

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Effectiveness and implementation of enhanced recovery after surgery programmes: a rapid evidence synthesis
<b>AUTHORS</b>	Paton, Fiona; Chambers, Duncan; Wilson, Paul; Eastwood, Alison; Craig, Dawn; Fox, Dave; Jayne, David; McGinnes, Erika

### VERSION 1 - REVIEW

<b>REVIEWER</b>	John MacFie York NHS FT UK  Have published extensively on this topic
<b>REVIEW RETURNED</b>	27-Mar-2014

<b>GENERAL COMMENTS</b>	<p>This is an excellent attempt to distil conclusions about ERAS from the World literature. It is comprehensive and well written</p> <p>In my opinion it does not achieve it's objectives. It concludes that there is at best marginal benefit for ERAS whilst recognising the heterogeneity of work they have reviewed. But the surgical reality is quite different.</p> <p>The "flaw" with this analysis is that they presume ERAS programmes are a defined entity. They are not. They merely represent what most surgeons would simply say are modern approaches to pre, peri and post op care.</p> <p>The original idea for ERAS was actually the multimodal studies published in the BJS. These were research (despite what authors say about this) and were based on the principle that a series of interventions based on available evidence would be beneficial because of marginal benefits of each. This was quite distinct to Henrique Kehlet who used early feeding and mobilisation only. As such authors miss the fundamental point about ERAS when they bemoan an ability to say which interventions are most effective.</p> <p>I suspect the authors need a surgical input into their analysis</p> <p>It is noteworthy that no surgical unit would now embark on so called ERAS studies because the factors involved are generally now standard and therefore it would now be unethical to set up such a study</p> <p>the main objective of ERAS is not cost saving. It is quality of patient care.</p>
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	I disagree with authors who state there is little published evidence about compliance. see khan et al
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<b>REVIEWER</b>	Henrik Kehlet Rigshospitalet, Denmark
<b>REVIEW RETURNED</b>	02-Apr-2014

<b>GENERAL COMMENTS</b>	<p>This review lacks a thorough discussion on the advances in enhanced recovery programs across surgical procedures compared to what already exists. Although the aim was to describe such programs in UK settings, the presented data may have local interest, but not more widespread.</p> <p>During the last 15 years, there has been an increased interest in enhanced recovery programs (or other synonyms). As mentioned in this “review”, there is a lot of data and many “systematic reviews” supporting the concept although most of the randomised trials do not involve the optimal implementation of the essential components of such programs.</p> <p>For this reviewer, it is difficult to see what new is available in the present review. There have been so many data on the results and the barriers for implementation as well as economic implications not covered in this review. In addition, the review fails to discuss in detail the different components of enhanced recovery programs in different procedures. Also, the review lacks all the information on such programs from other very common procedures, for instance major joint arthroplasty, where a lot of data are available and especially about the important aspects on post-discharge outcomes. Finally, quite a number of data have been published in gynaecological surgery, which is neither mentioned.</p> <p>In summary, although the aims and objectives of this review are fully valid – the information provided may not add significantly to the current available literature.</p> <p>Additional references:  Greco M, Capretti G, Beretta L, Gemma M, Pecorelli N, Braga M. Enhanced Recovery Program in Colorectal Surgery: A Meta-analysis of Randomized Controlled Trials. World J Surg 2013 (Epub).  Lee L, Li C, Landry T, Latimer E, Carli F, Fried GM, Feldman LS. A systematic review of economic evaluations of enhanced recovery pathways for colorectal surgery. Ann Surg 2014;259:670-676.  Neville A, Lee L, Antonescu I, Mayo NE, Vassiliou MC, Fried GM, Feldman LS. Systematic review of outcomes used to evaluate enhanced recovery after surgery. Br J Surg 2014;101:159-170.  Pearsall EA, Meghji Z, Pitzul KB, Aarts MA, McKenzie M, McLeod RS, Okrainec A. A Qualitative Study to Understand the Barriers and Enablers in Implementing an Enhanced Recovery After Surgery Program. Ann Surg 2014 (Epub).</p>
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### VERSION 1 – AUTHOR RESPONSE

Reviewer: 1  
Reviewer Name John MacFie  
Institution and Country York NHS FT UK

Please state any competing interests or state ‘None declared’: Have published extensively on this topic

This is an excellent attempt to distil conclusions about ERAS from the World literature. It is comprehensive and well written

- We thank the author for his kind remarks

In my opinion it does not achieve it's objectives. It concludes that there is at best marginal benefit for ERAS whilst recognising the heterogeneity of work they have reviewed. But the surgical reality is quite different.

The "flaw" with this analysis is that they presume ERAS programmes are a defined entity. They are not. They merely represent what most surgeons would simply say are modern approaches to pre, peri and post op care.

- We have not presumed that ERAS programmes are a defined entity and our inclusion criteria are reflective of this. Recognising that programmes vary across settings and specialties, we included reviews and studies that encompassed different combinations of the main preoperative, intraoperative and postoperative pathway elements described by the Dept of Health Enhanced Recovery Partnership Programme. We have amended the text to make this clearer.

The original idea for ERAS was actually the multimodal studies published in the BJS. These were research (despite what authors say about this) and were based on the principle that a series of interventions based on available evidence would be beneficial because of marginal benefits of each. This was quite distinct to Henrique Kehlet who used early feeding and mobilisation only. As such authors miss the fundamental point about ERAS when they bemoan an ability to say which interventions are most effective.

- To clarify, within finite budgets having a clear understanding of how best to implement ERAS programmes and the likely implications for service delivery is crucial. In our review we highlight a shortage of robust evidence evaluating the relative advantage of individual or combinations of components included in an enhanced recovery pathway. The degree to which success is dependent on the delivery of all, or just some combinations of elements (and the type and intensity – i.e. what sort of pre-op education or how much mobilisation delivered by whom) is not yet known.

I suspect the authors need a surgical input into their analysis

- Professor David Jayne, Consultant Surgeon at Leeds Teaching Hospitals, is a co-author of this review. He has practical experience of implementing an enhanced recovery programme in his own clinical setting and is currently leading an NIHR funded programme of research that is developing and translating new surgical technologies into clinical practice. Additional clinical input has been sought throughout the conduct of this review from the protocol stage through to the peer review undertaken by the funders.

It is noteworthy that no surgical unit would now embark on so called ERAS studies because the factors involved are generally now standard and therefore it would now be unethical to set up such a study

- Whilst we would also question the utility of further trials of ERAS v conventional care, there are a number of such studies currently being undertaken across the world (see NCT01938313, NCT01610726 by way of example).

the main objective of ERAS is not cost saving. It is quality of patient care.

- Quality of patient care is of course paramount in any service redesign. However, it is worth emphasising that this review was funded through an NIHR call to assess initiatives designed to reduce length of stay in secondary care. Likewise, the Dept of Health Enhanced Recovery Partnership Programme was established to support the further adoption and spread in clinical practice, improve patient experience and to help the NHS realise the associated productivity and efficiency gains enhanced recovery was thought to deliver. It is also worth noting that the primary

outcome in most of the studies included in this synthesis is length of stay.

I disagree with authors who state there is little published evidence about compliance. see Khan et al

- We are aware of Khan et al and have included it in our synthesis. The authors draw similar conclusions to our own with regard to the paucity and methodological quality of the available evidence.

Reviewer: 2

Reviewer Name Henrik Kehlet

Institution and Country Rigshospitalet, Denmark

Please state any competing interests or state 'None declared': None declared

This review lacks a thorough discussion on the advances in enhanced recovery programs across surgical procedures compared to what already exists. Although the aim was to describe such programs in UK settings, the presented data may have local interest, but not more widespread.

- We acknowledge that the evidence is aimed at the implementation of enhanced recovery programmes in UK settings, and we have further highlighted throughout the article that this is the case. The objective of the 'evidence synthesis' was to identify areas where savings could be made to reduce costs to the NHS and hopefully the amendments will further emphasise this. The evidence on the clinical and cost effectiveness of enhanced recovery programmes does, however, incorporate systematic reviews and RCTs conducted in other countries. As healthcare systems vary considerably across different countries, we did not feel it appropriate to generalise the findings on the success of implementing such programmes in UK settings to other healthcare settings.

During the last 15 years, there has been an increased interest in enhanced recovery programs (or other synonyms). As mentioned in this "review", there is a lot of data and many "systematic reviews" supporting the concept although most of the randomised trials do not involve the optimal implementation of the essential components of such programs.

For this reviewer, it is difficult to see what new is available in the present review. There have been so many data on the results and the barriers for implementation as well as economic implications not covered in this review. In addition, the review fails to discuss in detail the different components of enhanced recovery programs in different procedures. Also, the review lacks all the information on such programs from other very common procedures, for instance major joint arthroplasty, where a lot of data are available and especially about the important aspects on post-discharge outcomes. Finally, quite a number of data have been published in gynaecological surgery, which is neither mentioned.

- The purpose of the evidence synthesis under question was to bring together the evidence on enhanced recovery programmes. Although there are a number of publications on enhanced recovery, they aim to address questions in specific areas. For example, the publications suggested by reviewer 2 address questions on enhanced recovery programmes from limited perspectives. Lee's (2014) article is from an economical perspective only, Pearsall (2014) explores only barriers and facilitators to implementation, and Neville (2014) and Greco (2013) address the effectiveness of such programmes in abdominal/colorectal surgery. Although Nicholson (2014) investigates the effect of enhanced recovery programmes across a number of surgical specialities, this systematic review does not incorporate an economical evaluation or explore the barriers and facilitators for the successful implementation of these programmes. We feel that our evidence synthesis goes one step further than the evidence identified, by addressing a wider question and bringing together evidence from all relevant aspects on the current status of enhanced recovery programmes in UK settings.

- The reviewer rightly points out that certain evidence has not been covered in this synthesis. Evidence relating to enhanced recovery programmes may have been identified in our initial search of the literature. On screening by two independent reviewers, however, such evidence may not have met criteria for inclusion in the synthesis. We feel that the potential for missed data has been sufficiently highlighted in the article under 'strengths and weaknesses' (page 12).

- We agree with Reviewer 2 that there is a great deal of data available on such programmes from other surgical procedures such as joint arthroplasty and gynaecology. Our literature search did identify literature in these areas, (for example, approximately 35 articles relating to arthroplasty were located), but after screening by two independent reviewers, none of the articles met the specified eligibility criteria for inclusion in the evidence synthesis.

- We acknowledge that post-discharge outcomes are important in relation to enhanced recovery programmes. However, the original question being addressed in this evidence synthesis did not extend to post-discharge outcomes. A specific search for such outcomes was therefore not conducted. We briefly implied on page 13 (under ‘implications for research’) that further exploration into different discharge protocols is required to assess the effect they might have on the success of enhanced recovery programmes.

In summary, although the aims and objectives of this review are fully valid – the information provided may not add significantly to the current available literature.

- As the reviewer previously states, and as acknowledged in our evidence synthesis, there is a plethora of data on enhanced recovery programmes. In relation to this, we have also submitted a manuscript to BMJ Open Access highlighting the duplication of effort in this area as the systematic reviews identified by our literature search tended to include the same RCTs (Chambers D, Paton F, Wilson P, Eastwood A, Craig D, Fox D et al. Effect of enhanced recovery programmes on length of hospital stay in colorectal surgery: an overview and methodological assessment of systematic reviews. BMJ Open Access, in press).

Additional references:

Greco M, Capretti G, Beretta L, Gemma M, Pecorelli N, Braga M. Enhanced Recovery Program in Colorectal Surgery: A Meta-analysis of Randomized Controlled Trials. World J Surg 2013 (Epub).  
 Lee L, Li C, Landry T, Latimer E, Carli F, Fried GM, Feldman LS. A systematic review of economic evaluations of enhanced recovery pathways for colorectal surgery. Ann Surg 2014;259:670-676.  
 Neville A, Lee L, Antonescu I, Mayo NE, Vassiliou MC, Fried GM, Feldman LS. Systematic review of outcomes used to evaluate enhanced recovery after surgery. Br J Surg 2014;101:159-170.  
 Pearsall EA, Meghji Z, Pitzul KB, Aarts MA, McKenzie M, McLeod RS, Okrainec A. A Qualitative Study to Understand the Barriers and Enablers in Implementing an Enhanced Recovery After Surgery Program. Ann Surg 2014 (Epub).

- Thank you for listing the additional references. Unfortunately all four references were published after our last literature review search date and were therefore not identified for inclusion in the original evidence synthesis. We have acknowledged these references in the discussion section, but as stated above, the publications identified by the reviewer tend to present evidence from specific perspectives. Our synthesis draws together evidence from all of these perspectives.

**VERSION 2 – REVIEW**

<b>REVIEWER</b>	Henrik Kehlet Rigshospitalet, Denmark  Academic conflict of interest
<b>REVIEW RETURNED</b>	25-Jun-2014

<b>GENERAL COMMENTS</b>	The authors have provided minor revisions of the manuscript. This reviewer fails to see what is really new here unless actual data from UK (which are not presented) were compared to the existing data from the international literature (RCT’s, meta-analyses, systematic reviews and prospective detailed cohort studies). Thus, the manuscript continues to use much space for the systematic review
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	<p>of RCT's which has been done repeatedly before including the authors themselves (BMJ Open 2014). Consequently, this reviewer does not find any new information in this manuscript.</p> <p>This reviewer still finds nothing new in this manuscript. They repeat their analysis of the literature which has been done repeatedly before and as mentioned in the revised manuscript including new meta-analyses as well as the one published recently by the authors in BMJ Open 2014(Chambers). They emphasise that the paper is important for UK, but there is no specific data presentation from UK surveys in the manuscript (which would have been interesting) compared to published data from RCT's. Most importantly, this manuscript -as well as other reviews- fails to discuss the lack of compliance with the important ERAS elements thereby explaining the wide variability in length of stay etc. and therefore of limited value on what potentially is important for UK settings in the future. The review also fails to discuss the differences between not always well-performed RCT's and very detailed prospective consecutive studies with much better outcomes than in the RCT's with a low compliance of important ERAS elements.</p> <p>The manuscript would have benefited from a focus on actual UK data and then looking on only a few procedures and to compare it with existing scientific data from outside UK in order to discuss the potential implications in the UK settings. The discussion on economic savings etc. does not provide anything new compared to existing data.</p> <p>Finally, when discussing the future aspects of ERAS programs the paper lacks a discussion on the role of minimal invasive surgical techniques – but again where the literature is confusing because of lack of compliance to important elements of ERAS.</p> <p>In such a paper, it may be important and interesting to include a discussion on the results of detailed prospective studies with optimal compliance with the important ERAS elements, since those data are different from most of the RCT's and since in complex situations like perioperative care. Thus, RCT's may not always be the only necessary data – and especially in a paper where the aim was to discuss the potential of ERAS programs in the UK settings.</p> <p>Berwick DM. The science of improvement. JAMA 2008; 299:1182-1184.</p> <p>Slim K, Kehlet H. Commentary: Fast track surgery: the need for improved study design. Colorectal Dis 2012; 14:1013-1014.</p>
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## VERSION 2 – AUTHOR RESPONSE

Thank you to Professor Kehlet for his additional comments. We have made some changes to the manuscript and responded to try to address his comments.

The barriers and facilitators to the successful implementation of ERAS programmes using UK data are summarised in the manuscript. Given the space constraints for journal articles, we did not present further data, but such data are available in the full publication (in press). We have now alluded to this in the manuscript submission on page 9.

We acknowledge that the manuscript reviews evidence that has already been discussed in previous publications. The manuscript in question does however go a step further on previous publications by synthesising evidence from systematic reviews, RCTs, and case studies from the UK.

Compliance/adherence to ERAS protocols have been mentioned within the UK case study narrative and inferences have been made to the differences in ERAS protocols and their implementation, and lack of evidence on compliance/adherence to such protocols. We have further highlighted the lack of evidence on compliance on page 7, 9 and 10).

The authors have not discussed the differences between RCTs and prospective consecutive studies in the manuscript. The limitations of the RCTs and case studies included in the manuscript have, however, been alluded to and implications for further research discussed on page 14 highlight that further RCTs are not required. Rather what is needed is improved collection and reporting of how enhanced recovery programmes are implemented, resourced and experienced in NHS settings – which could include detailed prospective consecutive studies.

Unfortunately evidence from the UK in terms of RCTs was lacking (as highlighted in the manuscript) and as most of the published evidence has been in colorectal surgery, the authors' intentions were to try to identify evidence from other surgical areas to provide a broader perspective.

We acknowledge that the economic section does not provide anything new to existing data. A systematic search of the literature was, however, undertaken as part of the rapid evidence synthesis. The evidence presented therefore represents that which was identified by our review, and the manuscript highlights the limitations of this evidence and recommends further research in this area.

The manuscript does not discuss the role of minimal invasive surgical techniques as this was not part of the review remit. We have reported in the manuscript on pages 8 and 10 that differences in the findings may have been due to factors such as differences in procedures.

We acknowledge that RCTs may not always be the only necessary data and that was the reason for including case studies. As we state on page 15, had the reporting format originally proposed by the Enhanced Recovery Partnership Programme been adhered to, our knowledge of aspects relating to fidelity and compliance would have been enhanced. Unfortunately this was not the case. As such, we as authors have also recommend that further RCTs are not needed, and that further research for compliance/adherence in staff and patients is needed (page 15).