hemodialysis (hd) patients [abstract]. *Nephrol Dial Transplant [Internet]*.  
58  
59  
60

1  
2  
3 2001; 16(6):[A141 p.]. Available from:

4 <http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2168.2013.02903.x>

5  
6 60. Pearsall EA, Meghji Z, Pitzul KB, et al. A Qualitative Study to Understand the Barriers  
7 and Enablers in Implementing an Enhanced Recovery After Surgery Program. *Ann Surg.*  
8 2014 Mar 18.

9  
10 61. Hilty DM, Ferrer DC, Parish MB, et al. The effectiveness of telemental health: a 2013  
11 review. *Review. Telemedicine and e-Health.* 2013;19(6):444-54.

12  
13 62. Lee L, Li C, Landry T, Latimer E, et al. A Systematic Review of Economic  
14 Evaluations of Enhanced Recovery Pathways for Colorectal Surgery. *Ann Surg.*  
15 2014;259(4):670-6 10.

16  
17 63. Carroll C, Patterson M, Wood S, et al. A conceptual framework for implementation  
18 fidelity. *Implementation Science.* 2007;2(1):40.

19  
20 64. Coolson MME, van Dam RM, van der Wilt AA, et al. Systematic review and meta-  
21 analysis of enhanced recovery after pancreatic surgery with particular emphasis on  
22 pancreaticoduodenectomies: Supplementary Material. *World J Surg.* 2013; Published online  
23 09 April 2013.

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
<b>Colorectal/Colon surgery</b>							
Adamina (2011) <sup>(6)</sup>	✓	✓	UC	✓	UC	✓	✓
Ahmed (2012) <sup>(7)</sup>	✓	X	X	X	X	X	✓
Eskicioglu (2009) <sup>(10)</sup>	✓	✓	X	✓	✓	✓	✓
Gouvas (2009) <sup>(11)</sup>	✓	✓	X	✓	✓	✓	✓
Khan (2010) <sup>(13)</sup>	✓	✓	X	✓	X	✓	✓
Lv (2012a) <sup>(21)</sup>	✓	✓	X	X	✓	✓	✓
Rawlinson (2011) <sup>(15)</sup>	✓	X	X	✓	UC	X	UC
Spanjersberg (2011) <sup>(16)</sup>	✓	✓	✓	✓	✓	✓	✓
Varadhan (2010) <sup>(17)</sup>	✓	✓	X	✓	✓	✓	✓
Walter (2009) <sup>(18)</sup>	✓	✓	✓	✓	✓	✓	✓
Wind (2006) <sup>(19)</sup>	✓	✓	✓	✓	✓	✓	✓
<b>Gynaecological surgery</b>							
Lv (2012b) <sup>(20)</sup>	✓	X	X	X	X	✓	✓
<b>Liver/pancreatic surgery</b>							
Coolsen (2012) <sup>(8)</sup>	✓	✓	X	✓	X	✓	✓
Coolsen (2013) <sup>(9)</sup> Link to <sup>(64)</sup>	✓	✓	✓	✓	✓	✓	✓
Hall (2012) <sup>(12)</sup>	X	X	X	✓	X	✓	✓
<b>Various surgical specialities</b>							
Lemmens (2009) <sup>(14)</sup>	✓	X	X	✓	X	✓	✓
Sturm (2009) <sup>(5)</sup>	✓	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
<b>Bariatric surgery</b>									
Lemanu (2013) <sup>(27)</sup>	✓	✓	X	X	X	X	NA	UC	UC
<b>Colorectal/colon surgery</b>									
Garcia-Botello (2011) <sup>(24)</sup>	UC	X	UC	X	UC	X	NA	UC	✓
Ionescu (2009) <sup>(25)</sup>	✓	✓	X	X	UC	X	NA	UC	UC
Lee (2011) <sup>(26)</sup>	✓	✓	UC	X	UC	X	NA	UC	UC
Ren (2012) <sup>(28)</sup>	✓	✓	X	X	✓	X	NA	UC	UC
Wang (2011) <sup>(31)</sup>	UC	UC	UC	X	UC	X	NA	✓	✓
Wang (2012) <sup>(32)</sup>	UC	UC	X	X	✓	UC	UC	UC	UC
Yang (2012) <sup>(33, 34)</sup>	✓	UC	X	X	UC	X	NA	X	X
<b>Gastric surgery</b>									
Chen (2012) <sup>(22)</sup>	UC	UC	X	✓	✓	X	NA	UC	UC
Kim (2012) <sup>(23)</sup>	UC	UC	X	X	X	X	NA	UC	UC
Liu (2010) <sup>(28)</sup>	UC	X	X	X	X	X	NA	UC	UC
Wang (2010) <sup>(30)</sup>	UC	UC	X	X	UC	X	NA	X	X

UC: unclear reporting; NA: not applicable

Figure 1: Study flow diagram

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3 **Effectiveness and implementation of enhanced recovery after surgery programmes: a**  
4 **rapid evidence synthesis**  
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7 Fiona Paton, Duncan Chambers, Paul Wilson, Alison Eastwood, Dawn Craig, Dave Fox,  
8 David Jayne, Erika McGinnes  
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10

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12 stages. D Craig was involved in all stages of the economic evaluation including production of  
13 the final review write-up. D Chambers and FP were involved in all stages of the rapid  
14 synthesis including production of the final review write-up. DF conducted literature searches  
15 and contributed to the methods section of the review. DJ and EMcG provided advice  
16 throughout the rapid synthesis and commented on the draft review.  
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23 [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) and declare: no support from any organisation for the  
24 submitted work; no financial relationships with any organisations that might have an interest  
25 in the submitted work in the previous three years; no other relationships or activities that  
26 could appear to have influenced the submitted work.  
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32 **Transparency declaration:** The lead author (the manuscript's guarantor) affirms that this  
33 manuscript is an honest, accurate, and transparent account of the study being reported; that  
34 no important aspects of the study have been omitted; and that any discrepancies from the  
35 study as planned (and, if relevant, registered) have been explained.  
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39 **Data sharing:** No additional data available.  
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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: ~~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.
- Although 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.<sup>(1,2)</sup> 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<sup>(3)</sup> 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

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3 clinical and cost effectiveness of enhanced recovery programmes, and the implementation,  
4 delivery and impact of such programmes in secondary care settings in the UK.  
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### 7 **Methods**

8 Eight databases, including DARE, NHS EED and MEDLINE were searched to from 1990 to  
9 March 2013 without language restrictions. The PROSPERO database was searched to  
10 identify ongoing systematic reviews. Relevant reports and guidelines were screened for  
11 further studies. Reference lists of retrieved articles, reviews and evaluations were scanned,  
12 and relevant individuals contacted for additional evidence.  
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17 Systematic reviews, RCTs not included in the systematic reviews, economic evaluations,  
18 and UK NHS cost analysis studies were included if they evaluated the impact of enhanced  
19 recovery programmes (encompassing different combinations of the main preoperative,  
20 intraoperative and postoperative pathway elements described by the Enhanced Recovery Partnership  
21 Programme<sup>(4)</sup> on health or cost-related outcomes. Eligible studies included patients  
22 undergoing elective surgery in an acute hospital in the UK NHS or a comparable healthcare  
23 system. Comparators were only relevant to clinical and cost-effectiveness evaluations, and  
24 included conventional (usual/standard) care without a structured multimodal enhanced  
25 recovery patient pathway (as defined in the included studies). Case studies, impact  
26 assessments and surveys of patient experience that documented the experience of  
27 implementing enhanced recovery in a UK setting were also eligible.  
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36 Quality assessment of systematic reviews, RCTs and economic evaluations was based on  
37 existing CRD critical appraisal methods (<http://www.crd.york.ac.uk/crdweb/HomePage.asp>;  
38 CRD, 2009). Cost analysis studies, studies of patient experience, and case studies of  
39 implementation were not formally quality assessed.  
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43 All stages of the review process were performed by one researcher and checked by a  
44 second. Disagreements between reviewers were resolved by discussion or by recourse to a  
45 third reviewer where necessary.  
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49 The type and range of evidence precluded meta-analysis and we therefore performed a  
50 narrative synthesis, differentiating clinical outcomes (eg. mobilisation, mortality and  
51 morbidity, and length of hospital stay), patient-reported outcomes (eg. patient experience  
52 and satisfaction), resource use in secondary care (eg. workforce utilisation and costs), and  
53 implementation case studies.  
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## Results

Seventeen systematic reviews<sup>(5-21)</sup> and 12 additional RCTs<sup>(22-34)</sup> 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.<sup>(35)</sup> 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.<sup>(7)</sup> Ahmed (2012)<sup>(7)</sup> 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)<sup>(19)</sup> to 3.75 days (95% CI 5.11 to 2.40 days).<sup>(18)</sup> (Walter 2009) Evidence from

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3 individual RCTs in colorectal surgery also suggest reduced length of hospital stay following  
4 an ERAS programme (mean length of stay 4.15 days to 6.43 days) compared to  
5 conventional care (mean length of stay 6.6 days to 11.7 days). There were no significant  
6 differences in reported readmission rates, but it was unclear how readmissions were defined  
7 and measured in the reviews and RCTs.  
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12 Other surgical specialties showed greater variation in reported reductions in length of stay,  
13 but this is likely to reflect the greater uncertainty due to the more limited evidence base for  
14 these specialties. Statistical heterogeneity varied between reviews and was often not  
15 formally explored, but may have reflected differences in ERAS protocols, lack of compliance  
16 with important ERAS elements, and differences in surgical populations and procedures.  
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21 Deaths were rare and no significant differences between treatment groups were found in the  
22 systematic reviews and additional RCTs, regardless of surgical speciality. Morbidity was  
23 defined differently across systematic reviews and RCTs; rates between treatment groups  
24 were sometimes inconsistent, but generally indicated no statistically significant differences.  
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29 Mobilisation rates were inconsistent across systematic reviews, but most reported no  
30 significant differences in time to mobilisation between treatment groups. Mobilisation was  
31 rarely reported as an outcome in the additional RCTs.  
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35 Where systematic reviews and additional RCTs assessed quality of life and patient  
36 experience/satisfaction, equivocal findings were reported. Evidence on reintervention rates,  
37 pain and resource use was lacking in both systematic reviews and RCTs.  
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#### 40 41 **Other Reviews**

42 A systematic review in colorectal surgery, identified after the last literature search, showed  
43 similar findings to the systematic reviews discussed above.<sup>(36)</sup> Mean length of primary  
44 hospital stay was statistically significantly reduced in ERAS patients; mean difference (MD) -  
45 2.44 (95% CI -3.06 to -1.83; 11 RCTs) but with significant statistical heterogeneity ( $I^2=88\%$ ).  
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47 There was no evidence to suggest increased rates of readmissions, complications and  
48 mortality. Some of the individual RCT results for primary length of stay did not appear to be  
49 consistent with results reported in other systematic reviews, and this may have impacted on  
50 the estimated reduction in length of primary hospital stay.<sup>(36)</sup>  
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Two reviews<sup>(37, 38)</sup> 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. ~~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.<sup>(39-41)</sup> 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,<sup>(39, 42-44)</sup> 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,<sup>(45)</sup> the capacity to implement ERAS

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3 throughout the working week might ensure continuity of best care and help mitigate against  
4 such variation.  
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7 We included two published studies of patient experience of ERAS.<sup>(46, 47)</sup> Each study used  
8 qualitative research methods to analyse audiotaped material. The two studies provided  
9 limited evidence suggesting that patients who were willing to provide feedback took a  
10 positive view of their experience of treatment in an ERAS programme. The studies  
11 suggested that patients were willing to comment on their experience in a way that can help  
12 healthcare providers to identify areas for improvement.  
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### 17 **Cost-effectiveness**

18 Ten economic evaluations in adult populations undergoing various surgical procedures  
19 evaluated costs and outcomes over short time horizons ([see Table 5 supplementary table](#)  
20 [3](#)).<sup>(48-57)</sup> All of the evaluations suggested that programmes that achieve a reduction in length  
21 of stay are cost saving, and are not to the detriment of patients in terms of complication  
22 rates, readmission and health-related quality-of-life. The quality of the clinical studies on  
23 which these evaluations were based was variable, but generally poor. The generalisability of  
24 the results of these evaluations was limited by a lack of transparency in reporting, and the  
25 disparity in standard protocols and what had been evaluated across the settings made it  
26 unfeasible to select a cost-effective programme.  
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### 34 **Discussion**

#### 35 **Statement of Principal Findings**

36 Overall, the systematic reviews and additional RCTs suggest that length of hospital stay is  
37 reduced in ERAS patients compared to patients receiving conventional care. The evidence  
38 was based mainly on colorectal surgery and the applicability of findings to other surgical  
39 specialities remains less clear. Evidence for colorectal surgery suggests that enhanced  
40 recovery programmes may reduce hospital stays by 0.5 to 3.5 days compared with  
41 conventional care.  
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48 There were marked differences in length of stay across reviews and individual studies  
49 regardless of speciality. These differences may reflect differences in ERAS protocols,  
50 [compliance to ERAS programmes,](#) ~~and~~ health care systems [and procedures,](#) and/or  
51 outcome definitions. This raises questions regarding the magnitude of effect of the ERAS  
52 protocols on length of stay, which may be overstated in some reviews.  
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3 The evidence suggests that ERAS programmes do not compromise patient morbidity,  
4 mortality and readmission rates but outcome definitions varied across reviews and individual  
5 studies. Such differences make it difficult to determine the reliability and generalisability of  
6 the findings.  
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10 Equivocal findings were reported for quality of life and patient experience/satisfaction but the  
11 evidence was based on few studies, which utilised various methods to measure these  
12 outcomes. The limited evidence precludes conclusions on the effects of ERAS protocols on  
13 pain, mobilisation and reintervention.  
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18 The implementation evidence included resource use in terms of the professionals involved in  
19 delivery of enhanced recovery programmes, but details were very limited and did not add to  
20 the evidence synthesis. Most case studies were uncontrolled and represent experiences of a  
21 sample of centres that chose to report their data; their outcomes may not be representative  
22 of those achieved elsewhere in the UK NHS. Their main value as evidence is the light they  
23 shed on NHS clinicians' perceptions of requirements for successful implementation and  
24 barriers to implementation of ERAS.  
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30 The impact of surgical experience and surgical volume on clinical outcomes was not  
31 explored and any implications of differences in these areas remain unknown. As enhanced  
32 recovery invariably targets the fitter, more mobile patient, frailer patients may not receive  
33 parity of access to what may be considered optimal treatment and management. Managers  
34 and clinicians considering implementing such programmes should think about the likely  
35 implication on equity of access. Whether inequity is an unintended outcome of enhanced  
36 recovery, merits further investigation.  
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43 Our review of the cost effectiveness literature suggests that enhanced recovery programmes  
44 that achieve a reduction in length of stay may save costs without detrimental effects on  
45 complication rates, readmission and health-related quality of life. However, generalisability of  
46 the results of the economic evaluations is limited by a lack of transparency in reporting, use  
47 of different settings and populations and variable methodology in analyses. Data were  
48 lacking for resource use associated with the programmes evaluated and could not usefully  
49 inform the review of economic evaluations. In addition, the clinical effectiveness of some of  
50 the programmes considered in economic evaluations was not based on robust evidence.  
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### 55 56 **Strengths and weaknesses** 57 58 59 60



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3 The main strength of this study was our use of multiple approaches to acquire and  
4 synthesise evidence. The main limitations were poor methodological quality and poor  
5 reporting of the included studies, and the inherent difficulty of reviewing a complex  
6 intervention in different healthcare systems and surgical specialities. Current methods for  
7 synthesising such complex interventions are limited. The methodological limitations and are  
8 not discussed here as this was outside the scope of this project, but have been addressed in  
9 previous publications (eg. Noyes et al, 2013).<sup>(58)</sup> Another complication is that elements of  
10 early enhanced recovery programmes have become accepted practice within conventional  
11 care. This evolution makes combining studies over different periods and interpreting results  
12 of earlier studies in relation to the current context more difficult.  
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20 We found a large number of systematic reviews but there was substantial overlap in the  
21 included studies and evidence was not as abundant as the existence of multiple systematic  
22 reviews suggested. Most of the RCTs were small and not high quality. With the exception of  
23 one RCT, the remainder were single centre trials and therefore appear to have been  
24 undertaken to support implementation of an enhanced recovery programme in a specific  
25 setting rather than being planned as research studies. There were significant clinical and  
26 methodological differences between individual trials, and we therefore presented a narrative  
27 synthesis. Relatively few trials were conducted in the UK and this may limit the  
28 generalisability of evidence to UK NHS settings.  
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35 Lack of evidence on important outcomes including pain and quality of life is also an issue for  
36 research in this field. Trials tended not to report on adherence to the planned enhanced  
37 recovery programme. Assessing adherence to interventions and the impact this has on  
38 health outcomes is an important issue which is often overlooked in studies, and is a  
39 limitation in the evidence base in this review.  
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44 Three additional systematic reviews of effectiveness were brought to our attention during  
45 manuscript submission. One systematic review incorporates RCTs in colorectal surgery  
46 (Greco, 2013),<sup>(59)</sup> one incorporates RCTs and cohort studies in abdominal surgery (Neville,  
47 2014)<sup>(59)</sup> and one includes RCTs and quasi-RCTs across various surgical specialities  
48 (Nicholson, 2014).<sup>(59)</sup> The trials included in Greco (2013)<sup>(59)</sup> and Nicholson (2014)<sup>(59)</sup> overlap  
49 with those included in this review and the findings are consistent. The inclusion of these two  
50 reviews would therefore not have significantly altered the findings from this review. Neville  
51 (2014)<sup>(59)</sup> provides some additional data on patient-reported outcomes, including some  
52 evidence on post-discharge functional status. However, these outcomes were not frequently  
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3 [reported, and the additional evidence was mainly from study designs that would not have](#)  
4 [met the inclusion criteria for this review.](#)  
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8 An important feature of our review is the inclusion of evidence on the implementation of  
9 enhanced recovery programmes in the UK NHS. This evidence has not been synthesised  
10 previously and the original programme websites are archived, so future access is not  
11 assured. By summarising this evidence, we have ensured that the main findings continue to  
12 be publicly available. We sought evidence on the experience of health professionals and  
13 patients of a broad range of sources and study types. Important themes emerged from this  
14 evidence that may be of value for implementing and sustaining enhanced recovery  
15 programmes in UK NHS settings. Due to the rapid nature of the evidence synthesis, the list  
16 of sources searched to identify data on implementation and delivery of enhanced recovery  
17 programmes was not exhaustive and we acknowledge that relevant evidence may have  
18 been missed. Indeed, evidence from Scotland has been noted and eligible case studies  
19 have been identified from the NHS Scotland Quality Improvement Hub website. It should be  
20 noted that these are as limited as those included in the review. [A qualitative study was](#)  
21 [brought to our attention at peer review; the study was published after our final search date.](#)  
22 [Pearsall et al \(2014\)<sup>\(60\)</sup> conducted a qualitative study to explore the barriers and enablers in](#)  
23 [implementing an enhanced recovery after surgery programme in a University hospital in](#)  
24 [Canada. The themes identified are consistent with those reported in this review.](#)  
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35 However, case studies are susceptible to risk of bias. Use of a standard reporting format  
36 was a potential strength of the case studies but variation in what each site actually reported  
37 (particularly in terms of evidence of benefit from the introduction of enhanced recovery  
38 programmes) reduced the usefulness of the evidence.  
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42 We sought to incorporate published and unpublished evidence on patient experiences and  
43 views of enhanced recovery programmes. Evaluation of patient experience of care is  
44 increasingly important for the NHS, especially in view of unacceptable failures of care such  
45 as those highlighted in the Francis Report.<sup>(61)</sup> Though the evidence was generally positive for  
46 enhanced recovery, it was limited by a shortage of studies that used validated measures of  
47 patient experience and by study designs that could bias results in favour of enhanced  
48 recovery.  
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55 A further strength of this study was the consideration of cost-effectiveness evidence, but the  
56 nature of the evidence did not permit any analyses. There is a clear need to capture better  
57 evaluated data on costs and benefits of enhanced recovery programmes from a clearly  
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3 stated perspective. A systematic review of economic evaluations (Lee, 2014)<sup>(62)</sup> was brought  
4 to our attention during manuscript publication. The review confirmed the need for well-  
5 designed research to determine the cost-effectiveness of enhanced recovery programmes  
6 from both the institutional and societal perspectives.  
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### 10 **Implications for healthcare**

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13 Overall, there is consistent, albeit limited, evidence that enhanced recovery programmes can  
14 reduce length of patient hospital stay without increasing readmission rates. Data on re-  
15 intervention rates and patient-reported outcomes did not suggest significant differences  
16 between enhanced recovery and conventional care, but the evidence was very limited and  
17 based on small numbers of patients. The lack of evidence on patient outcomes, resource  
18 use and costs precludes firm conclusions on the overall value of enhanced recovery  
19 programmes.  
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26 ERAS does not appear to reduce complication or readmission rates; the only cost benefit  
27 may lie in a reduction in post-operative bed days. Optimal care is certainly the right thing to  
28 do, but the evidence does not identify which enhanced recovery programme elements and  
29 combinations of elements are most effective. As such, conclusions on which combinations  
30 provide greatest gains and how best to implement them cannot be made.  
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35 The extent to which managers and clinicians considering implementing enhanced recovery  
36 programmes can realise reductions and cost savings will therefore depend on length of stays  
37 achieved under their existing care pathway. Important themes emerged from the relevant  
38 evidence identified on implementation, including the role of ERAS facilitators and the need  
39 for full support from management. It appears that these components are essential for the  
40 successful implementation and sustained delivery of enhanced recovery programmes in  
41 NHS settings. Consideration of potential benefit also needs to take account of the costs of  
42 service redesign, the resource use associated with programmes of this nature, the potential  
43 for improvement in patient outcomes and the impact on equity of access.  
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### 50 **Implications for research**

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53 RCTs comparing an enhanced recovery programme with conventional care continue to be  
54 conducted and published, although mostly not in the UK. Given the available evidence,  
55 further single centre RCTs of this kind are not a priority. Rather, what is needed is improved  
56 collection and reporting of how enhanced recovery programmes are implemented, resourced  
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3 and experienced in NHS settings. Also, exploration into the effect that varying levels of  
4 surgical volume and surgical experience, and different discharge protocols might have on  
5 the success of an enhanced recovery pathway and subsequent outcomes. This will enhance  
6 our existing knowledge and understanding and provide evidence to support local decision-  
7 making about whether to adopt and how best to implement.  
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12 The two groups of implementation case studies included in our synthesis, although all were  
13 conducted in the UK, provide very limited information on how enhanced recovery  
14 programmes have actually been implemented in UK NHS settings. The standard reporting  
15 format originally proposed by The Enhanced Recovery Partnership Programme would  
16 enhance the value of future case studies if adhered to. Knowledge of how well the  
17 intervention has been implemented (fidelity) is essential for understanding how and why the  
18 intervention works and hence how outcomes can be further improved. Assessing fidelity may  
19 involve considering not only adherence to the requirements of the programme but also  
20 potential moderating factors, such as strategies used to assist delivery of the intervention,  
21 quality of delivery and participant responsiveness to new practices.<sup>(63)</sup> It would be helpful if  
22 future innovation programmes used standardised reporting. For multi-site programmes, a  
23 formal synthesis of findings from all participating sites should be undertaken as part of the  
24 evaluative process. This would ensure that the insights and contextual information which can  
25 inform the wider spread and adoption (or indeed discontinuation) would be systematically  
26 captured in a generalisable format.  
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36 Adherence/compliance to elements by staff and patients also requires further investigation.  
37 Rigorous data on patients' experiences of enhanced recovery programmes are lacking.  
38 Validated tools should be used and administered independently of those providing the  
39 service. Efforts should be made to obtain data from representative samples of patients  
40 receiving conventional care as well as those treated with enhanced recovery protocols,  
41 along with evidence on the experiences of their families/carers.  
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47 Evidence relating to the cost-effectiveness of enhanced recovery programmes in UK NHS  
48 settings is lacking. Whilst enhanced recovery programmes have the potential to deliver cost  
49 savings, improved measurement of costs and benefits is crucial to help decision-makers  
50 decide how best to make optimal use of limited resources.  
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For peer review only

## References

1. Øvretveit J. Does Improving Quality Save Money? A Review of Evidence of Which Improvements to Quality Reduce Costs for Health Service Providers. London: The Health Foundation, 2009.
2. Øvretveit J. Does Improving Care Coordination Save Money: A Review Of Research. London: The Health Foundation, 2011.
3. Kehlet H, Slim K. The future of fast-track surgery. *Br J Surg*. 2012 Aug;99(8):1025-6.
4. Enhanced Recovery Partnership Programme. Delivering enhanced recovery – Helping patients to get better sooner after surgery. London: Department of Health, 2010 March 31st.
5. Sturm L, Cameron AL. Brief review: Fast-track surgery and enhanced recovery after surgery (ERAS) programs. Melbourne: Australian Safety and Efficacy Register of New Interventional Procedures - Surgical (ASERNIP-S), 2009 Contract No.: 3.
6. Adamina M, Kehlet H, Tomlinson GA, Senagore AJ, Delaney CP. Enhanced recovery pathways optimize health outcomes and resource utilization: a meta-analysis of randomized controlled trials in colorectal surgery. *Surgery*. 2011;149(6):830-40. PubMed PMID: DARE-12011003749. Pubmed Central PMCID: Get SR
7. Ahmed J, Khan S, Lim M, Chandrasekaran TV, MacFie J. Enhanced recovery after surgery protocols - compliance and variations in practice during routine colorectal surgery. *Colorectal Dis*. 2012;14(9):1045-51.
8. Coolsen MME, Wong-Lun-Hing EM, van Dam RM, van der Wilt AA, Slim K, Lassen K, et al. A systematic review of outcomes in patients undergoing liver surgery in an enhanced recovery after surgery pathways. *HPB surgery : a world journal of hepatic, pancreatic and biliary surgery*. 2012;Early view online.
9. Coolsen MME, van Dam RM, van der Wilt AA, Slim K, Lassen K, Dejong CHC. Systematic review and meta-analysis of enhanced recovery after pancreatic surgery with particular emphasis on pancreaticoduodenectomies. *World J Surg*. 2013;Published online 09 April 2013.
10. Eskicioglu C, Forbes SS, Aarts M-A, Okrainec A, McLeod RS. Enhanced Recovery after Surgery (ERAS) programs for patients having colorectal surgery: a meta-analysis of randomized trials. *J Gastrointest Surg*. 2009 Dec;13(12):2321-9.
11. Gouvas N, Tan E, Windsor A, Xynos E, Tekkis PP. Fast-track vs standard care in colorectal surgery: a meta-analysis update. *Int J Colorectal Dis*. 2009 Oct;24(10):1119-31.
12. Hall TC, Dennison AR, Bilku DK, Metcalfe MS, Garcea G. Enhanced recovery programmes in hepatobiliary and pancreatic surgery: a systematic review. *Ann R Coll Surg Engl*. 2012;94:318-26.
13. Khan S, Wilson T, Ahmed J, Owais A, MacFie J. Quality of life and patient satisfaction with enhanced recovery protocols. *Colorectal Dis*. 2010;12(12):1175-82.

- 1  
2  
3 14. Lemmens L, van Zelm R, Borel Rinkes I, van Hillegersberg R, Kerkkamp H. Clinical  
4 and organizational content of clinical pathways for digestive surgery: a systematic review.  
5 *Dig Surg*. 2009;26(2):91-9.  
6
- 7 15. Rawlinson A, Kang P, Evans J, Khanna A. A systematic review of enhanced recovery  
8 protocols in colorectal surgery. *Ann R Coll Surg Engl*. 2011;93(8):583-8.  
9
- 10 16. Spanjersberg Willem R, Reurings J, Keus F, van Laarhoven Cornelis JHM. Fast track  
11 surgery versus conventional recovery strategies for colorectal surgery. *Cochrane Database*  
12 *of Systematic Reviews*. 2011 (2).  
13
- 14 17. Varadhan KK, Neal KR, Dejong CH, Fearon KC, Ljungqvist O, Lobo DN. The  
15 enhanced recovery after surgery (ERAS) pathway for patients undergoing major elective  
16 open colorectal surgery: a meta-analysis of randomized controlled trials. *Clin Nutr*.  
17 2010;29(4):434-40.  
18
- 19 18. Walter CJ, Collin J, Dumville JC, Drew PJ, Monson JR. Enhanced recovery in  
20 colorectal resections: a systematic review and meta-analysis. *Colorectal Dis*. 2009  
21 May;11(4):344-53.  
22
- 23 19. Wind J, Polle SW, Fung Kon Jin PH, Dejong CH, von Meyenfeldt MF, Ubbink DT, et  
24 al. Systematic review of enhanced recovery programmes in colonic surgery. *Br J Surg*. 2006  
25 Jul;93(7):800-9.  
26
- 27 20. Lv D, Wang X, Shi G. Perioperative enhanced recovery programmes for  
28 gynaecological cancer patients. *Cochrane Database of Systematic Reviews*. 2012 (12).  
29
- 30 21. Lv L, Shao Y-f, Zhou Y-b. The enhanced recovery after surgery (ERAS) pathway for  
31 patients undergoing colorectal surgery: an update of meta-analysis of randomized controlled  
32 trials. *Int J Colorectal Dis*. 2012;27:1549-54.  
33
- 34 22. Chen Hu J, Xin Jiang L, Cai L, Tao Zheng H, Yuan Hu S, Bing Chen H, et al.  
35 Preliminary experience of fast-track surgery combined with laparoscopy-assisted radical  
36 distal gastrectomy for gastric cancer. *J Gastrointest Surg*. 2012 Oct;16(10):1830-9.  
37
- 38 23. Kim JW, Kim WS, Cheong JH, Hyung WJ, Choi SH, Noh SH. Safety and efficacy of  
39 fast-track surgery in laparoscopic distal gastrectomy for gastric cancer: a randomized clinical  
40 trial. *World J Surg*. 2012 Dec;36(12):2879-87.  
41
- 42 24. Garcia-Botello S, Canovas de Lucas R, Tornero C, Escamilla B, Espi-Macias A,  
43 Esclapez-Valero P, et al. Implementation of a perioperative multimodal rehabilitation protocol  
44 in elective colorectal surgery. A prospective randomised controlled study. *Cir Esp*. 2011  
45 Mar;89(3):159-66.  
46
- 47 25. Ionescu D, Iancu C, Ion D, Al-Hajjar N, Margarit S, Mocan L, et al. Implementing fast-  
48 track protocol for colorectal surgery: a prospective randomized clinical trial. *World J Surg*.  
49 2009 Nov;33(11):2433-8.  
50
- 51 26. Lee TG, Kang SB, Kim DW, Hong S, Heo SC, Park KJ. Comparison of early  
52 mobilization and diet rehabilitation program with conventional care after laparoscopic colon  
53 surgery: a prospective randomized controlled trial. *Dis Colon Rectum*. 2011 Jan;54(1):21-8.  
54
- 55 27. Lemanu DP, Singh PP, Berridge K, Burr M, Birch C, Babor R, et al. Randomized  
56 clinical trial of enhanced recovery versus standard care after laparoscopic sleeve  
57 gastrectomy. *Br J Surg*. 2013 Mar;100(4):482-9.  
58  
59  
60

- 1  
2  
3 28. Liu XX, Jiang ZW, Wang ZM, Li JS. Multimodal optimization of surgical care shows  
4 beneficial outcome in gastrectomy surgery. *JPEN J Parenter Enteral Nutr.* 2010 May-  
5 Jun;34(3):313-21.  
6
- 7 29. Ren L, Zhu D, Wei Y, Pan X, Liang L, Xu J, et al. Enhanced Recovery After Surgery  
8 (ERAS) program attenuates stress and accelerates recovery in patients after radical  
9 resection for colorectal cancer: a prospective randomized controlled trial. *World J Surg.* 2012  
10 Feb;36(2):407-14.  
11
- 12 30. Wang D, Kong Y, Zhong B, Zhou X, Zhou Y. Fast-track surgery improves  
13 postoperative recovery in patients with gastric cancer: a randomized comparison with  
14 conventional postoperative care. *J Gastrointest Surg.* 2010;14(4):620-7.  
15
- 16 31. Wang G, Jiang ZW, Xu J, Gong JF, Bao Y, Xie LF, et al. Fast-track rehabilitation  
17 program vs conventional care after colorectal resection: a randomized clinical trial. *World J*  
18 *Gastroenterol.* 2011 Feb 7;17(5):671-6.  
19
- 20 32. Wang Q, Suo J, Jiang J, Wang C, Zhao YQ, Cao X. Effectiveness of fast-track  
21 rehabilitation vs conventional care in laparoscopic colorectal resection for elderly patients: a  
22 randomized trial. *Colorectal Dis.* 2012 Aug;14(8):1009-13.  
23
- 24 33. Yang DJ, Zhang S, He WL, Chen HY, Cai SR, Chen CQ, et al. Fast track surgery  
25 accelerates the recovery of postoperative insulin sensitivity. *Chin Med J.* 2012  
26 Sep;125(18):3261-5.  
27
- 28 34. Yang DJ, Zhang S, He WL, Huang WQ, Cai SR, Chen CQ, et al. Fast-track surgery  
29 accelerates the recovery of postoperative humoral immune function in elective operation for  
30 colorectal carcinoma: a randomized controlled clinical trial. *Chin Med J.* 2012 Apr  
31 24;92(16):1112-5.  
32
- 33 35. Vlug MS, Wind J, Hollmann MW, Ubbink DT, Cense HA, Engel AF, et al.  
34 Laparoscopy in combination with fast track multimodal management is the best perioperative  
35 strategy in patients undergoing colonic surgery: a randomized clinical trial (LAFAs-study). *Ann*  
36 *Surg.* 2011 Dec;254(6):868-75.  
37
- 38 36. Cheng-Le Z, Xing-Zhao Y, Xiao-Dong Z, Bi-Cheng C, Zhen Y. Enhanced recovery  
39 after surgery programs versus traditional care for colorectal surgery: A meta-analysis of  
40 randomized controlled trials. *Dis Colon Rectum.* 2013;56:667-78.  
41
- 42 37. Arsalani-Zadeh R, Elfadl D, Yassin N, MacFie J. Evidence-based review of  
43 enhancing postoperative recovery after breast surgery. *Br J Surg.* 2011 Feb;98(2):181-96.  
44
- 45 38. Hoffmann H, Kettelhack C. Fast-track surgery - conditions and challenges in  
46 postsurgical treatment: a review of elements of translational research in enhanced recovery  
47 after surgery. *Eur Surg Res.* 2012;49(1):24-34.  
48
- 49 39. Lin CH, Wang FC, Lin SC, Huang YH, Chen CC, Lane HY. Antipsychotic  
50 combination using low-dose antipsychotics is as efficacious and safe as, but cheaper, than  
51 optimal-dose monotherapy in the treatment of schizophrenia: A randomized, double-blind  
52 study. *Int Clin Psychopharmacol.* 2013;28(5):267-74.  
53
- 54 40. Werner D, Locke C. Experiences of chronic stress one year after the Gulf oil spill.  
55 *International Journal of Emergency Mental Health.* 2012;14(4):239-45.  
56  
57  
58  
59  
60



- 1  
2  
3 41. Advenier, Kapsambelis. Psychiatric diagnosis in the age of industrial medicine.  
4 French . References. Topique. 2013.  
5  
6 42. Christodoulou NG, Christodoulou GN. Financial crises: Impact on mental health and  
7 suggested responses. *Psychother Psychosom*. 2013;82(5):279-84.  
8  
9 43. Morrissey JP, Domino ME, Cuddeback GS. Assessing the effectiveness of recovery-  
10 oriented ACT in reducing state psychiatric hospital use. *Psychiatr Serv*. 2013;64(4):303-11.  
11  
12 44. Kirk Jr TA, Di Leo P, Rehmer P, Moy S, Davidson L. A case and care management  
13 program to reduce use of acute care by clients with substance use disorders. *Psychiatr Serv*.  
14 2013;64(5):491-3.  
15  
16 45. Aylin P, Alexandrescu R, Jen MH, Mayer EK, Bottle A. Day of week of procedure and  
17 30 day mortality for elective surgery: retrospective analysis of hospital episode statistics.  
18 *BMJ*. 2013 May;346:8.  
19  
20 46. Blazeby JM, Soulsby M, Winstone K, King PM, Bulley S, Kennedy RH. A qualitative  
21 evaluation of patients' experiences of an enhanced recovery programme for colorectal  
22 cancer. *Colorectal Dis*. 2010 Oct;12(10 Online):e236-42.  
23  
24 47. Taylor C, Burch J. Feedback on an enhanced recovery programme for colorectal  
25 surgery. *Br J Nurs*. 2011 2011 Mar;20(5):286-90.  
26  
27 48. Reilly KA, Beard DJ, Barker KL, Dodd CA, Price AJ, Murray DW. Efficacy of an  
28 accelerated recovery protocol for Oxford unicompartmental knee arthroplasty: a randomised  
29 controlled trial. *Knee*. 2005;12(5):351-7.  
30  
31 49. Archibald LH, Ott MJ, Gale CM, Zhang J, Peters MS, Stroud GK. Enhanced recovery  
32 after colon surgery in a community hospital system. *Dis Colon Rectum*. 2011;54(7):840-5.  
33  
34 50. Sammour T, Zargar-Shoshtari K, Bhat A, Kahokehr A, Hill AG. A programme of  
35 Enhanced Recovery After Surgery (ERAS) is a cost-effective intervention in elective colonic  
36 surgery. *N Z Med J*. 2010;123(1319).  
37  
38 51. King PM, Blazeby JM, Ewings P, Longman RJ, Kipling RM, Franks PJ, et al. The  
39 influence of an enhanced recovery programme on clinical outcomes, costs and quality of life  
40 after surgery for colorectal cancer. *Colorectal Dis*. 2006;8(6):506-13.  
41  
42 52. Nielsen PR, Andreasen J, Asmussen M, Tønnesen H. Costs and quality of life for  
43 prehabilitation and early rehabilitation after surgery of the lumbar spine. *BMC Health Serv*  
44 *Res [Internet]*. 2008 26/06/13; 8:[209 p.]. Available from:  
45 <http://www.biomedcentral.com/1472-6963/8/209>.  
46  
47 53. Jakobsen DH, Sonne E, Andreasen J, Kehlet H. Convalescence after colonic surgery  
48 with fast-track vs conventional care. *Colorectal Dis*. 2006 Oct;8(8):683-7.  
49  
50 54. McBride N, Farrington F, Midford R. Implementing a school drug education  
51 programme: reflections on fidelity. *International Journal of Health Promotion and Education*.  
52 2002;40(2):40-50.  
53  
54 55. Kariv Y, Delaney CP, Senagore AJ, Manilich EA, Hammel JP, Church JM, et al.  
55 Clinical outcomes and cost analysis of a fast track postoperative care pathway for ileal  
56 pouch-anal anastomosis. A case control study. *Dis Colon Rectum*. 2007;50(2):137-46.  
57  
58  
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60

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2  
3 56. Salhiyyah K, Elsobky S, Raja S, Attia R, Brazier J, Cooper GJ. A clinical and  
4 economic evaluation of fast-track recovery after cardiac surgery. *Heart Surgery Forum*.  
5 2011;14(6):E330-4.  
6  
7 57. Yanatori M, Tomita S, Miura Y, Ueno Y. Feasibility of the fast-track recovery program  
8 after cardiac surgery in Japan. *General Thoracic and Cardiovascular Surgery*.  
9 2007;55(11):445-9.  
10  
11 58. Noyes J, Gough D, Lewin S, Mayhew A, Michie S, Pantoja T, et al. A research and  
12 development agenda for systematic reviews that ask complex questions about complex  
13 interventions. *J Clin Epidemiol*. 2013 Nov;66(11):1262-70.  
14  
15 59. Eiselt J, Racek J, Trefil L, Opatrny Jr K. Ferric saccharate infusion enhances lipid  
16 peroxidation in hemodialysis (hd) patients [abstract]. *Nephrol Dial Transplant [Internet]*.  
17 2001; 16(6):[A141 p.]. Available from:  
18 <http://onlinelibrary.wiley.com/doi/10.1053/j.ajkd.2001.06.014>.  
19  
20 60. Pearsall EA, Meghji Z, Pitzul KB, Aarts MA, McKenzie M, McLeod RS, et al. A  
21 Qualitative Study to Understand the Barriers and Enablers in Implementing an Enhanced  
22 Recovery After Surgery Program. *Ann Surg*. 2014 Mar 18.  
23  
24 61. Hilty DM, Ferrer DC, Parish MB, Johnston B, Callahan EJ, Yellowlees PM. The  
25 effectiveness of telemental health: a 2013 review. *Review. Telemedicine and e-Health*.  
26 2013;19(6):444-54.  
27  
28 62. Lee L, Li C, Landry T, Latimer E, Carli F, Fried GM, et al. A Systematic Review of  
29 Economic Evaluations of Enhanced Recovery Pathways for Colorectal Surgery. *Ann Surg*.  
30 2014;259(4):670-6 10.  
31  
32 63. Carroll C, Patterson M, Wood S, Booth A, Rick J, Balain S. A conceptual framework  
33 for implementation fidelity. *Implementation Science*. 2007;2(1):40.  
34  
35 64. Coolson MME, van Dam RM, van der Wilt AA, Slim K, Lassen K, Dejong CHC.  
36 Systematic review and meta-analysis of enhanced recovery after pancreatic surgery with  
37 particular emphasis on pancreaticoduodenectomies: Supplementary Material. *World J Surg*.  
38 2013;Published online 09 April 2013.  
39  
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Figure 1: Study flow diagram

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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
<b>Colorectal/Colon surgery</b>							
Adamina (2011) <sup>(6)</sup>	✓	✓	UC	✓	UC	✓	✓
Ahmed (2012) <sup>(7)</sup>	✓	X	X	X	X	X	✓
Eskicioglu (2009) <sup>(10)</sup>	✓	✓	X	✓	✓	✓	✓
Gouvas (2009) <sup>(11)</sup>	✓	✓	X	✓	✓	✓	✓
Khan (2010) <sup>(13)</sup>	✓	✓	X	✓	X	✓	✓
Lv (2012a) <sup>(21)</sup>	✓	✓	X	X	✓	✓	✓
Rawlinson (2011) <sup>(15)</sup>	✓	X	X	✓	UC	X	UC
Spanjersberg (2011) <sup>(16)</sup>	✓	✓	✓	✓	✓	✓	✓
Varadhan (2010) <sup>(17)</sup>	✓	✓	X	✓	✓	✓	✓
Walter (2009) <sup>(18)</sup>	✓	✓	✓	✓	✓	✓	✓
Wind (2006) <sup>(19)</sup>	✓	✓	✓	✓	✓	✓	✓
<b>Gynaecological surgery</b>							
Lv (2012b) <sup>(20)</sup>	✓	X	X	X	X	✓	✓
<b>Liver/pancreatic surgery</b>							
Coolsen (2012) <sup>(8)</sup>	✓	✓	X	✓	X	✓	✓
Coolsen (2013) <sup>(9)</sup> Link to <sup>(64)</sup>	✓	✓	✓	✓	✓	✓	✓
Hall (2012) <sup>(12)</sup>	X	X	X	✓	X	✓	✓
<b>Various surgical specialities</b>							
Lemmens (2009) <sup>(14)</sup>	✓	X	X	✓	X	✓	✓
Sturm (2009) <sup>(5)</sup>	✓	X	X	✓	UC	✓	✓

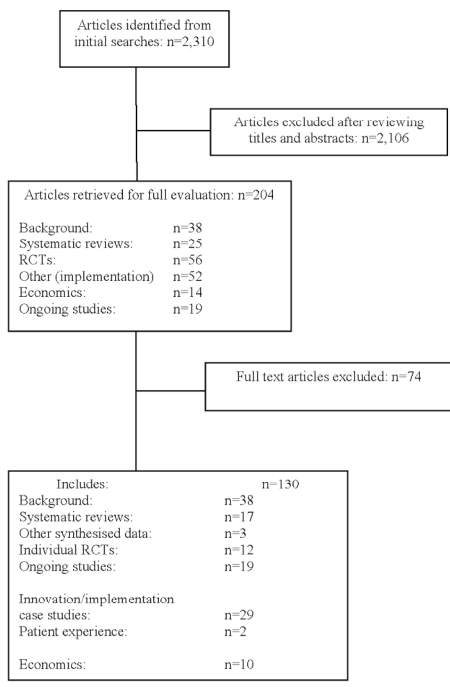
UC=unclear reporting

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
<b>Bariatric surgery</b>									
Lemanu (2013) <sup>(27)</sup>	✓	✓	X	X	X	X	NA	UC	UC
<b>Colorectal/colon surgery</b>									
Garcia-Botello (2011) <sup>(24)</sup>	UC	X	UC	X	UC	X	NA	UC	✓
Ionescu (2009) <sup>(25)</sup>	✓	✓	X	X	UC	X	NA	UC	UC
Lee (2011) <sup>(26)</sup>	✓	✓	UC	X	UC	X	NA	UC	UC
Ren (2012) <sup>(28)</sup>	✓	✓	X	X	✓	X	NA	UC	UC
Wang (2011) <sup>(31)</sup>	UC	UC	UC	X	UC	X	NA	✓	✓
Wang (2012) <sup>(32)</sup>	UC	UC	X	X	✓	UC	UC	UC	UC
Yang (2012) <sup>(33, 34)</sup>	✓	UC	X	X	UC	X	NA	X	X
<b>Gastric surgery</b>									
Chen (2012) <sup>(22)</sup>	UC	UC	X	✓	✓	X	NA	UC	UC
Kim (2012) <sup>(23)</sup>	UC	UC	X	X	X	X	NA	UC	UC
Liu (2010) <sup>(28)</sup>	UC	X	X	X	X	X	NA	UC	UC
Wang (2010) <sup>(30)</sup>	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		
<b>Adamina (2011)<sup>(8)</sup></b> 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)
<b>Ahmed (2012)<sup>(7)</sup></b> 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%)
<b>Eskicioglu (2009)<sup>(10)</sup></b> 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; $I^2=24\%$ )
<b>Gouvas (2009)<sup>(11)</sup></b> 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.
<b>Khan (2010)<sup>(13)</sup></b> 10 studies; 4 RCTs, 6 non-randomised comparative studies	Not applicable	Not applicable
<b>Lv (2012a)<sup>(21)</sup></b> 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, $I^2=0\%$ ).
<b>Rawlinson (2011)<sup>(19)</sup></b> 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.
<b>Spanjersberg (2011)<sup>(16)</sup></b> 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.
<b>Varadhan (2010)<sup>(12)</sup></b> 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; $I^2=9\%$ )
<b>Walter (2009)<sup>(18)</sup></b> 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/%)
<b>Wind (2006)<sup>(19)</sup></b> 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.
<b>Gynaecological surgery</b>		
<b>Lv (2012b)<sup>(20)</sup></b> 0 studies	Not applicable	Not applicable
<b>Liver/pancreatic surgery</b>		
<b>Coolsen (2012)<sup>(8)</sup></b> 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%
<b>Coolsen (2013)<sup>(9)</sup> Link to <sup>(63)</sup></b> 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)
<b>Hall (2012)<sup>(12)</sup></b> 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 to 14.6% (4 studies); liver 0 to 13 % (5 studies)
<b>Various surgical specialities</b>		
<b>Lemmens (2009)<sup>(14)</sup></b> 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
<b>Sturm (2009)<sup>(5)</sup></b> 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/%)
<b>Bariatric surgery</b>		
Lemanu (2013) <sup>(27)</sup>	Median days (interquartile range) Length of index admission: ERAS 1 (1 to 2); control 2 (0), 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.
<b>Colorectal/colon surgery</b>		
Ionescu (2009) <sup>(25)</sup>	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) <sup>(26)</sup>	ERAS 6.43 (3.41); control 9.16 (2.67), p=0.001	ERAS 0 (0); control 0 (0)
Ren (2012) <sup>(29)</sup>	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) <sup>(31)</sup>	Mean (SD) ERAS 5.7 (1.6); control 6.6 (2.4), p<0.001	Not reported
Wang (2012) <sup>(32)</sup>	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) <sup>(33, 34)</sup>	Median days: ERAS 5.5 (5 to 6); control 7.0 (6 to 8), p<0.001	Not reported
Ionescu (2009) <sup>(25)</sup>	Mean (SD) ERAS 6.0 (1.0); control 11.7 (3.8), p<0.05	No hospital readmissions due to complications.
<b>Gastric surgery</b>		
Chen (2012) <sup>(22)</sup>	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) <sup>(23)</sup>	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) <sup>(28)</sup>	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) <sup>(30)</sup>	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
<p><b>Salihyiah <i>et al</i> (2011)<sup>(55)</sup></b></p> <p>UK</p> <p>Hospital setting</p> <p><u>Study Population</u> Cardiac surgery Inpatients</p> <p><u>Time horizon</u> 6 months</p>	<p><u>Intervention</u> Fast-track transfer post-surgery to an independent theatre recovery unit 1-2-1 nursing (n=84)</p> <p><u>Comparator</u> Transfer post-surgery to hospital intensive care unit (n=52)</p>	<p>Economic evaluation based on a single study</p> <p><u>Perspective</u> Hospital</p> <p><u>Primary outcomes</u> Length of stay; Duration of intubation</p> <p><u>Direct Costs</u> Total expenditure of unit divided by number of patients</p> <p><u>Productivity Costs</u> n/a</p>	<p><u>Results</u> The costs and benefits were not synthesised</p> <p>mean cost FT: £4182 (SD:2284) mean cost C: £4553 (SD:1355) (p&lt;0.001)</p> <p>total LOS NSD</p> <p>8 patients failed FT &amp; were transferred to ICU</p> <p>5 patients (4 FT &amp; 1 C) required readmission</p> <p><u>Uncertainty</u> One-way &amp; multi-way sensitivity analysis demonstrated robustness in result that FT costs less than C</p>
<p><b>Lin <i>et al</i> (2011)<sup>(53)</sup></b></p> <p>China</p> <p>Hospital setting</p> <p><u>Study Population</u> Liver resection Inpatients</p> <p><u>Time horizon</u> Not reported</p>	<p><u>Intervention</u> 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 &lt;24 hours, planned discharge 6 days post-surgery (n=56)</p> <p><u>Comparator</u> Conventional pathway (limited reporting) (n=61)</p>	<p>Economic evaluation based on a single study</p> <p><u>Perspective</u> Hospital</p> <p><u>Primary outcomes</u> Length of stay; Complications; Mortality; Readmission</p> <p><u>Direct Costs</u> Hospital charges: operation and anaesthesia; pharmacy; auxiliary examination; other</p> <p><u>Productivity Costs</u> n/a</p>	<p><u>Results</u> The costs and benefits were not synthesised</p> <p>mean charge pre-pathway RMB 26,626 mean charge post-pathway RMB 21,004 (p&lt;0.05)</p> <p>LOS reduced from 11 days to 7 days (p&lt;0.005) Complications, mortality &amp; readmissions NSD</p> <p><u>Uncertainty</u> n/a</p>
<p><b>Kariv <i>et al</i> (2006)<sup>(55)</sup></b></p> <p>USA</p> <p>Hospital setting</p> <p><u>Study Population</u> Patients undergoing open ileoanal pouch surgery</p>	<p><u>Intervention</u> 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</p>	<p>Economic evaluation based on a single study</p> <p><u>Perspective</u> Hospital</p> <p><u>Primary outcomes</u> Length of stay; Readmission; Reoperation</p> <p><u>Direct Costs</u> Total costs for each of the categories were presented:</p>	<p><u>Results</u> The costs and benefits were not synthesised</p> <p>total per case cost FT US\$ 5,692 total per case cost C US\$ 6672 diff US\$980 (p=0.001)</p> <p>median postoperative los FT = 4 days C= 5 days (p=0.012) NSD in readmission outcomes</p>

Study Details	Study Comparators	Main Analytical Approaches, primary outcomes, and costs	Incremental cost-effectiveness (ICER) estimates and Decision Uncertainty
<p><u>Time horizon</u> 30 days</p>	<p>days (n=97)</p> <p><u>Comparator</u> 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)</p>	<p>per case of hospitalisation; operating room; radiology; anaesthesia; pharmacy; laboratory; ICU; and nursing care</p> <p><u>Productivity Costs</u> n/a</p>	<p><u>Uncertainty</u> n/a</p>
<p><b>Yanatori <i>et al</i> (2007)<sup>[57]</sup></b></p> <p>Japan</p> <p>Hospital setting</p> <p><u>Study Population</u> Cardiovascular surgery (cardiac arrest requiring cardiopulmonary bypass)</p> <p><u>Time horizon</u> 2 years</p>	<p><u>Intervention</u> Admitted 4 days prior to surgery, preoperative education by nurses, surgeons and rehab staff; discharge at day 7 post surgery</p> <p><u>Comparator</u> Conventional protocol – details not reported</p>	<p>Economic evaluation based on a single study</p> <p><u>Perspective</u> Healthcare provider/hospital</p> <p><u>Primary outcomes</u> Length of stay; Complications</p> <p><u>Direct Costs</u> Only total costs were presented</p> <p><u>Productivity Costs</u> n/a</p>	<p><u>Results</u> The costs and benefits were not synthesised</p> <p>Total mean cost for FT YEN 712,545 Total mean cost for C YEN 383,268 (p=0.038)</p> <p>Mean post-op LOS FT=15(12.4) C=36.7(6) (p=0.01)</p> <p><u>Uncertainty</u> n/a</p>
<p><b>Larsen <i>et al</i> (2009)<sup>[54]</sup></b></p> <p>Denmark</p> <p>Hospital setting</p> <p><u>Study Population</u> All patients for elective primary total hip/knee arthroplasty or unicompartmental knee arthroplasty</p> <p><u>Time horizon</u> One year</p>	<p><u>Intervention</u> 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)</p> <p><u>Comparator</u> Patients receive info on day of admission; patients randomly among wards, various nurses in charge of care; and various occupational and physiotherapists 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)</p>	<p>Economic evaluation based on a single study</p> <p><u>Perspective</u> Societal</p> <p><u>Primary outcomes</u> Length of stay; Adverse events (first 3months)</p> <p><u>Health-related quality-of-life</u> QALYS (EQ-5D) (baseline to 3 months)</p> <p><u>Direct Costs</u> 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</p> <p><u>Productivity Costs</u> Average wage rate for age-specific groups</p>	<p><u>Results</u> Accelerated intervention was both more effective and less costly than the comparator</p> <p>Average total cost for I DKK90,227 (+/- 47,475)</p> <p>Average total cost for C DKK71,344 (+/- 39,958)</p> <p>Average QALYs was 0.83 for the intervention and 0.78 in the comparator.</p> <p>Average QALY gain for hip patients I v C = 0.08 (CI: 0.02 to 0.05) (p=0.006)</p> <p>Average QALY gain for knee patients was NS</p> <p><u>Uncertainty</u> Bootstrapping, uni and multivariate</p>

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

Study Details	Study Comparators	Main Analytical Approaches, primary outcomes, and costs	Incremental cost-effectiveness (ICER) estimates and Decision Uncertainty
<p>Hospital setting</p> <p><u>Study Population</u> Lumbar fusion patients with degenerative lumbar disease</p> <p><u>Time horizon</u> 6 months</p>	<p>operation technique, better pain reduction, early nutrition and aggressive post-op mobilisation (n=28)</p> <p><u>Comparator</u> Standard care, not including components above (n=32)</p>	<p>Societal</p> <p><u>Primary outcome</u> Measured using 15D-score (self-reported at inclusion, day of surgery, day of discharge, and 1, 3 and 6 months post-op)</p> <p><u>Direct Costs</u> 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.</p> <p><u>Productivity costs</u> Based on return to work rates &amp; Danish average daily wage</p>	<p>Intervention direct cost 1,174 Euros per patient compared with 1,668 for standard care</p> <p>Intervention productivity costs were 8,021 Euros compared with 9,152 for standard care</p> <p>NS difference in HR quality of life scores</p> <p><u>Uncertainty</u> Optimistic and pessimistic scenarios varying individually pre-op costs, post-op hospital costs, direct costs, and productivity costs</p>
<p><b>Reilly et al(2005)<sup>(48)</sup></b></p> <p>UK</p> <p>Hospital setting</p> <p><u>Study Population</u> Patients undergoing unicompartmental knee arthroplasty</p> <p><u>Time horizon</u> Unclear</p>	<p><u>Intervention</u> Accelerated discharge: aim to discharge day after surgery (n=20)</p> <p><u>Comparator</u> Standard discharge: approx. 5 days post-surgery (n=21)</p>	<p>Economic evaluation based on a single study</p> <p><u>Perspective</u> Hospital</p> <p><u>Primary outcome</u> Oxford Knee Assessment</p> <p><u>Direct Costs</u> Fixed costs (surgical staff, anaesthetics, prosthesis, pharmacy), outpatient appointment, specialist registrar time.</p> <p><u>Productivity costs</u> n/a</p>	<p><u>Results</u> The costs and benefits were not synthesised</p> <p>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)</p> <p>Total costs for intervention per patient £3,391 compared with £4,634 for standard care</p> <p><u>Uncertainty</u> n/a</p>
<p><b>Archibald<sup>(49)</sup></b></p> <p>USA</p> <p>Hospital setting</p> <p><u>Study Population</u> Colorectal surgery patients</p> <p><u>Time horizon</u> unclear</p>	<p><u>Intervention</u> 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 &amp; 770 not enrolled)</p> <p><u>Comparator</u> Standard care historical baseline (n=1673)</p>	<p>Economic evaluation based on a study comparing two time periods, where ERAS was available in one and not in the other.</p> <p><u>Primary outcome</u> Length of stay ; POD; Readmission</p> <p><u>Direct Costs</u> Hospital costs (total direct and indirect costs identified via hospital billing system)</p> <p><u>Productivity costs</u> n/a</p>	<p><u>Results</u> The costs and benefits were not synthesised</p> <p>Mean LOS for the intervention was 8.4 days compared with 6.9 days for the comparator (p&lt;0.0001); Mean POD for the intervention was 7.6 days compared with 6.3 days (p&lt;0.0001)</p> <p>Mean hospital cost for the intervention population was US\$18,741 compared with US\$16,978 for the comparator.</p> <p><u>Uncertainty</u> n/a</p>

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Section/topic	#	Checklist item	Reported on page #
<b>TITLE</b>			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
<b>ABSTRACT</b>			
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
<b>INTRODUCTION</b>			
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
<b>METHODS</b>			
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

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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
<b>RESULTS</b>			
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
<b>DISCUSSION</b>			
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
<b>FUNDING</b>			
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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