QUERI

Enhanced Recovery After Surgery (ERAS) Programs for Patients Undergoing Colorectal Surgery

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PREFACE

The VA Evidence-based Synthesis Program (ESP) was established in 2007 to provide timely and accurate syntheses of targeted healthcare topics of particular importance to clinicians, managers, and policymakers as they work to improve the health and healthcare of Veterans. QUERI provides funding for four ESP Centers, and each Center has an active University affiliation. Center Directors are recognized leaders in the field of evidence synthesis with close ties to the AHRQ Evidence-based Practice Centers. The ESP is governed by a Steering Committee comprised of participants from VHA Policy, Program, and Operations Offices, VISN leadership, field-based investigators, and others as designated appropriate by QUERI/HSR&D.

The ESP Centers generate evidence syntheses on important clinical practice topics. These reports help:

- Develop clinical policies informed by evidence;
- Implement effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures; and
- Set the direction for future research to address gaps in clinical knowledge.

The ESP disseminates these reports throughout VA and in the published literature; some evidence syntheses have informed the clinical guidelines of large professional organizations.

The ESP Coordinating Center (ESP CC), located in Portland, Oregon, was created in 2009 to expand the capacity of QUERI/HSR&D and is charged with oversight of national ESP program operations, program development and evaluation, and dissemination efforts. The ESP CC establishes standard operating procedures for the production of evidence synthesis reports; facilitates a national topic nomination, prioritization, and selection process; manages the research portfolio of each Center; facilitates editorial review processes; ensures methodological consistency and quality of products; produces “rapid response evidence briefs” at the request of VHA senior leadership; collaborates with HSR&D Center for Information Dissemination and Education Resources (CIDER) to develop a national dissemination strategy for all ESP products; and interfaces with stakeholders to effectively engage the program.

Comments on this evidence report are welcome and can be sent to Nicole Floyd, ESP CC Program Manager, at Nicole.Floyd@va.gov.

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EXECUTIVE SUMMARY

INTRODUCTION

Enhanced recovery after surgery (ERAS), also referred to as an enhanced recovery program, fast-track rehabilitation, multimodal management, or similar descriptors, is a multidisciplinary approach to perioperative care. A protocol of components related to preadmission, preoperative, intraoperative, and postoperative care is implemented with the goal of improving patient recovery, facilitating earlier discharge from the hospital, and potentially reducing health care costs without increasing complications or hospital readmissions. The protocol components may contribute to minimizing, and/or improving the response to, physiological stress associated with surgery.

Although guidelines for ERAS related to colorectal surgery exist, variation in the number and definition of protocol components contributes to difficulties in determining effectiveness. Little is known about implementation barriers and facilitators as well as components (or combinations of components) key for improved clinical outcomes. In addition, protocol compliance, when reported, may be measured by percentage of elements applied or completed without standardization across elements (timing, regimens, doses, *etc*).

Preliminary literature searches conducted for topic refinement found several systematic reviews on enhanced recovery for colorectal surgery. However, none reported on subgroups based on surgical approach (open or laparoscopic surgery) or colorectal condition. While several noted the enhanced recovery protocol components from the included studies, the standard care protocols were not documented. None commented on barriers or facilitators to implementation of an enhanced recovery program.

The defining components of an enhanced recovery program for colorectal surgery have been revised over time and new trials have been published since the search dates of the existing reviews. We provide an updated review of randomized controlled trials (RCTs) and controlled clinical trials (CCTs) looking at comparative effectiveness and harms overall and by type of surgery, colorectal condition, and fidelity to an enhanced recovery protocol. We also review barriers and facilitators to implementation and provide a contextual discussion of compliance and outcomes.

With input from the topic nominator and a technical expert panel, we developed the following key questions:

KQ1: What is the comparative effectiveness of ERAS versus usual care or a subset of ERAS components for adults undergoing elective colorectal surgery?

KQ2: What are the harms of ERAS versus usual care or a subset of ERAS components for adults undergoing elective colorectal surgery?

KQ3: Do comparative effectiveness and harms vary by fidelity to ERAS components?

KQ4: Do comparative effectiveness and harms vary by type of, and clinical conditions for, colorectal surgery (*eg*, anatomical site, laparoscopic versus open surgery, reasons for open surgery, *etc*)?

KQ5: What are the barriers to and facilitators of implementation of ERAS programs?

METHODS

Data Sources and Searches

We searched MEDLINE (Ovid) and the Cumulative Index to Nursing and Allied Health Literature (CINAHL) for English language publications from 2011 to July 2017. Search terms included terms used synonymously with ERAS (*eg*, fast track, multimodal, accelerated, enhanced) and terms for colorectal surgery (both open and laparoscopic). We also obtained articles from reference lists of existing systematic reviews, reference lists of included studies, and suggestions from technical expert panel members.

Study Selection

Abstracts identified in the literature searches were independently reviewed by 2 researchers. Full-text review of potentially eligible studies was completed by one researcher with input from co-investigators. We included:

1) Studies of adults undergoing elective colorectal surgery (any colorectal procedure, open or laparoscopic surgery),
2) For effectiveness of ERAS programs (KQ1-KQ4):
    a. randomized controlled trial (RCT) or controlled clinical trial (CCT)
    b. comparator is usual care or subset of ERAS components (as defined by study authors),
3) For barriers to and facilitators of implementation (KQ5):
    a. any study design providing qualitative data on barriers and facilitators
    b. study conducted in healthcare system relevant to VA.

We excluded:

1) Non-English language publications,
2) Studies that compared laparoscopic and open surgery within an enhanced recovery protocol,
3) Studies reporting outcomes before and after implementation of an enhanced recovery protocol (*ie*, pre-post or case series with historical controls design); we included controlled clinical trials if data collection was concurrent,
4) Trials of single a component of enhanced recovery,
5) Studies that included post-operative components only (often referred to as “Post-operative Rehabilitation” or “Controlled Rehabilitation”).

Data Abstraction and Quality Assessment

For each eligible study for KQ1 to KQ4, we created a table indicating the included ERAS components and the ERAS components implemented as part of the usual care protocol.

We abstracted the following data onto evidence tables organized by type of surgery (open or laparoscopic):

1) Patient and study characteristics: study location (country); funding source; inclusion/exclusion criteria; length of follow-up; compliance with enhanced recovery protocol; patient age, gender, race/ethnicity, BMI or obesity status; comorbidity status; colorectal conditions; and surgical procedures

2) Outcomes (as defined above) for intervention and control groups.

Risk of bias of RCTs and CCTs was assessed using a modified Cochrane approach considering sequence generation, allocation, blinding, incomplete outcome reporting, and selective outcome reporting. Each study was rated as high, medium, low, or unclear risk of bias.

Data Synthesis and Analysis

Tables were developed with studies pertaining to KQ1 and KQ2 noting outcomes reported by fidelity to enhanced recovery components (KQ3) or type of surgery (KQ4). If applicable, data for critical outcomes were pooled. We qualitatively summarized findings for KQ5 (enhanced recovery barriers and facilitators).

We evaluated the overall strength of evidence for our critical outcomes using a method developed by the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) group.

RESULTS

Results of Literature Search

We reviewed 1789 citations and excluded 1629 studies at the abstract stage and another 117 after full-text review. Many of the excluded studies were observational studies that provided contextual information about adherence or compliance but did not meet inclusion criteria. We added 7 articles (including 6 trials published prior to 2011 identified from existing systematic reviews), resulting in a total of 50 included articles: 25 trials reported in 27 articles, 10 with information about implementation barriers and facilitators, and 13 systematic reviews.

Summary of Results for Key Questions

Thirteen RCTs compared open elective colorectal surgery with an enhanced recovery protocol to open surgery with a usual care protocol. Eight studies (6 RCTs and 2 CCTs) compared an enhanced recovery protocol to usual care in patients undergoing laparoscopic surgery. Three studies (2 RCTs and 1 CCT) included 4 groups of patients providing comparisons of enhanced recovery and usual care for both open and laparoscopic surgery. One RCT included both open and laparoscopic surgery with the surgeon deciding the surgical approach. None of the studies was conducted in the US. Indications for surgery included cancer and non-cancer conditions.

Key Question 1

Length of stay and overall perioperative morbidity were reduced in the enhanced recovery protocol groups compared to the usual care protocol groups. In pooled analyses, the mean reduction in length of stay was 2.59 days (95% CI -3.22, -1.97) and the risk ratio for experiencing complications was 0.66 (95% CI 0.54, 0.80). All-cause mortality was infrequent and did not differ significantly between the enhanced recovery and usual care protocol groups.

Readmissions, typically reported to 30 days post-surgery, were also similar (pooled risk ratio 1.11 (95% CI 0.82, 1.50). The incidence of ileus was not significantly different between enhanced recovery and usual care protocol groups, while gastrointestinal function (time to flatus and/or first bowel movement and time to oral intake of solid foods) were significantly shorter following surgery with an enhanced recovery protocol compared to a usual care protocol. Pain and quality of life were infrequently reported.

Key Question 2

Surgical site infection rates did not differ significantly between protocol groups. The pooled risk ratio was 0.75 (95% CI 0.52, 1.07). Other harms, including bleeding events, anastomotic leakage, need for re-operation, urinary tract infection, and cardiovascular complications also did not differ between groups.

Key Question 3

Few studies reported adherence to the enhanced recovery protocol components. We identified 11 studies that best differentiated the enhanced recovery protocol from the usual care protocol. We found pooled length of stay and overall morbidity in those studies, and in the remaining studies (*ie,* those with less differentiation of protocols), to be similar to the overall pooled estimates.

Key Question 4

For critical outcomes (length of stay, all-cause mortality, overall morbidity, readmissions, and surgical site infections) we found no difference between enhanced recovery and usual care protocols in studies performing open surgery or studies performing laparoscopic surgery or for studies of different colorectal conditions. We did not find outcomes reported for other subgroups of interest: comorbidity status, mobility status, frailty index, age, patient size, or right- versus left-side surgery.

Key Question 5

We included findings from interviews with providers and patients. Staffing and organizational barriers included difficulty adapting to change, need for flexibility to address individual patient needs, disagreement with the protocol recommendations, scheduling, and lack of resources to implement the protocol components. Facilitators included good communication and relationships across departments, leadership, integration of enhanced recovery protocols into order sets and computer order entry systems, audit and feedback with reporting of program data, and staff education. Patient-related barriers include characteristics of the population (*eg,* comorbidities, social support, health literacy) and concerns about care following discharge. Facilitators include patient education, early communication, and patient appreciation of early mobilization and hospital discharge.

DISCUSSION

Key Findings and Quality of Evidence

1) Enhanced recovery protocols significantly reduced length of stay (mean reduction 2.6 days) following colorectal surgery compared to usual care protocols (Quality of Evidence: Moderate). Length of stay reductions occurred across surgical approach (open and laparoscopic) as well as

clinical indication (*ie,* colorectal cancer, rectal cancer, a mix of colorectal cancer and benign conditions, or benign conditions alone).

2) Enhanced recovery protocols significantly reduced overall perioperative morbidity (mean absolute reduction 10%) associated with colorectal surgery compared to usual care protocols (Quality of Evidence: Moderate). Reductions due to enhanced recovery protocols did not significantly vary by type of, or clinical condition for, surgery.

3) Mortality, hospital readmissions, and surgical site infections were similar following colorectal surgery with an enhanced recovery protocol or a usual care protocol (Quality of Evidence for Mortality: Low) (Quality of Evidence for Readmissions: Low) (Quality of Evidence for Surgical Site Infections: Low). Outcomes were similar across surgical approach and clinical indication for surgery.

4) Few studies reported on clinically meaningful differences in pain or quality of life, though most studies noted an improvement in gastrointestinal function (typically passing flatus or bowel movement).

5) Enhanced recovery protocols varied across studies, little information was provided regarding component compliance, and evidence is insufficient regarding key components.

6) Commonly reported barriers to implementation include time, resources, and acceptability/feasibility of protocols to clinical staff and patients. Facilitators include organizational support, sufficient staff and electronic medical record resources, clear communication that is receptive to staff/patient feedback, and standardized yet adaptable and feasible protocols.

Implications for Practice

Few of the studies included in our review addressed compliance with the enhanced recovery protocols and only one related compliance to critical outcomes. Although representative data from observational studies (*not systematically reviewed*) suggest that outcomes vary depending on protocol compliance, there is no consensus on key components or a “bundle” of components necessary to achieve improved patient outcomes.

Limitations

Many studies were rated high or unclear risk of bias as methods of sequence generation, allocation concealment, and blinding were often not reported. Observed differences in outcomes across studies might be due to implementation of different enhanced recovery protocols, implementation of enhanced recovery in different healthcare systems and with different procedures (including discharge protocols), different patient populations (*eg*, exclusion of patients with ASA grades III or IV), and different outcome definitions.

Applicability of Findings to the VA Population

None of the trials and only 2 of the qualitative studies of barriers to and facilitators of implementation were done in the US. There is no direct evidence of the effectiveness or harms of an enhanced recovery protocol for colorectal surgery in the US or at VHA facilities. Hospital

length of stay, readmissions, and surgical complication rates from reported studies may not reflect US settings including those at VHA facilities. Although there are real potential benefits of enhanced recovery programs, particularly in reduced length of stay and possibly morbidity, rolling out a new protocol in "total quality improvement" fashion with evaluation and refinement might be the best approach due to limited applicability of existing RCT data, rapidly evolving standard practice, limited full understanding of implementation/adherence/standardization of enhanced recovery components, and possible barriers.

Research Gaps/Future Research

There is a need for data from the US, and, for the purpose of making decisions relevant to Veteran care, RCTs or quality improvement program processes with real-time evaluation across varying VHA facilities. While we found no empiric evidence, our key content experts and consultants suggest that many of the enhanced recovery components have been or over time are being adopted into standard perioperative care for colorectal surgery.

Studies designed to evaluate the benefits and harms of enhanced recovery protocols should provide detailed information describing enhanced recovery components, and specifically how they are implemented and compliance is assessed in the intervention and control groups. Surgeon experience and surgical volume should be considered. Outcomes should include patient and/or caregiver experiences.

Conclusions

Implementation of enhanced recovery protocols for elective colorectal surgery resulted in reduced length of stay and overall perioperative morbidity versus standard care protocols. Mortality, readmissions, and surgical site infections were similar between the groups. However, the enhanced recovery and standard care protocols varied across studies in number of components and combinations of components, with few trials reporting compliance with the protocols. There is no reliable evidence on enhanced recovery components, alone or in combination, that are key to improving patient outcomes. The value of investing time and resources into implementing all of the enhanced recovery components remains largely unknown.

ABBREVIATIONS TABLE

CCT	Controlled clinical trial
ERAS	Enhanced Recovery After Surgery
ERP	Enhanced Recovery Program
FT	Fast Track
RCT	Randomized controlled trial
UK	United Kingdom
US	United States
VA	Department of Veterans Affairs
VHA	Veterans Health Administration

EVIDENCE REPORT

INTRODUCTION

Enhanced recovery after surgery (ERAS), also referred to as an enhanced recovery program, fast-track rehabilitation, multimodal management, or similar descriptors, is a multidisciplinary approach to perioperative care. A protocol of components related to preadmission, preoperative, intraoperative, and postoperative care is implemented with the goal of improving patient recovery, facilitating earlier discharge from the hospital, and potentially reducing health care costs without increasing complications or hospital readmissions.[1-3] The protocol components may contribute to minimizing, and/or improving the response to, physiological stress associated with surgery.[1,2]

The ERAS Society has published guidelines for implementing an ERAS program for colorectal surgery.[2,4] However, variation in the number and definition of protocol components contributes to difficulties in determining effectiveness. Little is known about implementation barriers and facilitators as well as components (or combinations of components) key for improved clinical outcomes. In addition, protocol compliance, when reported, may be measured by percentage of elements applied or completed without standardization across elements (timing, regimens, doses, *etc*).

Enhanced recovery protocols are not limited to colorectal surgery. ERAS Society guidelines are available for at least 15 procedures.[2] However, given that the largest volume of evidence for comparative effectiveness of enhanced recovery and usual care protocols is available for colorectal surgery, we limit our review to studies of enhanced recovery for colorectal surgery.

Preliminary literature searches for topic refinement identified published systematic reviews on the topic. An overview of 13 systematic reviews published between 2011 and 2017 is presented in Appendix A.[5-17] Three focused only on laparoscopic surgery.[11,15,16] None of the existing reviews reported on subgroups based on surgical approach (open or laparoscopic surgery) or colorectal condition. While several noted the enhanced recovery protocol components from the included studies, the standard care protocols were not documented. Only one systematic review formally rated the overall quality of evidence.[17] None commented on barriers or facilitators to implementation of an enhanced recovery program.

The defining components of an enhanced recovery program for colorectal surgery have been revised over time[2] and new trials have been published since the search dates of the existing reviews. We provide an updated review of randomized controlled trials (RCTs) and controlled clinical trials (CCTs), looking at comparative effectiveness and harms overall and by type of surgery, colorectal condition, and fidelity to an enhanced recovery protocol. We also review barriers and facilitators to implementation and provide a contextual discussion of compliance and outcomes.

With input from the topic nominator and a technical expert panel, we developed the following analytic framework (Figure 1); population, intervention, comparator, outcomes (PICO); and key questions.

PICO

Population: Adults (18 and over) undergoing elective colorectal surgery

Intervention: Enhanced recovery program (as defined by study authors)

Comparator: Usual care or subset of enhanced recovery components not meeting author definition of a full enhanced recovery program

Outcomes:

Final Health Outcomes: Length of stay (initial stay, total); overall morbidity; mortality; readmission rate; ileus; clinically important difference in pain scores; and clinically meaningful changes in quality of life

Intermediate: Gastrointestinal function (time to oral feeding, bowel function, nausea), intravenous fluid administration, mobilization, pain scale scores

Harms: Surgical complications (infection, anastomotic leakage), non-surgical complications (cardiovascular, respiratory, urinary tract infection), need for re-operation, bleeding, Foley catheter re-insertion and complications, aspiration pneumonia, readmission

Key Questions

KQ1: What is the comparative effectiveness of ERAS versus usual care or a subset of ERAS components for adults undergoing elective colorectal surgery?

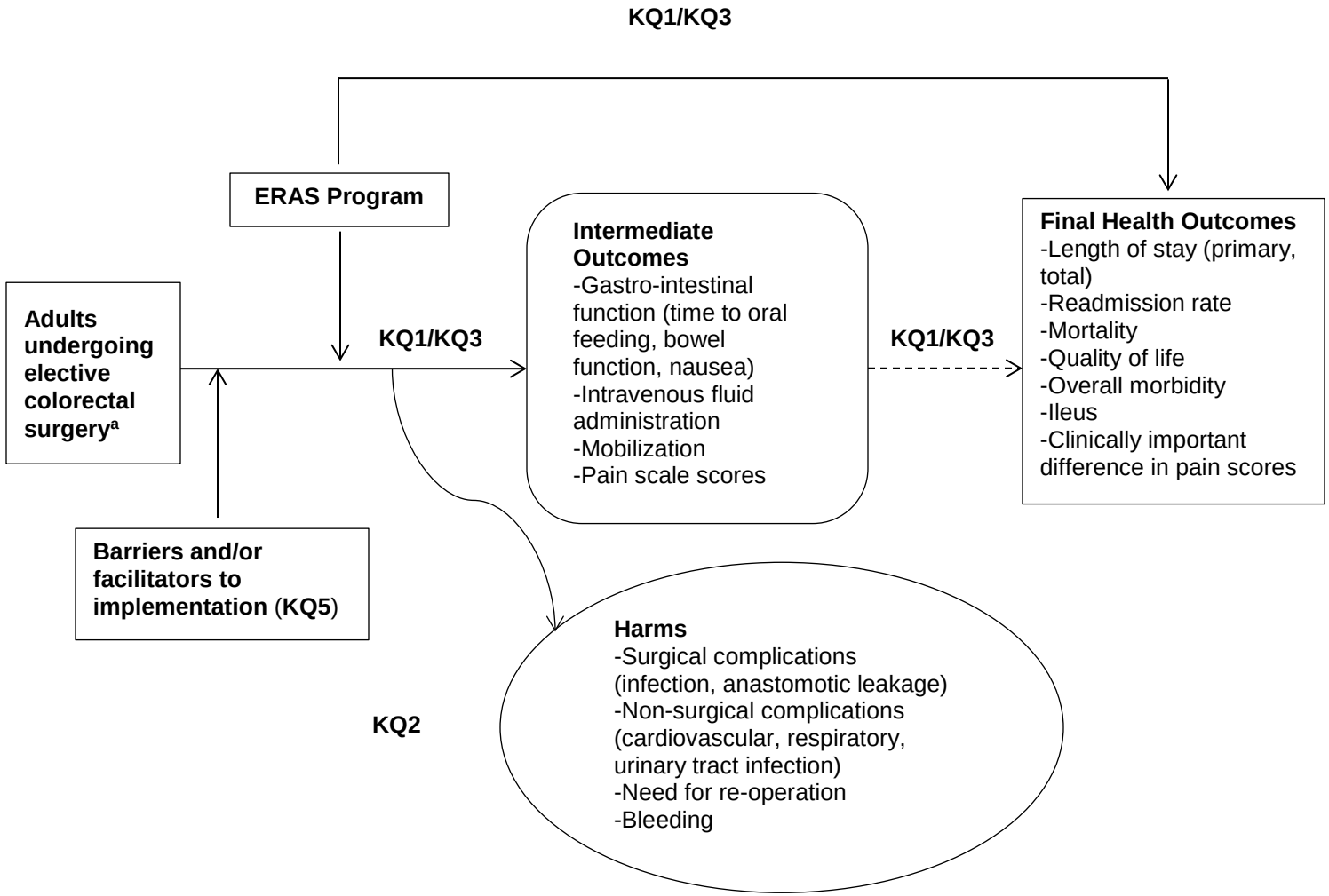
KQ2: What are the harms of ERAS versus usual care or a subset of ERAS components for adults undergoing elective colorectal surgery?

KQ3: Do comparative effectiveness and harms vary by fidelity to ERAS components?

KQ4: Do comparative effectiveness and harms vary by type of, and clinical conditions for, colorectal surgery (*eg*, anatomical site, laparoscopic versus open surgery, reasons for open surgery, *etc*)?

KQ5: What are the barriers to and facilitators of implementation of ERAS programs?

Figure 1. Analytic Framework



[a] Consider subgroups based on comorbidity status, mobility status, frailty index, age, patient size, right vs left side, laparoscopic vs open procedure, type of surgery **(KQ4)**

METHODS

TOPIC DEVELOPMENT

The topic was nominated for review by William Gunnar, MD, JD, National Director of Surgery.

SEARCH STRATEGY

We searched MEDLINE (Ovid) and the Cumulative Index to Nursing and Allied Health Literature (CINAHL) for English language publications from 2011 to July 2017. Search terms included terms used synonymously with ERAS (*eg*, fast track, multimodal, accelerated, enhanced) and terms for colorectal surgery (both open and laparoscopic). The search strategies are presented in Appendix B.

We obtained additional articles from reference lists of existing systematic reviews, reference lists of included studies, and suggestions from technical expert panel members.

STUDY SELECTION

Abstracts identified in the literature searches were independently reviewed by 2 researchers. Full-text review of potentially eligible studies was completed by one researcher with input from investigators. We included:

1) Studies of adults undergoing elective colorectal surgery (any colorectal procedure, open or laparoscopic surgery),

2) For effectiveness of ERAS programs (KQ1-KQ4):
   a. randomized controlled trial (RCT) or controlled clinical trial (CCT)
   b. comparator is usual care or subset of ERAS components (as defined by study authors),

3) For barriers to and facilitators of implementation (KQ5):
   a. any study design providing qualitative data on barriers and facilitators
   b. study conducted in healthcare system relevant to VA.

We excluded:

1) Non-English language publications,

2) Studies that compared laparoscopic and open surgery within an enhanced recovery protocol,

3) Studies reporting outcomes before and after implementation of an enhanced recovery protocol (*ie*, pre-post or case series with historical controls design); we included controlled clinical trials if data collection was concurrent,

4) Trials of single component of enhanced recovery,

5) Studies that included post-operative components only (often referred to as “Post-operative Rehabilitation” or “Controlled Rehabilitation”).

DATA ABSTRACTION

For each eligible study for KQ1 to KQ4, we created a table indicating the included ERAS components.[2,4] We also noted which of the ERAS components were implemented as part of the usual care protocol.

We abstracted the following data onto evidence tables organized by type of surgery (open or laparoscopic):

1) Patient and study characteristics: study location (country); funding source; inclusion/exclusion criteria; length of follow-up; compliance with enhanced recovery protocol; patient age, gender, race/ethnicity, BMI or obesity status; comorbidity status; colorectal conditions; and surgical procedures

2) Outcomes (as defined above) for intervention and control groups

QUALITY ASSESSMENT

Risk of bias of RCTs and CCTs was assessed using a modified Cochrane approach considering sequence generation, allocation, blinding, incomplete outcome reporting, and selective outcome reporting. Each study was rated as high, medium, low, or unclear risk of bias.[18]

DATA SYNTHESIS

Tables were developed with studies pertaining to KQ1 and KQ2 noting outcomes reported by fidelity to enhanced recovery components (KQ3) or type of surgery (KQ4). If applicable, data for critical outcomes were pooled and analyzed using DerSimonian and Laird random-effects models[19] in Cochrane Collaboration Review Manager software, Version 5.3 (The Nordic Cochrane Center, Copenhagen, Denmark). We calculated weighted mean differences (WMD) for length of stay and risk ratios (RR) for overall morbidity, all-cause mortality, readmissions, and surgical site infections. Peto odds ratios were applied when events were rare, such as mortality. Heterogeneity between studies was assessed by using the I^2 test, with a I^2 value greater than 50% considered substantial.[20] If length of stay data were reported in medians, data were extracted from previous systematic reviews or converted to estimates of means and standard deviations based on methods outlined by Hozo.[21]

We qualitatively summarized findings for KQ5 (enhanced recovery barriers and facilitators).

RATING THE BODY OF EVIDENCE

We evaluated the overall strength of evidence for our critical outcomes using a method developed by the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) group.(GRADEpro 2015 accessed at www.gradepro.org). The following domains were used to assess strength of evidence: 1) risk of bias; 2) consistency; 3) directness; and 4) precision. Strength of evidence ranges from high (indicating high confidence that the true effect lies close to that of the estimate of the effect) to very low (indicating very little confidence in the effect estimate and that the true effect is likely to be substantially different from the estimate of effect).

PEER REVIEW

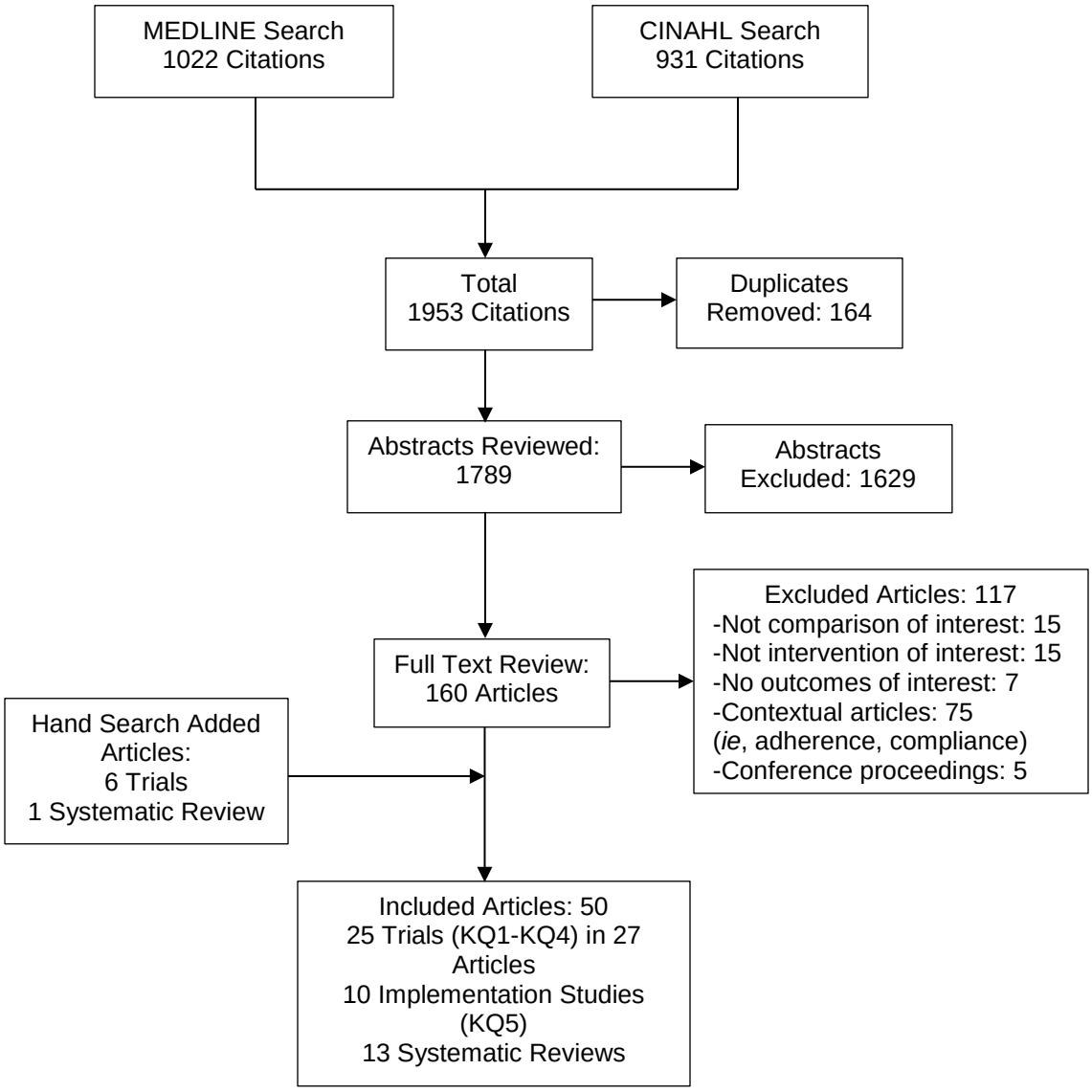
A draft version of this report was reviewed by content experts as well as clinical leadership. Reviewer comments and our responses are presented in Appendix C and the report was modified as needed.

RESULTS

LITERATURE FLOW

The literature searches yielded 1022 citations in MEDLINE and 931 citations in CINAHL. Combining the results and removing duplicates yielded 1789 citations. We excluded 1629 studies at the abstract stage and another 117 after full-text review. Many of the excluded studies were observational studies that provided contextual information about adherence or compliance but did not meet inclusion criteria. We added 7 articles (including 6 trials published prior to 2011 identified from existing systematic reviews) resulting in a total of 50 included articles: 25 trials reported in 27 articles, 10 with information about implementation barriers and facilitators, and 13 systematic reviews.

Figure 2: Literature Flow Chart



KEY QUESTION 1: What is the comparative effectiveness of ERAS versus usual care or a subset of ERAS components for adults undergoing elective colorectal surgery?

Overview of Studies

Open Surgery Studies

Sixteen studies (15 RCTs, 1 CCT) compared open surgery with an enhanced recovery protocol to open surgery with a conventional (usual care) protocol.[22-37] Three of these studies also reported results for laparoscopic surgery with an enhanced recovery protocol compared to laparoscopic surgery with a conventional protocol (see below).[25,34,35] We rated 4 studies low risk of bias, 4 medium risk of bias, 3 high risk of bias, and 5 unclear risk of bias. Study details are provided in Appendix D, Table 1.

No studies were conducted in the US. There were 6 from China,[23,27,32,35-37] 3 from the United Kingdom,[22,24,28] and one each from Italy,[31] India,[30] Greece,[25] the Netherlands,[34] Romania,[26] Switzerland,[29] and the Czech Republic.[33]

Seven studies included patients undergoing elective surgery for colorectal cancer.[23,26-28,32,36,37] Three studies reported the percentage of colon and rectal surgeries.[23,26,28] One study enrolled patients age 70 and older.[27] Sample sizes in the colorectal cancer studies ranged from 62[37] to 597.[32] Mean or median ages ranged from 55 to 73 years; in the study of elderly patients, the mean age was 75 years. The study population was more than 55% male in all but one study.[28] Three studies reported BMI with values of 22,[37] 22.5,[32] and 24.[23] No study included participants with preoperative American Society of Anesthesiologists (ASA) physical status classification IV.

Five studies included mixed groups of patients – colorectal cancer or benign conditions,[22,24,29,34,35] though the majority of participants underwent surgery for colon cancer. Sample sizes in these studies ranged from 25[22] to 191[34] with mean or median ages ranging from 55 to 68 years. In all but one study,[22] more than 50% of participants were male. All 5 studies reported BMI with mean or median values of 27 or lower. As with the colorectal cancer studies, no colorectal cancer/benign condition study included participants with preoperative ASA score IV.

Two studies included patients undergoing rectal cancer surgery.[25,31] Both enrolled fewer than 100 patients. Mean ages were 67[31] and 64[25] years and more than 50% were male. Mean BMI was 28 in one study;[25] the other reported that 38% had a BMI less than 25.[31] In one study, 88% were ASA I or II;[25] in the other, 90% were ASA II or III.

The remaining 2 studies enrolled patients undergoing colorectal surgery that was primarily non-cancer related. In the study from India, 3% of participants had a cancer diagnosis[30] while in the study from the Czech Republic,[33] 7% had a cancer diagnosis and 78% had Crohn's disease. Sample sizes in the 2 studies were 60 and 103, respectively, with mean ages of 34 and 36 years. Approximately 50% were male in both studies; neither reported BMI or ASA scores.

Laparoscopic Studies

Eleven studies (8 RCTs, 3CCTs) compared an enhanced recovery program to usual care in patients undergoing laparoscopic surgery for colorectal conditions.[25,34,35,38-46] Three of these studies also reported results for open surgery (see above).[25,34,35] Five studies were from China[35,38,44-46] and 3 were from Italy,[40,41,43] with one each from Japan,[42] Greece,[25] and The Netherlands.[34] Three were rated unclear risk of bias, 5 medium risk of bias, 2 high risk of bias, and one low risk of bias. Study details are provided in Appendix D, Table 1.

Five studies included patients with colon cancer[35,44,45] or colorectal cancer.[42,46] Sample sizes ranged from 78[46] to 320.[42] One study enrolled patients over 65 years; median ages were 71 in the enhanced recovery group and 72 in the usual care group.[46] In the other 4 studies, mean or median ages were in the 50s[35,44,45] or 60s.[42] Across the 4 studies, 47%[45] to 66%[35] were male and in 3 studies reporting BMI, means or medians were 22 to 24.[35,44,45] No study reporting ASA included grade IV; 2 studies excluded ASA III or IV.[42,45]

One study included 209 patients with cancer and benign conditions[34] and 2 included patients with cancer (69%-75%) or diverticular disease (25%-31%).[40,41] In the study with cancer and benign conditions, mean age was 57 years, 58% were male, and mean BMI was 26.[34] Patients with ASA IV were excluded. In the studies with cancer and diverticular disease, the mean or median ages were 66 years, approximately 50% were male, and mean BMI was 26.5.[40,41] ASA IV was also an exclusion criterion. A subgroup analysis of one of these studies included only patients 70 years of age and older.[39]

Two studies enrolled patients exclusively with rectal cancer.[25,38] Mean ages were 55 years in a study of 116 patients[38] and 66 years in a study of 75 patients.[25] In one study the populations was 66% male with a mean BMI of 22.[38] In the second study, the population was 44% male with a mean BMI of 28.[25] One study excluded patients with ASA III or IV[38]; in the other study there were no patients with ASA IV.[25]

One study enrolled 227 women with bowel endometriosis.[43] Mean age was 35 years and mean BMI was 22.

We identified one additional report of laparoscopic surgery with enhanced recovery compared to usual perioperative care in elderly patients with colorectal cancer.[47] However, the authenticity of the paper has been questioned.[48] We do not report findings from this study.

Mixed Open and Laparoscopic Study

One low risk of bias RCT included 324 patients who underwent either open or laparoscopic surgery (the surgeon's choice) for colon (46%) or rectal (54%) disease.[49,50] Overall, 79% of cases were malignant. Median ages were 65 (ERAS group) and 66 (usual care group), 54% were male, and 63% were ASA II. A subgroup analysis divided patients into 3 age groups: ≤65 years, 66 to 79 years, and ≥80 years.[49]

Enhanced Recovery Components

Ljungqvist et al organized the ERAS components into 4 phases: preadmission, preoperative, intraoperative, and postoperative.[2] We merged the ERAS components from this recent

description with those from 2013 guidelines.[2,4] We charted the enhanced recovery protocol components specified in the enhanced recovery protocols and usual care protocols for each of the studies included in our review (Appendix E). Some studies used identical protocols resulting in 24 unique protocols (13 for open surgery, 10 for laparoscopic surgery, and one for open or laparoscopic surgery). We tracked 3 preadmission components, 8 preoperative components, 6 intraoperative components, and 9 postoperative components.

We found wide variation in the number of enhanced recovery components contained in the study protocols. Of 26 possible enhanced recovery components, enhanced recovery group protocols were found to include between 4 and 18 enhanced recovery components (4 studies with fewer than 10 components, 10 studies with 10-12 components, 8 studies with 13-15 components, and 2 studies with more than 15 components). The standard care group protocols included between 0 and 10 enhanced recovery components (16 with 0-2 components, 4 with 3-6 components, and 4 with more than 6 components).

The number of studies including each component (in either the enhanced recovery protocol or the usual care protocol) is presented in Table 1. No study included the preadmission components. Of the preoperative components, the most frequently included in enhanced recovery protocols were carbohydrate treatment, no routine use of mechanical bowel preparation, and a fasting protocol allowing clear fluids until 2 hours before surgery and solid until 6 hours before surgery. Eight protocols from our included studies had 2 or fewer of the 8 preoperative components, 2 had 3 components, 6 had 4 components, 6 had 5 components, and 2 had 6 components.

Of the 6 intraoperative components, the most frequently included were removal of nasogastric tubes before reversal of anesthesia (and no routine use of nasogastric tubes) and a standardized anesthesia protocol. One study protocol included only one intraoperative component. Most protocols included between 3 and 5 components. One protocol from a study of laparoscopic surgery included all 6 components.

Among the 9 postoperative components, early intake of oral fluids and solids was included in all enhanced recovery protocols. Other frequently included components were early mobilization, multimodal approach to opioid-sparing pain control, and early removal of urinary catheters and intravenous fluids. One protocol included only one postoperative component. The rest included at least 2 of the 9 components, with most including between 4 and 6 components.

Table 1. Count of ERAS Components in Study Protocols for ERAs and Standard Care

Phases	ERAS Components	ERAS Protocol	Standard Care Protocol
PREADMISSION	Smoking/alcohol cessation	0	0
	Nutritional screening/support	0	0
	Medical optimization of chronic disease	0	0
PREOPERATIVE	Structured information/patient and caretaker engagement	12	0
	Bowel preparation (no routine use of mechanical bowel prep)	16	2
	Pre-operative fasting (clear fluids to 2 hours and solids to 6 hours before surgery)	16	3
	Carbohydrate treatment	18	0
	Thrombosis prophylaxis	4	2
	Infection prophylaxis and/or skin preparation with chlorhexidine-alcohol	11	8
	Nausea and vomiting prophylaxis	5	2
	Pre-anesthetic sedative medication (no routine use)	3	0
INTRAOPERATIVE	Minimal invasive surgical techniques	2+10 Lap	0+10 Lap
	Standardized anesthesia protocol – may use thoracic epidural blocks with local anesthetics and low-dose opioids for open surgery and spinal analgesia or patient-controlled morphine as alternative to thoracic epidural for laparoscopic surgery	16	9
	Maintain fluid balance; vasopressors for blood pressure control	14	3
	Restrictive use of surgical site drains	15	5
	Remove nasogastric tubes before reversal of anesthesia (and no routine use)	21	5
	Control of body temperature	9	4
	Early mobilization	22	4
	Early intake of oral fluids and solids	23	1
POSTOPERATIVE	Early removal of urinary catheters and intravenous fluids	18	2
	Chewing gum, laxatives, peripheral opioid-blocking agents	7	1
	Protein and energy-rich nutritional supplements	11	0
	Glucose control	1	0
	Multimodal approach to opioid-sparing pain control – consider thoracic epidural analgesia (open surgery) or spinal analgesia (laparoscopic surgery); also NSAIDS and paracetamol	21	6
	Multimodal approach to control of nausea and vomiting	0	0
	Prepare for early discharge	2	1

Overview of Outcomes

Table 2 provides an overview of outcomes reported. An “up arrow” (-) indicates a statistically significant benefit with the enhanced recovery protocol compared to the usual care protocol. A “side-to-side arrow” («) indicates results were not significantly different between the enhanced recovery protocol and the usual care protocol. A “down arrow” (¯) indicates a significantly worse outcome with the enhanced recovery protocol compared to the usual care protocol. Complete outcomes data are provided in Appendix D, Tables 2-6. Outcome reporting varied across studies. No study reported on all our outcomes. All studies reported a measure of length of stay. Most studies reported on mortality, perioperative complications (including overall morbidity), hospital readmissions, and some aspect of gastrointestinal function. Few studies reported on clinically meaningful changes in quality of life or pain.

Table 2. Summary of Outcomes (Enhanced Recovery vs Usual Care)

Author Year Population	Length of Stay	Overall Mortality	Overall Morbidity	Readmissions	Quality of Life (Clinically Meaningful Change)	Pain (Clinically Meaningful Change)	Gastrointestinal Function			Surgical Complications				Non-Surgical Complications	
							Ileus	Time to Oral Solid Foods	Other (*eg*, Flatus, Bowel Movement)	Surgical Site Infection	Bleeding	Need for Re-operation	Other Surgical Complication	Foley Catheter Re-insertion/ Complication	Aspiration Pneumonia/ Pulmonary Infection
OPEN SURGERY STUDIES															
Feng 2016[23] Colorectal cancer	- [b]		-				«	-	-	«	«		«		«
Pappalardo 2016[31] Rectal cancer	-	«							-				«		
Jia 2014[27] Colorectal cancer (elderly)	-	«							-	«			«		-
Nanavati 2014[30] Gastrointestinal surgery (3% cancer)	-	«		«			«		-	«		«	«		
Gouvas 2012[25] *CCT* Rectal cancer	- [c]	«	«	«			-		-		«	«	«		-
Ren 2011[32] Colorectal cancer	-	«	«						-	«			«		
Wang 2012[35] Colon cancer	- [a]	«	«	«									«		
Yang 2012[37] Colorectal cancer	-		«	«				-	-	«			«		«

Author Year Population	Length of Stay	Overall Mortality	Overall Morbidity	Readmissions	Quality of Life (Clinically Meaningful Change)	Pain (Clinically Meaningful Change)	Gastrointestinal Function			Surgical Complications				Non-Surgical Complications	
							Ileus	Time to Oral Solid Foods	Other (*eg*, Flatus, Bowel Movement)	Surgical Site Infection	Bleeding	Need for Re-operation	Other Surgical Complication	Foley Catheter Re-insertion/ Complication	Aspiration Pneumonia/ Pulmonary Infection
Vlug 2011[34] Cancer and benign disease	- [c]	«	«	«			«	-	-	«		«	«		
Wang 2011[36] Colorectal cancer	-	«	-	«					-	«		«	«	«	
Ionescu 2009[26] Rectosigmoid (58%) or colon (42%) cancer	-			«				-	-	«		«	«		
Muller 2009[29] Colon surgery (87% malignant) with primary anastomosis	-		-	«			«			«	«		«		«
Šerclová 2009[33] Intestinal resection (78% Crohn's disease, 7% cancer)	-	«	-	«		-		-	-				-		
Khoo 2007[28] Colon (67%) or rectal (33%) cancer	- [c]	«		«				-	-				«	«	
Gatt 2005[24] Colon surgery (69% malignant)	- [c]	«	«	«			«	-		«					«

Author Year Population	Length of Stay	Overall Mortality	Overall Morbidity	Readmissions	Quality of Life (Clinically Meaningful Change)	Pain (Clinically Meaningful Change)	Gastrointestinal Function			Surgical Complications				Non-Surgical Complications	
							Ileus	Time to Oral Solid Foods	Other (*eg*, Flatus, Bowel Movement)	Surgical Site Infection	Bleeding	Need for Re-operation	Other Surgical Complication	Foley Catheter Re-insertion/ Complication	Aspiration Pneumonia/ Pulmonary Infection
Anderson 2003[22] Colon surgery (72% malignant)	-	«		«			«	-		«					
LAPAROSCPIC SURGERY STUDIES															
Ota 2017[42] CCT Colorectal cancer	-	«		«			«	-	-	«	mixed	«	«		
Scioscia 2017[43] Bowel endometriosis	-			«							«	«			
Mari 2016[40] Colorectal cancer (75%) or diverticular disease (25%)	-	«	«				«	-	mixed	«	«		«		«
Wang 2015[45] *CCT* Colon cancer	-	«	«		«	«	«		-	«			«		«
Feng 2014[38] Rectal cancer	-	«	-	«			«		-	«		«	«		«
Mari 2014[41] Colon cancer (69%) or diverticular disease (31%)	-	«	«	«				-	-				«		
Gouvas 2012[25] *CCT* Rectal cancer	-	«	-	«			«		-		«	«	«		«

Author Year Population	Length of Stay	Overall Mortality	Overall Morbidity	Readmissions	Quality of Life (Clinically Meaningful Change)	Pain (Clinically Meaningful Change)	Gastrointestinal Function			Surgical Complications				Non-Surgical Complications	
							Ileus	Time to Oral Solid Foods	Other (*eg*, Flatus, Bowel Movement)	Surgical Site Infection	Bleeding	Need for Re-operation	Other Surgical Complication	Foley Catheter Re-insertion/ Complication	Aspiration Pneumonia/ Pulmonary Infection
Wang 2012[35] Colon cancer	- [a]	«	«	«									«		
Wang 2012[44] Colon cancer	- [a]	«	«	«				-	-	«		«	«	«	
Wang 2012[46] Colorectal cancer (elderly)	-		-						-	«			«		«
Vlug 2011[34] Cancer and benign disease	-	«	«	«			«	-	-	«		«	«		
MIXED OPEN AND LAPAROSCOPIC SURGERY STUDIES															
Forsmo 2016[50] Colorectal cancer and benign disease	-	«	«	«			«	«	-	«		«	«		«

- =benefit with enhanced recovery protocol
« =no difference between enhanced recovery protocol and usual care protocol
¯=poorer outcome with enhanced recovery protocol
mixed=more than one outcome and results varied
[a] total length of stay
[b] calculated P value
[c] median values (reported in study) indicate benefit with enhanced recovery protocol; calculated means (Figure 3) indicate no benefit

Length of Stay

All but one of the included studies reported mean or median length of stay. In most studies, this was the "initial" length of stay following the surgery date. In 2 studies, one of which provided data for both open surgery and laparoscopic surgery, readmissions were also considered providing a "total" length of stay.[35,44] Excluding those 2 studies, mean length of stay ranged from 3.0 to 8.5 days in the enhanced recovery group and 6.0 to 13.2 days in the control group. All studies found a reduced length of stay in the enhanced recovery group compared to the usual care group. Pooling results from the studies reporting initial length of stay yielded a mean difference of -2.59 days (95% CI -3.22, -1.97) (Figure 3). Statistical heterogeneity was high (I^2=92%). Quality of evidence for reduced length of stay with enhanced recovery protocols compared to usual care protocols was rated as moderate (Table 3 and Appendix F).

The remaining study reported the day on which patients met discharge criteria (*ie*, normal oral feeding, complete canalization, drains and catheters removed, no fever, no need for intravenous therapy).[31] The study included patients with rectal cancer undergoing open surgery. Overall, patients in the enhanced recovery protocol group achieved discharge status sooner than those in the traditional care group (P<.05) with 68% of the enhanced recovery group patients and 16% of the traditional care group meeting criteria on post-operative day 4. All of the enhanced recovery group patients met discharge criteria by post-operative day 6 while 28% of the traditional care group did not meet criteria until post-operative day 7 or longer.

Figure 3. Pooled Analysis for Length of Stay

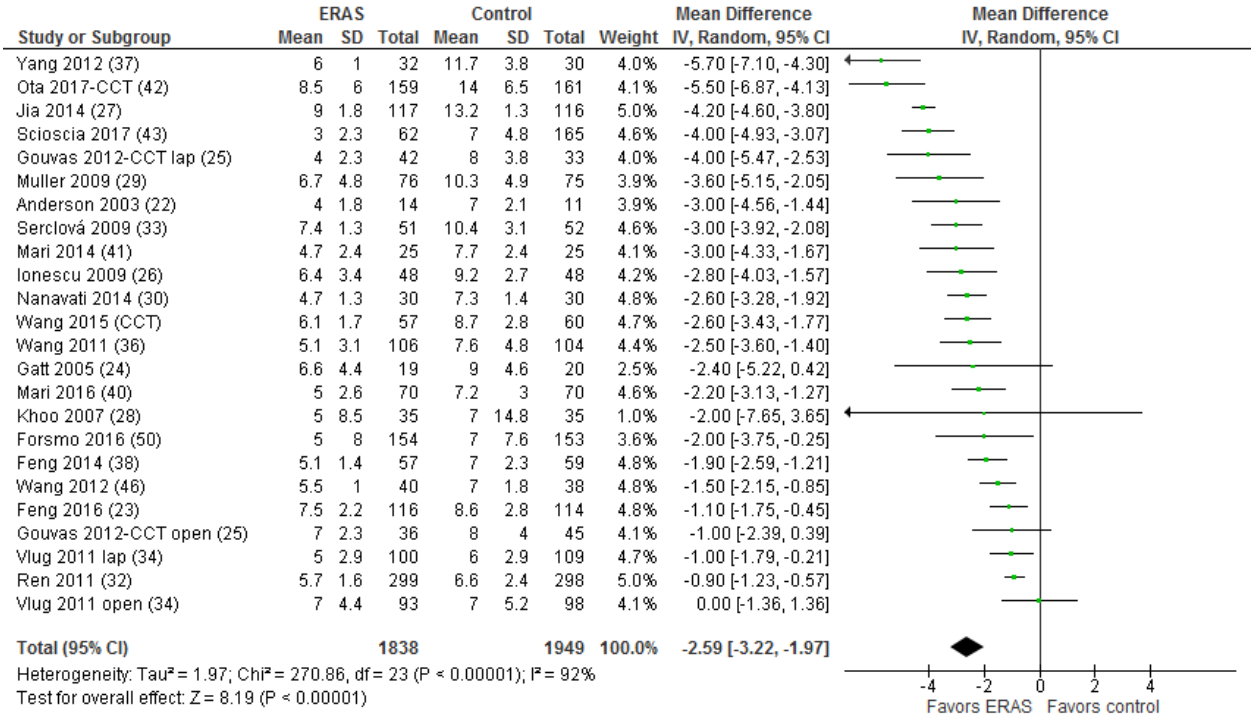


Table 3. Summary of Findings for ERAS Compared to Control for Colorectal Surgeries

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without ERAS	With ERAS	Difference		
Length of stay № of participants: 3787 (24 RCTs)				MD **2.6 days lower** (3.2 lower to 2.0 lower)	⊕⊕⊕◯ MODERATE [a,b]	Duration of hospital stay was lower with ERAS in both open and laparoscopic procedure groups compared with respective control groups. Subgroup results based on condition were comparable to the overall findings.
Mortality № of participants: 3255 (22 RCTs)	**OR 1.79** (0.81 to 3.95)	0.6%	**1.0%** (0.4 to 2.1)	**0.4% more** (0.1 fewer to 1.6 more)	⊕⊕◯◯ LOW [a,c]	No statistically significant differences between groups.
Perioperative morbidity № of participants: 2919 (19 RCTs)	**RR 0.66** (0.54 to 0.80)	29.1%	**19.2%** (15.7 to 23.3)	**9.9% fewer** (13.4 fewer to 5.8 fewer)	⊕⊕⊕◯ MODERATE [a]	Fewer complications in both open and laparoscopic ERAS groups versus respective controls. Subgroup results based on condition were comparable to the overall findings.
Readmissions № of participants: 2515 (19 RCTs)	**RR 1.11** (0.82 to 1.50)	6.4%	**7.1%** (5.2 to 9.6)	**0.7% more** (1.1 fewer to 3.2 more)	⊕⊕◯◯ LOW [a,d]	No statistically significant differences between groups.
Surgical site infection № of participants: 2880 (17 RCTs)	**RR 0.75** (0.52 to 1.07)	4.8%	**3.6%** (2.5 to 5.1)	**1.2% fewer** (2.3 fewer to 0.3 more)	⊕⊕◯◯ LOW [a,d]	No statistically significant differences between groups.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **MD:** Mean difference; **RR:** Risk ratio; **OR:** Odds ratio

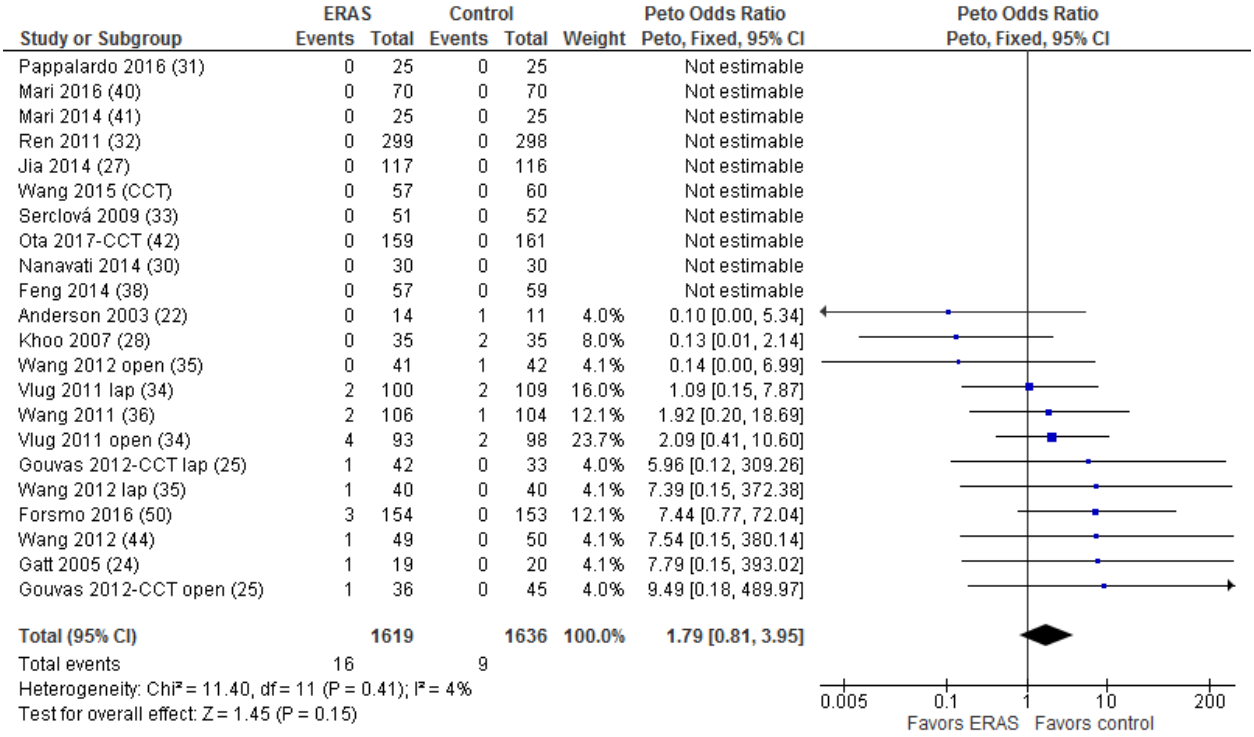
GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations
a. Mostly moderate, high or unclear risk of bias
b. I-square indicated substantial statistical heterogeneity although all but 2 studies reported lower duration with ERAS. Strong association observed.
c. Wide confidence intervals and very few events
d. Wide confidence intervals

All-cause Mortality

All-cause mortality, typically assessed until 30 days post-surgery, was reported in 19 studies. Three of the studies[25,34,35] reported results for both open and laparoscopic surgery, resulting in a total of 22 comparisons of enhanced recovery and usual care protocols. Mortality was generally infrequent (approximately 1%) with 10 studies reporting no deaths.[27,30-33,38,40-42,45] No study reported a significant difference in mortality between the enhanced recovery and usual care protocols. The pooled odds ratio was 1.79 (95% CI 0.81, 3.95) (Figure 4). Quality of evidence for no difference in all-cause mortality with enhanced recovery or usual care protocols was rated as low (Table 3 and Appendix F).

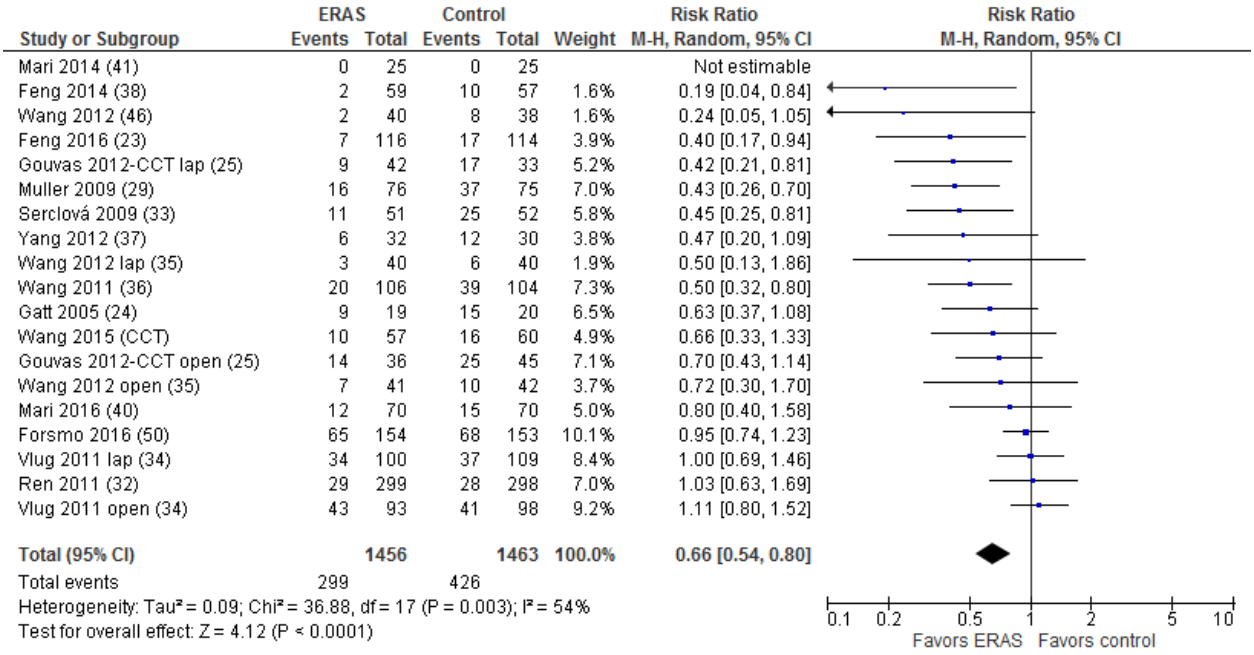
Figure 4. Pooled Analysis for Mortality



Overall Morbidity

Perioperative morbidity was reported in 17 studies. The 3 studies reporting outcomes for both open and laparoscopic surgery reported morbidity resulting in a total of 20 comparisons of enhanced recovery and usual care protocols. One study noted no major complications in either group.[41] In 11 of the remaining comparisons of enhanced recovery and usual care protocols, no significant difference in morbidity was observed. In 7 comparisons, overall morbidity was significantly lower in the enhanced recovery protocol groups compared to usual care. The pooled risk ratio was 0.66 (95% CI 0.54, 0.80) (Figure 5). One additional study reported the proportion of patients with one or more complications, finding no significant difference between the enhanced recovery and usual care protocols.[44] Quality of evidence for reduced overall morbidity with enhanced recovery protocols compared to usual care protocols was rated as moderate (Table 3 and Appendix F).

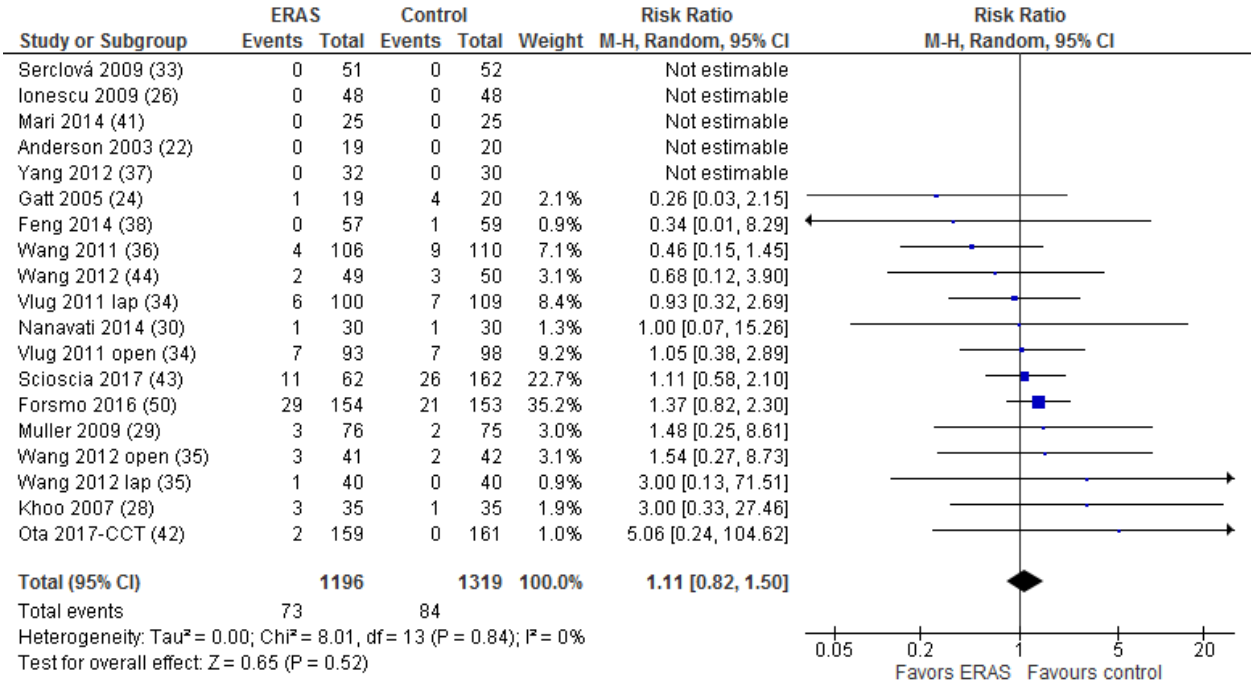
Figure 5. Pooled Analysis for Morbidity



Readmissions

Eighteen studies (21 comparisons) reported readmissions. In one study with both open surgery and laparoscopic surgery results, readmission rates ranged from 9.5% to 15% but were not reported by group.[25] The authors reported that differences between groups were not significant. The pooled risk ratio for studies reporting readmission rates by study group is presented in Figure 6. Five studies reported no readmissions.[22,26,33,37,41] The pooled estimate was 1.11 (95% CI 0.82, 1.50) (absolute difference =-0.7%, 95% CI -1.1, 3.2), indicating no significant difference in risk of readmission following colorectal surgery with an enhanced recovery protocol compared to a usual care protocol. Quality of evidence for no significant difference in readmissions between enhanced recovery and usual care protocols was rated as low (Table 3 and Appendix F).

Figure 6. Pooled Analysis for Readmissions



Pain and Quality of Life

Few studies reported pain or quality of life outcomes (Appendix D, Tables 3 and 4). One study comparing enhanced recovery and usual care protocols associated with open surgery for benign conditions (78% Crohn's disease) reported clinically significant lower pain for the enhanced recovery group on post-operative days 0 to 5.[33] A difference of one point on a visual analog pain scale of 0 to 10 was considered a clinically important difference. Scores ranged from 1.6 for the enhanced recovery group and 3.2 for the usual care group on the day of surgery to 0 and 1, respectively, on post-surgery day 5 (Appendix D, Table 4).

Another study, enrolling patients with colon cancer undergoing laparoscopic surgery, reported European Organization for Research and Treatment of Cancer (EORTC OLQ-C30) scores for pain and quality of life.[45] The scale was administered pre-operatively and post-operatively and change scores were reported. A change of at least 5 points on a 0 to 100 scale was considered clinically significant with further gradations for "little," "moderate," or "very much" change (either better or worse). For pain, changes from before surgery to 3 days post-surgery did not differ significantly between the enhanced recovery and usual care protocol groups. Both groups experienced changes of greater than 20 points ("very much" worse pain). At post-operative day 28, the change from baseline pain was "little" worse for the enhanced recovery group and "moderate" worse for the usual care group (P=.05).

For quality of life, the change from baseline to post-operative day 3 was "moderate" for both the enhanced recovery and usual care groups but the difference between groups was significant (P<.001). By post-operative day 28, both groups rated quality of life similar to pre-surgery levels (P=.11 between groups).

Several studies reported pain scale scores without assessing whether clinically meaningful changes were observed (Appendix D, Table 4). A study of both open and laparoscopic surgery for colon cancer and benign disease reported that SF-36 Bodily Pain Scale scores returned to baseline at 4 weeks after surgery with no significant differences between enhanced recovery and usual care protocols.[34] Another study reported no difference between groups in pain scores.[24]

Three studies reported pain scores during the post-operative period. One study of open colon surgery (72% malignant) reported that median pain scores at rest, on movement, and on coughing were significantly higher in the usual care protocol group on post-operative day 1 but by day 7, only pain on coughing was significantly higher.[22] Two studies of laparoscopic surgery reported significantly higher pain in the enhanced recovery protocol group in the immediate post-operative period[41] or on post-operative days 1 and 3.[38] The first study, enrolling patients with colon cancer or diverticular disease, found the difference was not significant at 5 hours post-surgery. The enhanced recovery group experienced lower pain (although not significantly) starting on post-operative day 1.[41] The second study, enrolling patients with rectal cancer, found higher pain in the enhanced recovery group persisted on post-operative day 3 but was not significantly different from the usual care group at post-operative day 5.[38]

One study of open rectal surgery reported quality of life scores from the EORTC OLQ-C38.[31] The authors administered the questionnaire prior to discharge and at the 1 month follow-up but did not identify the time point associated with the reported scores. Overall, there was no significant difference between enhanced recovery and traditional care groups with 56% and 48%, respectively, reporting excellent quality of life and only 4% in each group (1 patient) reporting poor quality of life.

Gastrointestinal Function

Most studies reported measures of gastrointestinal function. Twelve studies (14 comparisons) reported ileus (Appendix D, Table 3). One study found significantly lower incidence of ileus in the enhanced recovery protocol group with open surgery but a non-significant difference between protocols for laparoscopic surgery.[25] The remaining studies found no significant difference between enhanced recovery and usual care protocols for open surgery,[22-24,29,30,34] laparoscopic surgery,[34,38,40,42,45] or mixed open and laparoscopic surgery.[50]

Twenty studies (22 comparisons) reported significantly shorter time to flatus and/or first bowel movement in the enhanced recovery protocol group compared to the usual care protocol group (Appendix D, Table 4). The difference was observed for open surgery,[23,25-28,30-34,36,37] laparoscopic surgery,[25,34,38,40-42,44-46] and mixed surgery approaches[50] across colorectal conditions.

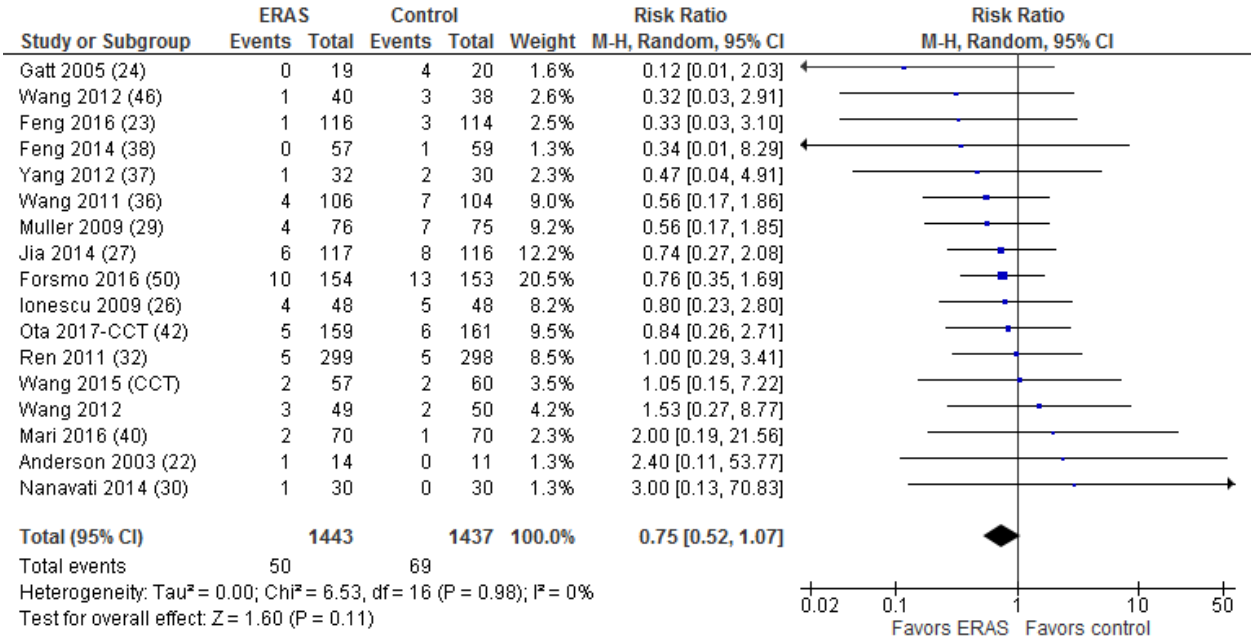
The time to oral intake of solid foods was also significantly shorter following surgery with an enhanced recovery protocol compared to a usual care protocol in 8 open surgery[22-24,26,28,33,34,37] and 5 laparoscopic surgery[34,40-42,44] studies (Appendix D, Table 4). The study with mixed open and laparoscopic surgery found median days until able to tolerate solid food did not differ significantly between the enhanced recovery protocol group (2 days, range 0-9) and standard care group (1 day, range 0-12).[50]

KEY QUESTION 2: What are the harms of ERAS versus usual care or a subset of ERAS components for adults undergoing elective colorectal surgery?

Surgical Site Infections

Surgical site infection rates were reported in 18 studies (19 comparisons of enhanced recovery and usual care protocols) and typically infrequent in both groups (Appendix D, Table 5). No study found a significant difference in surgical site infections between the 2 protocols. One study reported total number of infections for both open surgery and laparoscopic surgery with no difference between enhanced recovery and usual care protocols within the surgery types.[34] The remaining studies reported infection rates. Pooled results indicate no difference in the risk of surgical site infection with enhanced recovery or usual care protocols (RR 0.75 [95% CI 0.52, 1.07]) (Figure 7). Quality of evidence for no significant difference in surgical site infections between enhanced recovery and usual care protocols was rated as low (Table 3 and Appendix F).

Figure 7. Pooled Analysis for Surgical Site Infection



Other Harms (Appendix D, Tables 5 and 6)

Few bleeding events were observed with no significant differences between enhanced recovery and usual care protocol groups for either open or laparoscopic surgery.[23,25,29,40,42,43] Need for re-operation was reported on 10 studies (11 comparisons) with no significant differences between protocol groups for either surgery type.[25,26,30,34,36,38,42-44,50]

Many studies reported anastomotic leakage with no differences between enhanced recovery and usual care protocols for either open or laparoscopic surgery.[23,25-32,34,36-38,40-42,44-46,50] Unspecified surgical complications either were not significantly different between enhanced recovery and usual care protocol groups[25,35,42] or were significantly lower in the enhanced recovery protocol group.[33]

Foley catheter re-insertion was reported in 3 studies with no significant difference between enhanced recovery protocols and usual care protocols for open surgery[28,36] or laparoscopic surgery.[44] Pneumonia and other chest infections were reported in 11 studies (12 comparisons). Two open surgery studies found a significantly lower incidence in the enhanced recovery protocol group[25,27] while 4 found no difference between the enhanced recovery and usual care protocols.[23,24,29,37] Five laparoscopic studies[25,38,40,45,46] and one study with mixed open and laparoscopic procedures[50] found no significant difference in pulmonary infections between enhanced recovery and usual care protocol groups.

Five open surgery studies and one laparoscopic surgery study reported post-operative nausea, vomiting, or diarrhea with no significant difference between the enhanced recovery and usual care protocol groups.[24,26,32,33,35,40] One study of elderly patients (70 to 88 years old) undergoing open surgery for colorectal cancer found post-operative delirium was significantly less likely in the enhanced recovery protocol group.[27] Two other studies found no difference between protocol groups for delirium or post-operative confusion.[42,50] Other commonly reported non-surgical complications with no significant differences between protocol groups included intestinal obstruction,[25,27,32,36,44,46] urinary tract infection,[22,24,26-29,36,38,44,50] urinary retention,[23,25,29,34,36,38,40,50] deep vein thrombosis or pulmonary embolism,[24-27,36,38,42,44,50] and cardiovascular and/or cerebrovascular complications.[22,27-29,31,32,34,36,37,40,42,44,45,50]

KEY QUESTION 3: Do comparative effectiveness and harms vary by fidelity to ERAS components?

Adherence to Specific Enhanced Recovery Components

Four studies reported adherence or compliance data. A CCT from Japan with predominantly laparoscopic surgery for colorectal cancer reported compliance (*ie*, the component was "applied") with enhanced recovery components.[42] Across 17 components, the average compliance was 85%. Seven of the 17 components were also applied in more than 50% of the conventional care group including avoidance of fluid overload, no use of drains, antimicrobial prophylaxis, epidural anesthesia, early removal of nasogastric tubes, routine postoperative laxative, and ambulation on post-operative day 1. The study reported significantly shorter length of stay in the enhanced recovery group with no differences in mortality, readmissions, or surgical site infections. Among enhanced recovery group patients, increased adherence to the protocol was associated with shorter length of stay (P=.01) but not overall rate of complications (P=.29).

In a 4-arm study with enhanced recovery and usual care groups for both open and laparoscopic surgery (mainly for colorectal cancer), 15 enhanced recovery components were evaluated for each patient.[34] Successful application of each component was noted. A mean of 11.2 (SD 2.2) of the 15 components were applied in the laparoscopic surgery with enhanced recovery group (n=100) and 11.1 (SD 2.2) components in the open surgery with enhanced recovery group. The authors noted that "applied" does not mean that the component was successfully achieved. Vlug et al found no significant differences in mortality, overall morbidity, or hospital readmissions with enhanced recovery for either open or laparoscopic surgery. Length of stay was significantly shorter in the enhanced recovery groups compared to the usual care groups for both open and laparoscopic surgery.[34]

A study of open or laparoscopic surgery (surgeon's decision) for colorectal cancer or benign conditions reported adherence to 22 enhanced recovery components for both the enhanced recovery and standard care group.[50] Adherence was similar in the 2 groups for 7 components: omission of bowel preparation, no preoperative fasting, no premedication, antimicrobial prophylaxis, thoracic epidural analgesia, prevention of hypothermia, and intra-operative fluid loading level. The study reported significantly shorter length of stay in the enhanced recovery group compared to standard care with no differences in overall morbidity, mortality, readmissions, or surgical site infections.

A fourth study monitored adherence to 5 enhanced recovery components (intraoperative intravenous intake, first 24-hour intravenous intake, effective epidural analgesia, mobilization time on post-operative day 1, and oral nutrition on post-operative days 1 and 4) during open surgery, mainly for colorectal cancer.[29] The authors noted significant differences between the enhanced recovery and usual care protocol groups in median intraoperative intravenous intake, first 24-hour median intravenous intake, and oral nutrition on post-operative days 1 and 4 as evidence of "excellent compliance." The 2 protocol groups did not differ significantly on "effective" epidural analgesia or median mobilization time on day 1. Muller et al found no difference in surgical site infections or readmissions but did report a reduction in length of stay and overall morbidity in the enhanced recovery group versus usual care.

Inclusion of Recommended ERAS Components in a Perioperative Protocol

We used our charting of ERAS components in the enhanced recovery and standard care protocols of each of the included RCTs and CCTs to identify studies that best differentiated an enhanced recovery protocol from a standard care protocol. We looked at a) overlap of enhanced recovery components between the 2 protocols and b) inclusion of 2 enhanced recovery components that require a multidisciplinary team to successfully execute (intra-operative standardized anesthesia protocol and post-operative multimodal approach to opioid-sparing pain control). Based on these 2 criteria, we identified 11 studies (of the 25 included in the review) that appeared to best differentiate an enhanced recovery protocol from a usual care protocol.[22,23,27,28,32,33,35,36,40,44,46] We pooled data from these 11 studies (provided they reported outcomes of interest in a way that permitted pooling) and from the remaining studies for 2 critical outcomes – length of stay (Figure 8) and overall morbidity (Figure 9). The results were similar to the overall pooled estimates with no interaction for the subgroup analysis for either outcome. Heterogeneity was substantial for the length of stay analysis (I^2 values ≥84%) but nearly all studies favored the enhanced recovery protocol.

Figure 8. Pooled Analysis for Length of Stay in Studies with More vs Less Definitive Differentiation of ERAS vs Control Protocols

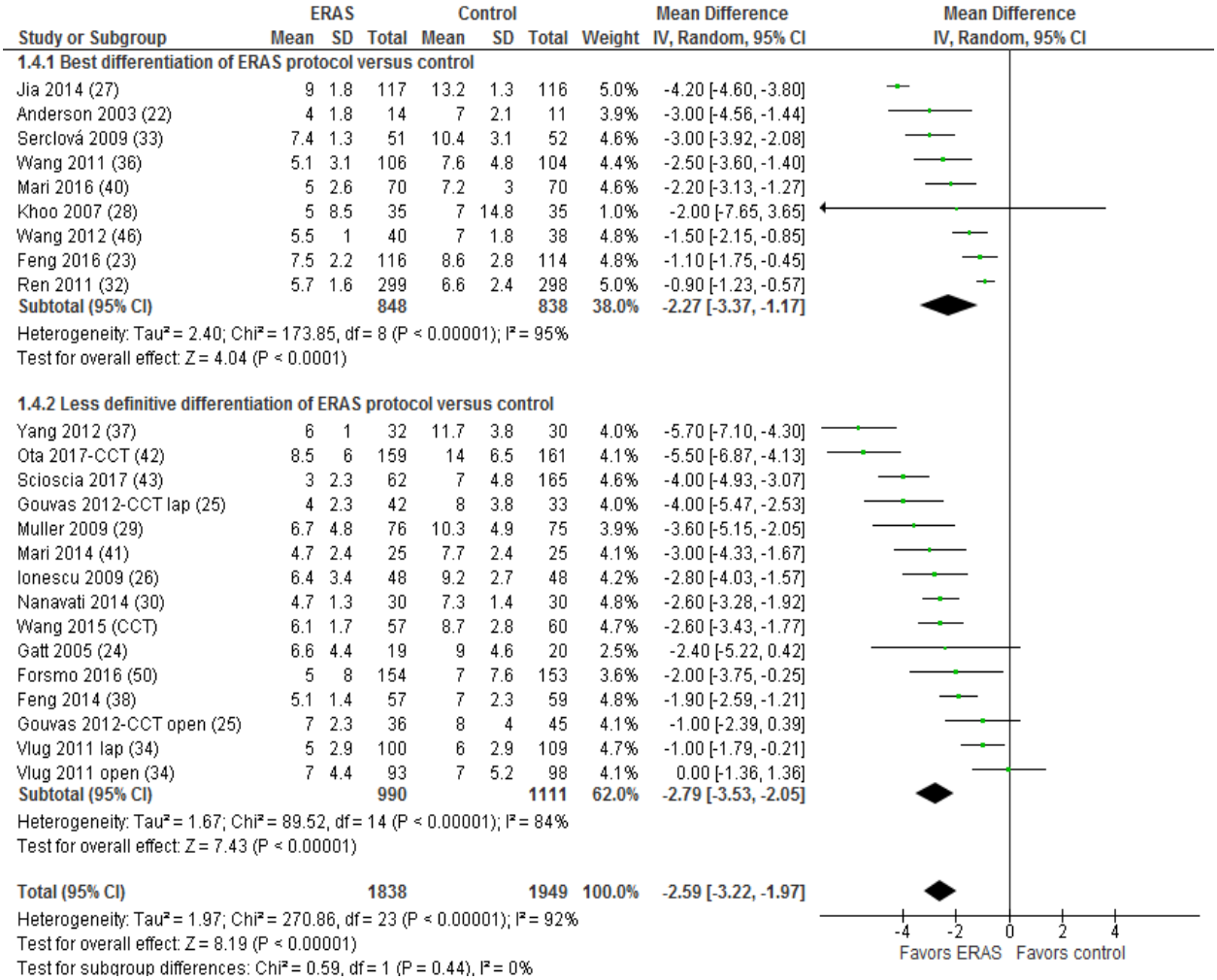
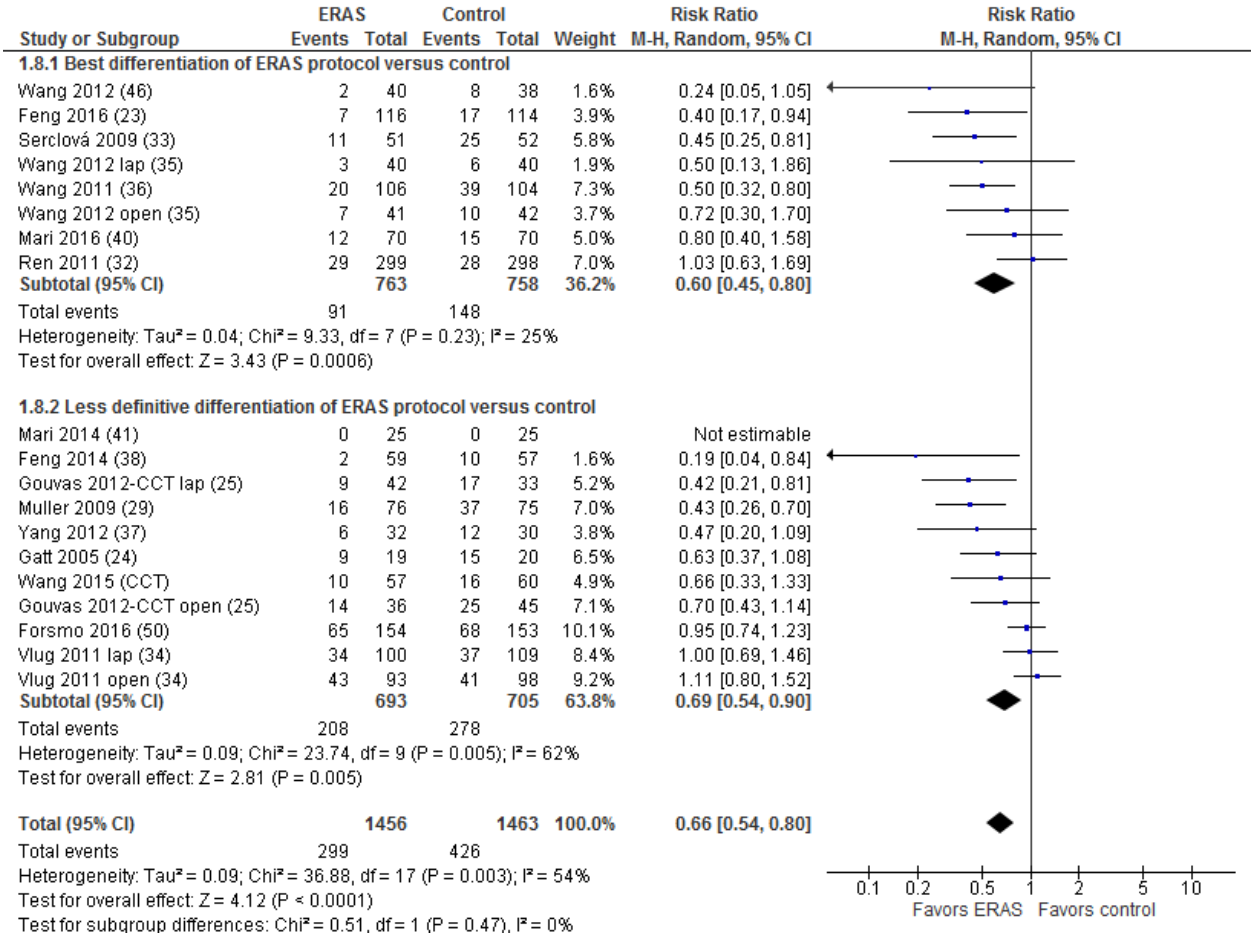


Figure 9. Pooled Analysis for Morbidity in Studies with More vs Less Definitive Differentiation of ERAS vs Control Protocols



KEY QUESTION 4: Do comparative effectiveness and harms vary by type of, and clinical conditions for, colorectal surgery (*eg*, anatomical site, laparoscopic versus open surgery, reasons for open surgery, *etc*)?

For critical outcomes, we grouped studies by surgery type (open or laparoscopic) and by colorectal condition (colorectal cancer, rectal cancer, a mix of colorectal cancer and benign conditions, or benign conditions alone). Findings for other outcomes, including pain, quality of life, gastrointestinal function, and harms as described under Key Questions 1 and 2 (above), did not appear to differ between studies of open surgery and studies of laparoscopic surgery. We did not find outcomes reported for other subgroups of interest: comorbidity status, mobility status, frailty index, age, patient size, or right- versus left-side surgery.

Length of Stay

Length of stay reductions due to ERAS did not significantly differ by type of, or clinical condition for, surgery. We pooled results separately for studies using laparoscopic techniques and studies using open surgery. The resulting estimates for mean difference were similar to that of the overall mean difference for both groups (Appendix G, Figure 1). The interaction was not significant (P=.69).

We also pooled results separately for studies of surgery for different colorectal conditions (colorectal cancer, rectal cancer, a mix of colorectal cancer and benign conditions, or benign conditions alone). Pooled estimates for the mean differences were similar to that of the overall mean difference for all 4 groups (Appendix G, Figure 2). The interaction was not significant (P=.29).

All-cause Mortality

We found no difference in mortality between enhanced recovery and usual care protocols observed in studies performing open surgery or in studies performing laparoscopic surgery (Appendix G, Figure 3). The interaction was not significant (P=.43).

Across colorectal conditions, there was no difference in mortality between enhanced recovery and usual care protocols for colorectal cancer, rectal cancer, or a mix of colorectal cancer and benign conditions (Appendix G, Figure 4). The interaction was not significant (P=.42). There were no deaths in the 2 studies of benign conditions alone.[30,33]

Overall Morbidity

Perioperative morbidity reduction between enhanced recovery and usual care protocols did not differ in studies performing open surgery and in studies performing laparoscopic surgery (Appendix G, Figure 5). The risk ratios were similar to the overall risk ratio. The interaction was not significant (P=.79).

The effect of ERAS on overall morbidity also did not vary by clinical condition (P for interaction=0.13). Perioperative morbidity was significantly lower in the enhanced recovery groups compared to usual care (Appendix G, Figure 6).

Readmissions

No difference in risk of readmission between enhanced recovery and usual care protocols was observed in studies regardless of surgical approach (open or laparoscopic surgery) (P for interaction =.65) (Appendix G, Figure 7). The pooled risk ratio for each subset of studies was similar to the overall risk ratio.

Across colorectal conditions, risk of readmission was not significantly different between enhanced recovery and usual care protocols for colorectal cancer, rectal cancer, a mix of colorectal cancer and benign conditions, or benign conditions alone (Appendix G, Figure 8). The interaction was not significant (P=.87).

Surgical Site Infections

No difference in surgical site infection rates between enhanced recovery and usual care protocols was observed in studies performing open surgery or in studies performing laparoscopic surgery (Appendix G, Figure 9). The pooled estimates were similar to the overall risk ratio and the interaction was not significant (P=.54).

Across colorectal conditions, risk of surgical site infection did not differ significantly between enhanced recovery and usual care protocols for colorectal cancer, rectal cancer, or a mix of colorectal cancer and benign conditions (Appendix G, Figure 10). The interaction was not significant (P=.81).

KEY QUESTION 5: What are the barriers to and facilitators of implementation of ERAS programs?

We identified 10 studies that provided information on barriers and facilitators to implementing an enhanced recovery program. Five of the 7 studies interviewed representatives from a multidisciplinary team,[51-55] 2 interviewed patients,[56,57] 2 surveyed surgeons,[58,59] and one interviewed nurses.[60] The studies were conducted in the US,[51,59] Canada,[53,55] Australia/New Zealand,[54,58] the Netherlands,[52] and the UK.[56,57,60] Table 4 provides an overview of the studies.

Table 4. Studies of Barriers and Facilitators

Author, year Country	Hospital type	ERAS protocol in place at time of interview/survey?	Persons interviewed/surveyed
Alawadi 2016[51] US	Safety net hospital (single site)	No	Colorectal care surgeons, anesthesiologists, nurses; colorectal surgery patients
Keller 2016[59] US	Not applicable	70% of responders did not have an enhanced recovery protocol at their institution; 42% reported using enhanced recovery concepts	Surgeons, members of Society of American Gastrointestinal and Endoscopic Surgeons (SAGES)
Pearsall 2015[55] Canada	University-affiliated adult teaching hospitals (7 sites)	No	Surgeons, anesthesiologists, ward nurses (not limited to colorectal care)
Conn 2015[53] Canada	Academic hospitals (15 sites)	Yes; 8 sites with experience; 7 sites with limited experience	Colorectal care surgeon champions, anesthesiologist champions, nurse champions, coordinators
Lyon 2014[54] Australia	Quaternary referral hospital (single site)	Yes	Colorectal care surgeons, stoma therapist, dietetics, physiotherapist medical administration
Ament 2014[52] Netherlands	Hospitals that successfully implemented ERAS[a] (10 sites)	Yes	Gastrointestinal surgeons, physician assistants, coordinators, nurses
Kahokehr 2011[58] New Zealand and Australia	Not applicable	45% of responders routinely or “sometimes” followed a formalized ERAS pathway	Colorectal surgeons (members of Colorectal Surgical Society of Australia and New Zealand)
Jeff 2014[60] United Kingdom	District general hospital	Yes	Ward nurses
Bernard 2014[56] United Kingdom	Not specified	Yes	Patients
Taylor 2011[57] United Kingdom	Tertiary colorectal unit	Yes	Patients

[a] Success defined as median length of stay of 6 days or less and protocol adherence rates above 70%

Adapting the framework reported by Alawadi et al,[51] barriers and facilitators reported in the studies are organized by staff-related factors, organizational factors, and patient factors. Commonly reported barriers to implementation include time, resources, and acceptability/feasibility of protocols to clinical staff and patients. Facilitators include organizational support, sufficient staff and electronic medical record resources, clear communication that is receptive to staff/patient feedback, and standardized yet adaptable and feasible protocols.

Staff-related Factors

Frequently mentioned staff-related barriers to implementation included difficulty adapting to change and perceived resistance to change by co-workers and colleagues from other specialty areas (Table 5). Other barriers included lack of agreement with the enhanced recovery recommendations (including a sense that there wasn't sufficient evidence to support some components) and lack of staff or staff time.

Staff-related facilitators to implementation included strong team collaboration and communication, support from leadership, ongoing staff education, and engagement of ERAS coordinators and physician champions.

Table 5. Staff-related Barriers and Facilitators

Barriers	Facilitators
Resistance to "cook book" approach[51]	Team cohesion/collaboration (problem solving, addressing barriers, support)[51,53,55,60]
Difficulty adapting to change (culture, personal preferences, resistance); need to change staff attitudes and behavior[51,53-55,60]	Good communication among team members; especially if there is need to modify the protocol for specific patient needs[51,54,55]
Perceived reluctance of others to adopt components of ERAS and to work cooperatively; lack of colleague or co-specialty support[51,55,58-60]	Creation of opportunities to build relationships across departments; avoid sense of coercion or "top-down" approach[53]
Need for flexibility to address special needs of patients[51,54,60]	Leadership team builds a "community of practice" with other centers (networking, shared best practices)[53]
Shortened preoperative fasting may require cases to be cancelled if a patient is moved forward on the operative schedule[55]	Physician champions[55]
Setting shortened discharge date might discourage patient if goal is not achieved[55]	An ERAS coordinator responsible for systematic checks and monitoring of outcomes and adherence[52-55]
Lack of agreement with recommendations, don't believe in it, not enough evidence[53,55,58,60]	Support from institution and departmental leaders[53,55,60]
Lack of staff to implement ERAS components (*eg,* more frequent mobilization)[55]	Staff education (ongoing) on the evidence behind change in practice; knowledge of program[52,54,55,60]
Lack of time[55,58]	
Lack of weekend staffing for some components (*eg,* stoma therapy nurse) delays discharge[54]	
Lack of individual confidence in following ERAS; concern about adverse consequences of accelerated patient discharge[60]	
Nurses not perceiving themselves as having ownership and ability to foster development of the program[60]	
Staff education[59]	
Lack of awareness about enhanced recovery[59]	

Organizational Factors

At the organizational level, commonly mentioned barriers include lack of institutional or departmental support, lack of resources, issues with staff scheduling, and difficulty coordinating across different departments (Table 6).

Facilitators of implementation of an enhanced recovery program included evidence-based pathways and standardized order sets, administrative reminders and/or integration of the enhanced recovery components into computer order entry systems, and use of outcomes data to build interest in the program. Setting performance targets, audit and feedback, and periodic updates were suggested as beneficial for sustaining a program.

Table 6. Organizational Barriers and Facilitators

Barriers	Facilitators
Need department-level "buy-in"; lack of institutional support[55,58,59]	ERAS pathway provides evidence-based standard of care; standardized order sets would reduce variation in practice[51,53,55]
Integration of ERAS with staff scheduling[53]	Protocol endorsed by a national organization[59]
Rotating residents could be a challenge to establishing consistency of practice[51]	Availability and use of data to drive effective implementation; provide updates to build and sustain interest in the ERAS program (*eg,* data reports with uptake, outcomes)[52,53,59]
Coordinating ERAS across different departments; need for education for entire perioperative multidisciplinary team, patients, and families[51,55]	Audit and feedback to sustain program[52,53,55]
Inconsistencies with partners or covering physicians following the same protocol[59]	Integration of ERAS into computer order entry systems[53]
Satisfaction with current results[58]	Administrative reminders integrated in daily practice (*eg,* checklists in patient files)[54]
Limited resources: equipment, staff, space[51,55,59,60]	Embed ERAS components in local protocols and performance targets for sustainability[52]
Lack of discharge resources (*ie,* rural areas may lack specialist experience and facilities required to care for patients after discharge)[54]	Cluster ERAS patients in a specific department or room[52]
	Uniformity in procedure for planning and discussing timing of discharge[52]
	Reaching the point where ERAS becomes the standard of care[53]

Patient Factors

Three studies interviewed patients,[51,56,57] and several others mentioned patient factors related to implementation of an enhanced recovery program (Table 7). Potential barriers included the characteristics of the patient population (potentially limiting early discharge and compliance with recommendations), patient preferences and expectations (particularly related to home recovery), and concern about availability of support and community resources following discharge. Patient and family/caregiver education and early communication of expectations were mentioned as facilitators of patient acceptance of an enhanced recovery program.

Table 7. Patient Factors

Barriers	Facilitators
Characteristics of patient population served by facility (*eg,* high comorbidity rate, advanced disease at presentation, social support, health literacy)[51,54]	Patient education component may increase patient satisfaction and compliance with care; family involvement[51,55,57]
Patient preferences and expectations (reflective of culture and values) might affect acceptance of ERAS program[54,55]	Early communication with the patient about expectations and discharge[52,54,57]
Amount of patient information provided and level of complexity may need to be tailored to individual patient preferences[56]	Frequent contact with multidisciplinary team can improve patient confidence in the rehabilitation process[57]
Lack of quiet and privacy hinders patient recovery[51]	Patients welcomed early mobilization and speedier recovery/release[51,56,57]
Concerns about protocol being too difficult for all patients[56]	Patient appreciation of earlier return to usual activities following discharge[57]
Concerns about pain control options[57]	
Recovery at home hindered by inadequate instructions and education on what to expect during home recovery and difficulty contacting specialist support[51,57]	
Need for support of family and friends after discharge[56]	
Patient fear that early release could be unsafe (*eg,* complications, pain management) particularly if no social support or community resources not available[51,56]	

SUMMARY AND DISCUSSION

KEY FINDINGS AND QUALITY OF EVIDENCE

1) Enhanced recovery protocols significantly reduced length of stay (mean reduction 2.6 days) following colorectal surgery compared to usual care protocols (Quality of Evidence: Moderate). Length of stay reductions occurred across surgical approach (open and laparoscopic) as well as clinical indication (*ie*, colorectal cancer, rectal cancer, a mix of colorectal cancer and benign conditions, or benign conditions alone).

2) Enhanced recovery protocols significantly reduced overall perioperative morbidity (mean absolute reduction 10%) associated with colorectal surgery compared to usual care protocols (Quality of Evidence: Moderate). Reductions due to enhanced recovery protocols did not significantly vary by type of, or clinical condition for, surgery.

3) Mortality, hospital readmissions, and surgical site infections were similar following colorectal surgery with an enhanced recovery protocol or a usual care protocol (Quality of Evidence for Mortality: Low) (Quality of Evidence for Readmissions: Low) (Quality of Evidence for Surgical Site Infections: Low). Outcomes were similar across surgical approach and clinical indication for surgery.

4) Few studies reported on clinically meaningful differences in pain or quality of life, though most studies noted an improvement in gastrointestinal function (typically passing flatus or bowel movement).

5) Enhanced recovery protocols varied across studies, little information was provided regarding component compliance, and evidence is insufficient regarding key components.

6) Commonly reported barriers to implementation include time, resources and acceptability/feasibility of protocols to clinical staff and patients. Facilitators include organizational support, sufficient staff and electronic medical record resources, clear communication that is receptive to staff/patient feedback, and standardized yet adaptable and feasible protocols.

DISCUSSION

Our review of 25 RCTs and CCTs (with 28 comparisons of enhanced recovery and standard care protocols) found moderate quality evidence of significantly reduced length of stay and overall morbidity in enhanced recovery protocol groups compared to standard care protocol groups. Mortality, readmissions, and surgical site infections were similar in the 2 groups (low quality evidence). Among other outcomes assessed, measures of gastrointestinal function (*eg*, time to first oral solid foods, flatus, and first bowel movement) were improved with enhanced recovery protocols compared to standard care protocols. Ileus, other surgical complications, and non-surgical complications were similar. Few studies reported on clinically meaningful change in pain or quality of life scores. Results were similar for open surgery and laparoscopic surgery and regardless of colorectal condition. We found insufficient evidence on whether the effects of enhanced recovery protocols vary by components, whether certain components are essential, or if

certain components are unnecessary and perhaps burdensome. Our review also describes commonly reported barriers and facilitators to implementation.

Of the existing systematic reviews (Appendix A), the review by Greco et al[8] had the greatest overlap of included studies with our review. The review was limited to RCTs published to June 2012 with no language restrictions. Sixteen RCTs were included, 5 of which were rated high risk of bias. As in our review, no significant differences were observed between the enhanced recovery group and the standard treatment group for mortality, surgical complications (limited to surgical site infections in our review), and readmissions. Overall morbidity and length of stay were significantly reduced in the enhanced recovery group compared to the control group. In the Greco review, findings were similar when only low and medium risk of bias studies were included. The number of enhanced recovery components in the included studies ranged from 4 to 13. No measure of compliance was reported and no subgroup analyses based on enhanced recovery components were performed.[8]

A critical overview of the methodology used in 10 systematic reviews and meta-analyses (to March 2013) of ERAs programs for colorectal surgery was published in 2014.[61] Differences in study inclusion criteria (type of surgery allowed, number of enhanced recovery components), methods for meta-analyses, definitions of outcomes (particularly length of stay), handling of missing data, accuracy of extraction of data components, and reporting of key decisions in the review methodology are likely responsible for observed differences in pooled estimates across systematic reviews. The authors noted a high level of redundancy and encouraged readers of systematic reviews (particularly those seeking input for decision-making) to look for multiple reviews and to assess the quality of the review as one means of understanding differences in findings between reviews.

IMPLICATIONS FOR PRACTICE

Few studies addressed compliance with the enhanced recovery protocols.[62] Only 4 of the trials included in our review addressed fidelity to the ERAs protocol.[29,34,42,50] Only one related adherence to critical outcomes.[42] Our analysis of studies with higher differentiation or lesser differentiation of enhanced recovery protocols from standard care protocols found results similar to the overall pooled estimates with no interaction for the subgroup analysis for either length of stay or overall morbidity.

Representative data from recent observational studies (*not systematically reviewed*) suggest that outcomes vary depending on compliance with the enhanced recovery protocol.[63-66] A Canadian study included 347 patients, 66% with cancer, who underwent bowel resection.[64] A laparoscopic approach was used in 72%. The enhanced recovery protocol included 23 components, each with defined criteria for adherence. Adherence to the individual components ranged from 26% to 100% with only 2 components less than 50%. Patients were adherent to a median of 18 components (range 16-20). Adherence was significantly associated with successful recovery, a composite outcome with length of day 4 days or less, no 30-day post-operative complications, and no hospital readmissions (OR 1.39 [95% CI 1.24, 1.57] for every additional protocol component). Adherence was inversely associated with length of stay. A study from Poland with 251 patients who underwent laparoscopic resection for colorectal cancer under a 16-item enhanced recovery protocol created 3 groups of patients: those with >90% compliance (defined as “interventions fulfilled”), those with 70-90% compliance, and those with <70% compliance.

Length of stay was significantly lower (mean of 4.5 days) in the >90% compliance group than in the <70% compliance group (mean of 7.8 days).[65] A multi-nation database (Europe and New Zealand) with over 2,300 patients who underwent resection for colorectal cancer included data on compliance with 13 enhanced recovery components. Compliance was inversely associated with length of stay (median of 6 days with greater than 90% compliance; median of 8 days with less than 50% compliance) and development of complications (33% of those with greater than 90% compliance; 48% of those with less than 50% compliance).[63] An analysis of data from over 4,300 colorectal surgery patients in the UK found a weak but significant inverse correlation between length of stay and compliance with 19 enhanced recovery components ($r = -0.18$, $P<.001$).[66] The median length of stay was 7 days if compliance was 70% or higher and 9 days if compliance was less than 50% ($P<.001$).

Furthermore, although observational studies have attempted to identify key components or subsets of components (see, for example, Loftus et al,[67] Pecorelli et al,[64] ERAS Compliance Group 2015[63]) there is no consensus on how many, or which specific, components are necessary to implement to achieve improved patient outcomes. There may be a specific "bundle" of practices that would improve care and patient outcomes, a concept identified by the Institute for Healthcare Improvement to describe an approach to reduce variation in practice, develop a collaborative environment, and ultimately improve outcomes.[68]

Only one of our included trials reported cost data.[32] The study was done in China with all patients undergoing open surgery for colorectal cancer. The total cost of the procedure was $2,441 per patient in the enhanced recovery protocol group and $2,711 per patient in control group ($P<.001$). The postoperative expenses were $548 per patient in the enhanced recovery protocol group and $804 per patient in the control group ($P<.001$). The study did not provide details about what was included in the reported costs. Although not part of our systematic review, we identified one study that modeled costs of implementing an enhanced recovery program in a colorectal surgery program at The Johns Hopkins Hospital.[69] Total first year costs were $117,875 and $552,783 for 100 and 500 cases per year, respectively or approximately $1,100 per patient. Net savings based on 500 cases per year and 1.9 day average reduction in length of stay were over $395,000. We also identified a second study from the US that reported total actual costs (including labor, supplies, and facilities) for patients undergoing colorectal surgery before and after implementation of a perioperative consult service with enhanced recovery components.[70] Median total cost per patient decreased by 17% from pre-implementation to the extended follow-up period (5 to 14 months following implementation) ($P<.05$). During the same time period, median length of stay decreased from 4.2 days to 3.3 days ($P<.01$). Readmission and reoperation rates were not significantly different from pre- to post-implementation. The authors noted that the combination of decreased length of stay and costs achieved post-implementation meant that 4 patients could be cared for in the same time as 3 patients pre-implementation at significantly reduced cost.

Other concerns in practice include workload and sustainability of the intervention. We identified 3 studies (again, not part of our systematic review) that provide information on these topics. A study from Switzerland used a standardized point system for measuring nursing tasks associated with patient care before and after implementation of an enhanced recovery protocol.[71] Compliance with the 21 component enhanced recovery protocol was also tracked. Nursing workload was significantly lower following introduction of the enhanced recovery protocol

(point values: 61.2 before implementation, 51.6 in the year after implementation, P<.002). Relative to pre-implementation, the average time saving per patient each day was 48 minutes. There was a significant inverse correlation between nursing workload and compliance with the enhanced recovery protocol (r =-0.42, P<.001).

A study from the Netherlands reported sustainability at 3 to 5 years after implementing an enhanced recovery protocol.[72] The analysis included data from 10 hospitals that were initially successful in implementing the protocol with success defined as length of stay 6 days or lower and protocol adherence greater than 70%. Length of stay increased from 5.25 days to 6.0 days (P>.05). Overall protocol compliance decreased from 75% to 67% (P<.01). Variation among the hospitals was noted. A study from Switzerland assessed sustainability using data from consecutive patients undergoing elective colorectal surgery at an academic hospital during the implementation process and for 3 years after.[73] Median length of stay, readmissions, and complications (including mortality) did not differ significantly over time and were similar to pre-implementation values. Functional recovery components (day of first passage of flatus, day at which oral pain control is achieved, and mobilization of 4 hours or more on post-operative day 1) were also unchanged over the implementation and post-implementation period. Adherence to components of the enhanced recovery protocol increased from 41% before implementation to 73% during implementation and 77% during year 3. Adherence decreased significantly, however, from year 3 to year 4 (P<.05).

LIMITATIONS

Although there is evidence from randomized controlled trials comparing enhanced recovery protocols to standard care, many studies were rated high or unclear risk of bias as methods of sequence generation, allocation concealment, and blinding were often not reported. Differences in the characteristics of the individual trials limits the interpretation and application of findings.

Observed differences in outcomes across studies might be due to implementation of different enhanced recovery protocols.[62] In the RCTs and CCTs included in our review, we found enhanced recovery group protocols included between 4 and 18 enhanced recovery components while standard care group protocols included between 0 and 10 enhanced recovery components.

Other differences across studies include implementation of enhanced recovery in different healthcare systems and with different procedures (including discharge protocols), different patient populations (*eg*, exclusion of patients with ASA grades III or IV), and different outcome definitions.[62]

APPLICABILITY OF FINDINGS TO THE VA POPULATION

None of the trials and only 2 of the qualitative studies of barriers to and facilitators of implementation were done in the US. There is no direct evidence of the effectiveness or harms of an enhanced recovery protocol for colorectal surgery in the US or at VHA facilities. Hospital length of stay, readmissions, and surgical complication rates from reported studies may not reflect US settings including those at VHA facilities. Resource needs, sustainability, or patient and provider acceptance of ERAS protocols are also not well-known. Before widely implementing an enhanced recovery protocol, discussions are needed with key staff, patients, and system groups. Although there are real potential benefits of enhanced recovery programs,

particularly in reduced length of stay and possibly morbidity, rolling out a new protocol in "total quality improvement" fashion with evaluation and refinement might be the best approach due to limited applicability of existing RCT data, rapidly evolving standard practice, limited full understanding of implementation/adherence/standardization of enhanced recovery components, and possible barriers. Two recent publications describe implementation of an enhanced recovery program across multiple sites within a health care system in Canada[74] and the US.[75]

RESEARCH GAPS/FUTURE RESEARCH

There is a need for data from the US, and, for the purpose of making decisions relevant to Veteran care, RCTs or quality improvement program processes with real time evaluation across varying VHA facilities. While we found no empiric evidence, our key content experts and consultants suggest that many of the enhanced recovery components have been or, over time, are being adopted into standard perioperative care for colorectal surgery. A recent commentary described enhanced recovery as modern perioperative care tailored to individual patients.[76] The author noted that some components of surgical practice are not typically included in enhanced recovery protocols including the concept of "prehabilitation."

Studies designed to evaluate the benefits and harms of enhanced recovery protocols should provide detailed information describing enhanced recovery components and specifically how they are implemented and compliance is assessed in the intervention and control groups. Compliance should be documented for each patient with details of the anesthesiology and analgesia protocol (*eg*, specific medications and doses used, timing of administration), timing of pre- and post-operative solids and fluids intake, degree of mobilization, etcetera. Surgeon experience and surgical volume should be considered. Outcomes should include patient and/or caregiver experiences.[62]

CONCLUSIONS

Implementation of enhanced recovery protocols for elective colorectal surgery resulted in reduced length of stay and overall perioperative morbidity versus standard care protocols. Mortality, readmissions, and surgical site infections were similar between the groups. However, the enhanced recovery and standard care protocols varied across studies in number of components and combinations of components with few trials reporting compliance with the protocols. There is no reliable evidence on enhanced recovery components, alone or in combination, that are key to improving patient outcomes. The value of investing time and resources into implementing all of the enhanced recovery components remains largely unknown.

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APPENDIX A. CITATION OF INCLUDED RCTS AND CCTS IN PRIOR SYSTEMATIC REVIEWS OF ENHANCED RECOVERY IN COLORECTAL SURGERY (2011-2017)

	SYSTEMATIC REVIEWS (See Footnotes for Detailed Inclusion Criteria)												
	Open or Open and Laparoscopic Surgery										Laparoscopic Surgery Only		
	Adamina 2011[5]	Rawlinson 2011[13]	Spanjers-berg 2011[14]	Lv 2012[12]	Zhuang 2013[17]	Bagnall 2014[a6]	Greco 2014[8]	Grant 2017[7]	Lau 2017[9]	Launay-Savary 2017[a10]	Li 2013[11]	Tan 2014[15]	Zhao 2014[16]
RCTs Only	ü		ü	ü	ü		ü	ü	ü		ü	ü	
Required number of components	ü	ü	ü		ü				ü		ü		ü
Multiple languages allowed	ü	NR	ü	ü	ü	NR	ü			ü		ü	
OPEN SURGERY STUDIES													
Feng 2016[23]													
Pappalardo 2016[31]													
Jia 2014[a27]						ü			ü	ü			
Nanavati 2014[30]									ü				
Gouvas 2012[25] (CCT)[b]													ü
Ren 2012[32]					ü		ü		ü				
Wang 2012[b35]							ü		ü		ü		ü
Yang 2012[37]					ü		ü		ü				
Vlug 2011[b34]				ü	ü		ü		ü		ü	ü	ü
Wang 2011[36]							ü		ü		ü		

	SYSTEMATIC REVIEWS (See Footnotes for Detailed Inclusion Criteria)												
	Open or Open and Laparoscopic Surgery										Laparoscopic Surgery Only		
	Adamina 2011[5]	Rawlinson 2011[13]	Spanjers-berg 2011[14]	Lv 2012[12]	Zhuang 2013[17]	Bagnall 2014[a6]	Greco 2014[8]	Grant 2017[7]	Lau 2017[9]	Launay-Savary 2017[a10]	Li 2013[11]	Tan 2014[15]	Zhao 2014[16]
Ionescu 2009[26]					ü		ü		ü				
Muller 2009[29]	ü	ü	ü	ü	ü		ü		ü				
Šerclová 2009[33]	ü	ü	ü	ü	ü		ü		ü				
Khoo 2007[28]	ü	ü	ü	ü	ü		ü		ü				
Gatt 2005[24]	ü	ü	ü	ü	ü		ü		ü				
Anderson 2003[22]	ü	ü	ü	ü	ü		ü		ü				
LAPAROSCOPIC SURGERY STUDIES													
Ota 2017[42] (CCT)													
Scioscia 2017[43]													
Mari 2016[40]													
Wang 2015[45] (CCT)													
Feng 2014[38]									ü				ü
Mari 2014[41]									ü				
Gouvas 2012[25] (CCT)[b]													ü
Wang 2012[b35]							ü				ü		ü
Wang 2012[44]					ü		ü		ü			ü	
Wang 2012[a46]					ü	ü	ü			ü	ü	ü	ü
Vlug 2011[b34]				ü	ü		ü				ü	ü	ü

	SYSTEMATIC REVIEWS (See Footnotes for Detailed Inclusion Criteria)												
	Open or Open and Laparoscopic Surgery										Laparoscopic Surgery Only		
	Adamina 2011[5]	Rawlinson 2011[13]	Spanjersberg 2011[14]	Lv 2012[12]	Zhuang 2013[17]	Bagnall 2014[a6]	Greco 2014[8]	Grant 2017[7]	Lau 2017[9]	Launay-Savary 2017[a10]	Li 2013[11]	Tan 2014[15]	Zhao 2014[16]
MIXED OPEN AND LAPAROSCOPIC SURGERY STUDIES													
Forsmo 2016[50]													

CCT=controlled clinical trial; RCT=randomized controlled clinical trial

[a] Elderly (≥65 years)

[b] 4-arm study: open surgery with enhanced recovery, open surgery with usual care, laparoscopic surgery with enhanced recovery, and laparoscopic surgery with usual care

Systematic Review Inclusion Criteria (Literature Search Dates)

Adamina 2011 (Search 1966 – June 2010): RCT comparing ERP with traditional care (any indication for colorectal surgery); adult population; minimum 30 day follow-up; documented compliance to ≥4 of 5 key components a) patient information, b) preservation of gastrointestinal function, c) minimizing organ dysfunction; d) active pain control; e) promotion of patient's autonomy); publication in English, German, French, Spanish, or Danish

Rawlinson 2011 (Search to February 2011): RCT or CCT with prospective intervention group that compared enhanced recovery perioperative program with traditional care; open or laparoscopic elective colorectal surgery (any indication); adult population; documented protocol with at least 4 components of enhanced recovery covering pre-, intra-, and post-operative periods); reporting at least one outcome of interest (length of stay, complications, readmission rates, mortality); language limitation not reported

Spanjersberg 2011 (Search 1990 – 2009): RCT comparing any type of enhanced recovery strategy for resections in colorectal disease to conventional recovery strategies; open or laparoscopic surgery; at least 7 enhanced recovery items in the intervention group and no more than 2 enhanced recovery items in the conventional care group; any language

Lv 2012 (Search 1966 – April 2012): RCTs comparing enhanced recovery with conventional perioperative care in major colorectal surgery (resection); minimum 30 day follow-up; any language

Zhuang 2013 (1966 – July 2012): RCTS comparing enhanced recovery with traditional care for elective colorectal surgery; open or laparoscopic surgery; malignant or benign disease; enhanced recovery program should include at least 7 of 20 components; adult population; reporting at least one outcome of interest (length of stay, readmission rates, complications, mortality); any language

Bagnall 2014 (1947 – February 2014): any study design; evaluating enhanced recovery program in elderly (65 years or older) population undergoing colorectal surgery (or with elderly cohort as a subgroup analysis); language limitation not reported

Greco 2014 (Search to June 2012): RCTs comparing enhanced recovery to standard treatment in colorectal surgery; no restriction on primary or secondary outcomes; any language

Grant 2017 (Search to June 2015): RCTs comparing enhanced recovery to standard care for perioperative care in adults undergoing general anesthesia for abdominal and pelvic surgery; reporting healthcare-associated infection; English language

Lau 2017 (1966 – February 2016): RCTs comparing enhanced recovery to standard care; age range not specified; any surgery (site or approach); enhanced recovery program included at least 4 components; reporting primary clinical outcomes (length of stay, 30-day readmission, 30-day mortality, total costs); English language abstract and/or full text

Launey-Savary 2017 (2000 – 2015): any study design; comparing feasibility of enhanced recovery in elderly (65 years or older) to younger population or to traditional management; elective colorectal surgery; reporting main endpoints (feasibility, efficacy, compliance); English or French

Li 2013 (Search to May 2013): RCTs (including abstracts) comparing laparoscopic colorectal surgery with enhanced recovery to laparoscopic colorectal surgery with conventional care; adult population; at least 7 of 17 enhanced recovery components; one month follow-up for complications and readmissions; reported at least one outcome of interest; English language
Tan 2014 (Search 1991 – February 2013): RCTs comparing enhanced recovery to traditional care in elective laparoscopic colorectal surgery; any language
Zhao 2014 (Search to April 2014): RCTs or CCTs comparing enhanced recovery with conventional care in laparoscopic colorectal cancer surgery; clear description of enhanced recovery protocol; applied at least 6 enhanced recovery components; reporting at least one outcome of interest (length of stay, time to first flatus, time of first bowel movement, complications, readmissions, mortality); English language

APPENDIX B. SEARCH STRATEGIES

MEDLINE (Ovid)

1	((fast and track) or fast-track or ERAS or ERP).mp.
2	(enhanced and recovery and surg$).mp.
3	(enhanced and recovery and program$).mp.
4	((multimodal or enhanced or accelerated) and (optimization or management or rehabilitation or protocol or package or program or pathway)).mp.
5	1 or 2 or 3 or 4
6	(resection or surgical or surgically or surgery or laparo$ or procedure).mp.
7	exp Colon/
8	exp Rectum/
9	exp Colon, Sigmoid/
10	(bowel or rectal or colonic or colon or colorectal or rectum or sigmoid).mp.
11	7 or 8 or 9 or 10
12	6 and 11
13	exp Colorectal Surgery/
14	exp Rectum/su [Surgery]
15	exp Colon/su [Surgery]
16	13 or 14 or 15
17	5 and 12
18	5 and 16
19	17 or 18
20	limit 19 to (english language and yr="2011 -Current")

CINAHL

S1	TX (fast and track) OR fast-track OR ERAS OR ERP OR (enhanced AND recovery AND (surg* OR program*)) OR ((multimodal OR enhanced OR accelerated) AND (optimization OR management OR rehabilitation OR protocol OR program OR pathway))
S2	TX (resection OR surg* OR laparo* OR procedure)
S3	TX (bowel OR rectal OR colonic OR colon OR colorectal OR rectum OR sigmoid)
S4	S3 AND S3
S5	S1 AND S4
S6	S1 AND S4 (Published Date: 20110101-20161231)
S7	S6 (English language)

APPENDIX C. PEER REVIEW COMMENTS/AUTHOR RESPONSES

Question	Reviewer's Response	Author's Responses
Are the objectives, scope, and methods for this review clearly described?	Yes	Thank you
	Yes	
	Yes	
	Yes	
	Yes	
	Yes	
Is there any indication of bias in our synthesis of the evidence?	No	Thank you
	No	
	No	
	No	
	No	
	No	
Are there any published or unpublished studies that we may have overlooked?	No	Thank you
	No	
	No	
	No	
	No	
	No	
Additional suggestions or comments can be provided below. If applicable, please indicate the page and line numbers from the draft report.	None	Thank you
	Spelling: should read Morbidity on page 32 line 4	This has been corrected.
	This is a well done systematic review of ERAS and colorectal surgery. Unfortunately most of the studies were of poor quality so the conclusions are weak. One element that is important to consider is the idea of 'bundling' and standardization and the benefit that this component of ERAS may have -- it was included in the HICPAC guidelines.	Thank you. We agree with the reviewer's comment about the quality of the studies. We added the concept of "bundling" to the "Implications for Practice" section.
	This might not be appropriate for the purpose of this paper: My only suggestion would be that the VA could exploit the advantages of being a large system and come up with templated preadmission educational materials, CPRS notes/order sets and ways to facilitate obtaining CHO drinks preop for patients to facilitate adoption of this. These are items that I am currently working on-- could be adopted and edited by facilities as needed, but would help overcome a lot of the time barriers that we encounter.	Thank you for the suggestion. As the reviewer suspected, specific strategies for implementation are outside the scope of the review.

APPENDIX D. EVIDENCE TABLES

Table 1. Study Characteristics

Author, year Country Funding Source	Inclusion/Exclusion Criteria	Intervention (n) Control (n) Follow-up	Demographics	Risk of Bias
Open Surgery Studies				
Feng 2016[23] China Government funding	Inclusion: age 18-70 years; histological diagnosis of colorectal cancer; no radiotherapy or chemotherapy treatment; no severe diarrhea, liver and kidney function failure, or cardiopulmonary insufficiency; ASA I-III; BMI 18.5-30; abdominal CT with no obvious lymph node or distant metastasis Exclusion: history of abdominal surgery; endocrine or immune system dysfunction (*eg,* diabetes, thyroid disease, multiple sclerosis, rheumatoid arthritis); recent blood transfusions; preoperative treatment with opioids, hormones, non-steroidal anti-inflammatory drugs, or other immunomodulatory substances; contraindications for epidural anesthesia	Intervention: fast-track surgery (n=121) Control: traditional care (n=120) Follow-up: 30 days Compliance: NR	N=241 (data for 230) Colorectal conditions (%): 44 colon, 56 rectum Procedures (%): NR Age (mean): 58 Gender (% male): 56 BMI: 24 Comorbidity status: ASA I (27), ASA II (50), ASA III (23)	Sequence generation: NR Allocation concealment: unclear Blinding: unclear; treatment team and patient/family not blinded; data collectors were not involved in patient management Incomplete outcome data: adequate (5% excluded from analysis due to non-compliance, ostomy surgery) Selective outcome reporting: no *Risk of bias:* medium
Pappalardo 2016[31] Italy No funding indicated	Inclusion: extraperitoneal tumor location (within 12 cm above anal verge); cT2-T4 tumors with or without positive lymph nodes, elective procedure; neoadjuvant therapy where indicated Exclusion: tumor >12 cm above anal verge, cT1 or M1, urgent procedure, ASA >3, operated on with abdominoperineal resection or Hartmann's procedure, refusing neoadjuvant therapy where indicated, refusing or unable to follow fast-	Intervention: fast-track protocol (n=25) Control: traditional care (n=25) Follow-up: 30 days Compliance: NR	N=50 Colorectal conditions (%): 100% rectal cancer Procedures (%): anterior resection (62), ultra-low anterior resection (36) Castrini technique (4) Age (mean): 67 Gender (% male): 52	Sequence generation: NR Allocation concealment: NR Blinding: adequate (outcome assessors) Incomplete outcome data: yes (mean data not reported) Selective outcome reporting: yes (data not reported at time points identified in methods)

Author, year Country Funding Source	Inclusion/Exclusion Criteria	Intervention (n) Control (n) Follow-up	Demographics	Risk of Bias
	track protocol, coagulation disorder contraindicating epidural catheter insertion NOTE: 56% of fast-track and 52% of traditional care groups received neoadjuvant therapy		BMI: 38% <25; 20% >30 Comorbidity status: ASA I (10), ASA II (42), ASA III (48)	*Risk of bias:* high
Jia 2014[27] China No funding indicated	Inclusion: elderly patients with colorectal carcinoma admitted for open curative resection Exclusion: history of dementia, Parkinson's disease, alcohol intake of ≥250 g/day, long-term use of sleeping pills or anxiolytics, and those who received anesthesia within the past 30 days	Intervention: fast-track surgery (n=120) Control: traditional care (n=120) Follow-up: NR, perioperative period Compliance: NR	N=240 (all elderly, ages 70-88) (data for 233) Colorectal conditions (%): colon cancer (49); rectal cancer (51) Procedures (%): colectomy (45); Dixon (32), Miles (23) Age (mean): 75 Gender (% male): 63 BMI: NR Comorbidity status: NR	Sequence generation: adequate Allocation concealment: NR Blinding: NR Incomplete outcome data: 3% (n=7, including 3 who went to ICU) not included in analyses Selective outcome reporting: no *Risk of bias:* medium
Nanavati 2014[30] India No funding indicated	Inclusion: age 16-66 years, undergoing anastomosis anywhere distal to the ileum Exclusion: uncontrolled comorbid conditions (*eg,* diabetes mellitus, hypertension) and emergency bowel surgeries	Intervention: fast-track peri-operative care (n=30) Control: traditional perioperative care (n=30) Follow-up: 30 days Compliance: NR	N=60 Colorectal conditions (%): ileostomy closure 42 colostomy closure 28 abdominal pain 13 ileocolostomy closure 8 other 9 Age (mean): 34 Gender (% male): 53 BMI: NR Comorbidity status: NR	Sequence generation: NR Allocation concealment: unclear Blinding: NR Incomplete outcome data: no loss to follow-up Selective outcome reporting: no *Risk of bias:* unclear

Author, year Country Funding Source	Inclusion/Exclusion Criteria	Intervention (n) Control (n) Follow-up	Demographics	Risk of Bias
Gouvas 2012[25] CCT Greece No funding indicated 2 X 2 study (open vs laparoscopic and fast track vs usual care)	Inclusion: diagnosed with adenocarcinoma of lower 2/3 of rectum Exclusion: emergency cases, tumor other than adenocarcinoma, distant metastases, neuromuscular disability, unsuitable for epidural anesthesia; ASA IV, refusal to consent to fast-track care or laparoscopy, different operation performed than originally scheduled	Intervention: open surgery combined with fast track (n=36) Control: open surgery usual care (n=45) Follow-up: 30 days Compliance: NR	N=81 Colorectal conditions (%): rectal cancer (100) Age (mean): 64 Gender (% male): 67 (fast track 53% vs 78% usual care, P=.001 across groups) BMI: 28 Comorbidity status (%): ASA I (42); ASA II (46), ASA III (12)	Sequence generation: NA (CCT) Allocation concealment: NA, grouped according to surgeon's preference Blinding: NR Incomplete outcome data: no Selective outcome reporting: no *Risk of bias:* high
Ren 2011[32] China Government funding	Inclusion: age 20-80 years, single colorectal lesion, medically eligible for radical colorectal surgery Exclusion: emergency surgery, synchronous resection of other organs, past abdominopelvic surgical history, affliction with a disease that would affect recovery	Intervention: ERAS group (n=299) Control: usual care (n=298) Follow-up: 30 days Compliance: NR	N= 676 (Data for 597) Procedures (%): right hemicolectomy (28), left hemicolectomy (6), low anterior resection (44), abdominoperineal resection (13), other (9) Age (median): 59 (ERAS), 61 (control) Gender (% male): 62 BMI (median): 22.5 Comorbidity status: ASA (mean) Control 1.4 (0.4) ERAS 1.4 (0.3)	Sequence generation: adequate Allocation concealment: NR Blinding: adequate (outcomes assessment) Incomplete outcome data: 0% (79 were randomized but then found to not meet inclusion criteria) Selective outcome reporting: no *Risk of bias:* low
Wang 2012[35] China	Inclusion: no disease of immune system, no pre-operative radiotherapy or chemotherapy, no history of operation on abdominal and distant metastases, ASA	Intervention: open surgery combined with fast track (n=42)	N=86 (data for 83) Colorectal conditions (%): colon cancer 100	Sequence generation: NR Allocation concealment: adequate

Author, year Country Funding Source	Inclusion/Exclusion Criteria	Intervention (n) Control (n) Follow-up	Demographics	Risk of Bias
No funding indicated 2 X 2 study (open vs laparoscopic and fast track vs usual care)	score I–III, and self-care function prior to hospitalization Exclusion: association with other organ resection, conversion from laparoscopic operation to laparotomy, inability to place an epidural catheter, inability to infuse drugs, need for a stoma, and emergency operation	Control: open surgery usual care (n=44) Follow-up: 30 days Compliance: NR	Age (median): 55 (fast track), 57 (usual care) Gender (% male): 59 BMI: 22.5 Comorbidity status (%): ASA I (40), ASA II (46), ASA III (14)	Blinding: NR Incomplete outcome data: 3% (n=3) excluded from analyses Selective outcome reporting: no *Risk of bias:* unclear
Yang 2012[37] China No funding indicated	Inclusion: age 18-80, diagnosed with colorectal carcinoma, no preoperative chemotherapy or radiotherapy, ASA score I-II, BMI 17.5-27.5, preoperative serum albumin ≥30g/L, elective open colorectal resection with tracheal intubation and general anesthesia Exclusion: immune-related disease, primary diabetes mellitus or impaired glucose tolerance, hiatus hernia, gastroesophageal reflux disease (GERD), pregnancy, bowel obstruction, difficult airway access, drug intake that may affect bowel movement and function, failure of thoracic epidural catheter insertion, intraoperative blood transfusion, stoma requirement, unresectable carcinoma	Intervention: fast-track group (n=35) Control: conventional care (n=35) Follow-up: 30 days Compliance: Use of checklists to maintain compliance. Did not report results of checklists	N= 70 (data for 62) Procedures (%): right hemicolectomy (21), left hemicolectomy (8); sigmoidectomy (21), Dixon operation (50) Age (median): 57 (fast track), 60 (usual care) Gender (% male): 68 BMI (median): 22 Comorbidity status: NR	Sequence generation: adequate Allocation concealment: adequate Blinding: adequate (outcome assessment) Incomplete outcome data: 11% (n=8) not included in analysis Selective outcome reporting: no *Risk of bias:* low
Vlug 2011[34] *LAFA-study* The Netherlands (multisite) Industry 2 X 2 study (open vs laparoscopic	Inclusion: ages 40-80 years; ASA I, II, or III; elective segmental colectomy for histologically confirmed adenocarcinoma or adenoma; without evidence of metastatic disease Exclusion: prior midline laparotomy, unavailability of a laparoscopic surgeon, emergency surgery, or a planned stoma	Intervention: open surgery combined with fast track (n=103) Control: open surgery usual care (n=108) Follow-up: 30 days Compliance: 15 components monitored for compliance,	N=211 (data for 191) Colorectal conditions (%): colon cancer and benign disease 100 Procedures (%): right colectomy (45), left colectomy (55) Age (mean): 66	Sequence generation: NR Allocation concealment: adequate Blinding: patients and medical staff blinded for surgical approach (laparoscopic vs open) until day of discharge

Author, year Country Funding Source	Inclusion/Exclusion Criteria	Intervention (n) Control (n) Follow-up	Demographics	Risk of Bias
and fast track vs usual care)		11.1 of 15 components successfully applied per patient in fast-track group;.5.8 components of fast track successfully applied per patient in usual care group	Gender (% male): 59 BMI: 26 Comorbidity status (%): ASA I or II (79), III (21)	Incomplete outcome data: 10% (n=20) were excluded from analyses (9 of 20 [45%] withdrew consent) Selective outcome reporting: no *Risk of bias:* medium
Wang 2011[36] China Social Development Fund	Inclusion: NR Exclusion: non-selective admission, preoperative distant metastases, stoma, emergency situation, scheduled total colectomy or abdominoperineal resection, contraindications for epidural anesthesia or early ambulation	Intervention: fast-track rehabilitation (n=106) Control: conventional care (n=104) Follow-up: 30 days Compliance: NR	N=230 (data for 210) Colorectal condition (s)(%): colon (65), rectum (35) Procedures (%): right hemicolectomy (26), left hemicolectomy (20), sigmoid colectomy (29), anterior resection (25) Age (median): 57 (fast track), 55 (conventional care) Gender (% male): 60 BMI: NR Comorbidity status (%): ASA I (28), ASA II (55), ASA III (17)	Sequence generation: NR Allocation concealment: NR Blinding: NR Incomplete outcome data: 0% Selective outcome reporting: no *Risk of bias:* unclear
Ionescu 2009[26] Romania No funding indicated	Inclusion: ASA score I-III, admitted to hospital for elective open colorectal surgery for neoplasm Exclusion: previous abdominal surgery, extensive neoplasm, severe malnutrition, surgery for complications (bowel obstruction), and palliative surgical procedures	Intervention: fast-track protocol (n=48) Control: conventional care program (n=48) Follow-up: NR (perioperative; patients asked to mention	N=96 (Data for N=96) Colorectal conditions (%): rectosigmoid (58); colon (42) Procedures: right hemicolectomy (29). left hemicolectomy (11), segmental	Sequence generation: adequate Allocation concealment: adequate Blinding: NR Incomplete outcome data: 0%

Author, year Country Funding Source	Inclusion/Exclusion Criteria	Intervention (n) Control (n) Follow-up	Demographics	Risk of Bias
		inclusion in study in case of readmission) Compliance: NR	colonic resection (1), rectosigmoidian resection (58) Age (mean): 62 Gender (% male): 64 BMI: NR Comorbidity status (%): ASA I (52), ASA II (45), ASA III (3) Subgroups noted [a]: None	Selective outcome reporting: no *Risk of bias:* low
Muller 2009[29] Switzerland No funding indicated	Inclusion: age >18, elective open colonic resection with a primary anastomosis Exclusion: emergency situations, contraindication to epidural anesthesia, scheduled total colectomy or rectum resection, preoperatively immobile	Intervention: fast-track program (n=76) Control: standard care (n=75) Follow-up: 30 days Compliance: adherence reported for intraoperative intravenous intake, first 24-hour intravenous intake, effective epidural analgesia, mobilization time day 1, and oral nutrition day 1 and day 4 NOTE: study stopped prematurely after reaching significant difference for primary endpoint (total complications to 30 days after surgery)	N= 156 (data for 151) Procedures (%): sigmoid resection or left hemicolectomy (67), resection of transverse colon (1), right hemicolectomy (32) Age (median): 62 (fast track), 59 (standard care) (P=.04) Gender (% male): 51 BMI (median): 24 (fast track), 26 (standard care) Comorbidity status (%): ASA I (3), ASA II (69); ASA III (28)	Sequence generation: NR Allocation concealment: unclear Blinding: no Incomplete outcome data: 3% (n=5) not included in analysis Selective outcome reporting: did not report data from BADL (need for personal care) nor IADL (ability to perform physical activities) *Risk of bias:* high
Šerclová 2009[33] Czech Republic	Inclusion: age 18-70 years, ASA score between I or II, open intestinal resection	Intervention: fast-track group (n=53)	N= 105 (data for 103) Colorectal conditions (%): Crohn's disease (78), ulcerative	Sequence generation: adequate

Author, year Country Funding Source	Inclusion/Exclusion Criteria	Intervention (n) Control (n) Follow-up	Demographics	Risk of Bias
Government	Exclusion: pelvic radiation, multi-organ resections, cancer, pregnant women	Control: conventional care (n=52) Follow-up: 30 days Compliance: NR	colitis (9), familial adenomatous polyposis (5), carcinoma (7), other (2) Procedures (%): simple bowel resection (54), multiple (25), resection and stomy (20) Age (mean): 36 Gender (% male): 50 BMI (median): NR Comorbidity status (%): NR	Allocation concealment: adequate Blinding: NR Incomplete outcome data: 2% (n=2) not included in analysis Selective outcome reporting: no *Risk of bias:* low
Khoo 2007[28] UK No funding indicated	Inclusion: elective surgery for colorectal cancer. Exclusion: unable to mobilize independently over 100 meters at preoperative assessment, contraindications to thoracic epidurals, preexisting clinical depression, palliation, a joint operation involving another surgical specialty	Intervention: multimodal package (n=35) Control: usual care (n=35) Follow-up: 10-14 days Compliance: Both arms were protocol-driven, with checklists	N=81 (data for 70) Colorectal conditions (%): colon cancer (67), rectal cancer (33) Age (median): 69 (multimodal), 73 (usual care) Gender (% male): 39 BMI: NR Comorbidity status (%): ASA I (11), ASA II (74), ASA III (14)	Sequence generation: adequate Allocation concealment: adequate (telephone) Blinding: NR Incomplete outcome data: 14% (n=11 withdrawn, 7 due to metastatic disease 3 withdrew consent) Selective outcome reporting: no *Risk of bias:* medium
Gatt 2005[24] UK No funding indicated	Inclusion: requiring elective colorectal surgery, living independently at home Exclusion: age<18 years, pregnancy, intolerance to probiotics and/or preantibiotics, contraindication to one or more optimization strategy,	Intervention: multimodal optimization (n=19) Control: usual care (n=20) Follow-up: 30 days	N=39 Colorectal conditions (%): malignant disease (69) Procedures (%): right hemicolectomy (28), left	Sequence generation: unclear Allocation concealment: unclear Blinding: no

Author, year Country Funding Source	Inclusion/Exclusion Criteria	Intervention (n) Control (n) Follow-up	Demographics	Risk of Bias
	contraindications to early postoperative discharge, prescribed medications that may independently prolong hospital stay (*eg,* anticoagulants), advanced malignancy on preoperative assessment, palliative or emergency surgery, failure to perform colonic or rectal resection	Compliance: NR	hemicolectomy (5), anterior resection (38), sigmoid colectomy (5), subtotal colectomy (8), abdominoperineal resection (5), other (11) Age (median): 67 (both groups) Gender (% male): 59 BMI: medians 24 (multimodal), 27 (usual care) Comorbidity status: POSSUM score (medians) 28 (multimodal), 32 (usual care); ASA (median)=2 (both groups)	Incomplete outcome data: all included in the analyses Selective outcome reporting: no *Risk of bias:* unclear
Anderson 2003[22] UK No funding indicated	Inclusion: lived independently at home and required left or right hemicolectomy Exclusion: NR	Intervention: multimodal optimization (n=14) Control: usual care (n=11) Follow-up: 30 days Compliance: NR	N=25 Colorectal conditions (%): malignant disease 72% Age (medians): 64 (multimodal), 67 (usual care) Gender (% male): 44 BMI: medians 24 (multimodal), 26 (usual care) Comorbidity status: POSSUM score (median) 26 (both groups); ASA I/II 92%, III 8%	Sequence generation: NR Allocation concealment: unclear Blinding: no Incomplete outcome data: no Selective outcome reporting: no *Risk of bias:* unclear
Laparoscopic Studies				
Ota 2017[42] Japan	Inclusion: ASA grade I or II, elective surgery for colonic or rectosigmoid cancer in 1 of 6 hospitals, white blood cell count	Intervention: enhanced recovery after surgery (n=159)	N=320	Sequence generation: NA, not randomized

Author, year Country Funding Source	Inclusion/Exclusion Criteria	Intervention (n) Control (n) Follow-up	Demographics	Risk of Bias
CCT No funding indicated	≥3000/μL, platelet count ≥100,000/μL, serum aspartate aminotransferase or alamine aminotransferase level ≤100IU/μL, total bilirubin ≤2mg/dl, serum creatinine ≤1.5 mg/dl Exclusion: emergency surgery, bowel obstruction preoperatively, routine use of steroids, history of cancer treatment using irradiation or chemotherapy, previous laparotomy other than for appendectomy, oophorectomy, or caesarean section	Control: conventional perioperative care (n=161) Follow-up: 30 days Compliance: average rate of compliance with each ERAS intervention in ERAS group was 85%; over 50% of ERAS components were implemented in conventional care group; improved adherence to ERAS protocol significantly associated with reduced length of stay (P=.01) but not overall complications (P=.29)	Colorectal locations (%): cecum (16), ascending (29), transverse (12), descending (7), sigmoid (29), rectosigmoid (14) Age (medians): 69 (ERAS), 68 (conventional care) Gender (% male): 50 BMI: NR Comorbidity status (%): ASA I (37), ASA II (63)	Allocation concealment: NA, grouped according to hospital where operation was performed Blinding: NR Incomplete outcome data: no Selective outcome reporting: no *Risk of bias:* high
Scioscia 2017[43] Italy No funding indicated	Inclusion: age >18 years, preoperative evidence of bowel endometriosis (imaging or other), primary laparoscopic approach Exclusion: surgery for reasons other than endometriosis, laparotomy or vaginal approach, endometriosis without bowel involvement, did not consent to intestinal surgery	Intervention: fast-track care (n=62) Control: conventional care (n=165) NOTE: 1:3 ratio for randomization Follow-up: 30 days Compliance: NR	N=227 Colorectal conditions (%): bowel endometriosis (100) Procedure (%): bowel segmental resection (86) Age (mean): 35 Gender (% male): 0 BMI: 22 Comorbidity status: Barthel index (median) 100 for both groups (complete independence)	Sequence generation: unclear; based on scheduled day of surgery Allocation concealment: unclear; day of surgery assigned by secretary blind to study Blinding: surgeons and anesthetists blinded to the group assigned to them Incomplete outcome data: adequate (no loss to follow-up) Selective outcome reporting: no *Risk of bias:* medium

Author, year Country Funding Source	Inclusion/Exclusion Criteria	Intervention (n) Control (n) Follow-up	Demographics	Risk of Bias
Mari 2016[40] Italy No funding indicated	Inclusion: indication for major colorectal surgery, age 18-80 years, ASA I to III, autonomous for mobilization and walking, eligible for laparoscopic technique Exclusion: no additional criteria reported	Intervention: ERAS (n=70) Control: standard care (n=70) Follow-up: 5 days Compliance: 90% accordance with ERAS guidelines	N=140 Colorectal conditions (%): diverticulitis (25), adenocarcinoma (75) (left 43%, right 31%, rectal 26%) Age (mean): 66 Gender (% male): 53 BMI: 27 Comorbidity status (%): ASA I (23), ASA II (64), ASA III (14)	Sequence generation: adequate Allocation concealment: unclear Blinding: unclear Incomplete outcome data: adequate; ITT analysis, 4% (n=5) from ERAS group discharged before day 5 blood sample Selective outcome reporting: no *Risk of bias:* medium
Wang 2015[45] China CCT No funding indicated	Inclusion: underwent colonic surgery (radical resection of colonic cancer) by one surgical group (July 2012-Oct 2013) Exclusion: NR	Intervention: ERAS program (n=57) Control: usual care (n=60) Follow-up: 28 days Compliance: NR	N=117 Colorectal conditions (%): cancer 100 (right side 79%, left side 21%) Age (mean): 59 Gender (% male): 47 BMI: 24 Comorbidity status: ASA score=1 72%, ASA score=2 28%	Sequence generation: NA (CCT) Allocation concealment: NA (CCT) Blinding: self-administered questionnaire Incomplete outcome data: 96% response rate overall Selective outcome reporting: no *Risk of bias:* medium
Feng 2014[38] China	Inclusion: age 18-75 years; diagnosed with rectal cancer based on clinical symptoms, imaging, and pathological evidence, with no findings of tumor invasion to adjacent organs, local, or distal	Intervention: fast-track surgery (n=60) Control: usual care (n=60)	N=120 (data for n=116) Colorectal condition (s): rectal cancer	Sequence generation: adequate Allocation concealment: adequate

Author, year Country Funding Source	Inclusion/Exclusion Criteria	Intervention (n) Control (n) Follow-up	Demographics	Risk of Bias
National Natural Scientific Foundation of China Laparoscopic (94%)	metastasis; no preoperative radiotherapy or chemotherapy; ASA physical status I or II Exclusion: pregnant or lactating women; primary diabetes; complete bowel obstruction; severe cardiopulmonary or immune related diseases; human immunodeficiency virus infection or acquired immunodeficiency syndrome related diseases; palliative or emergency operation; combined resection of spleen or pancreas; severe adverse events (*eg,* cerebrovascular accident or massive hemorrhage); history of radio-chemotherapy	Follow-up: 4 weeks Compliance: NR	Procedure: radial anterior resection with TME Age (mean): 55 Gender (% male): 66 BMI: 22 Comorbidity status (%): ASA I (4), ASA II (96)	Blinding: adequate (outcomes assessment) Incomplete outcome data: 3% (n=4, unresectable tumor and withdrawal of consent) not included in analyses Selective outcome reporting: no *Risk of bias:* low
Mari 2014[41] Italy No funding indicated	Inclusion: age 18-85 years, total laparoscopic high anterior resection, ASA score I-III, BMI <30, no intestinal diversion Exclusion: NR	Intervention: fast-track program (n=26) Control: usual care (n=26) Follow-up: 30 days Compliance: NR	N=52 (data for 50) Colorectal condition (s) (%): colon cancer (69), diverticular disease (31) Age (median): 66 (29-83) Gender (% male): 48 BMI: 25 Comorbidity status (%): ASA, I (67), ASA II (29), ASA III (2)	Sequence generation: NR Allocation concealment: unclear Blinding: NR Incomplete outcome data: 4% (n=2) not included in analyses Selective outcome reporting: BADL not reported *Risk of bias:* unclear
Gouvas 2012[25] CCT Greece No funding indicated 2 X 2 study (open vs laparoscopic	Inclusion: diagnosed with adenocarcinoma of lower 2/3 of rectum Exclusion: emergency cases, tumor other than adenocarcinoma, distant metastases, neuromuscular disability, unsuitable for epidural anesthesia; ASA IV, refusal to consent to fast-track care or laparoscopy,	Intervention: laparoscopy combined with fast track (n=42) Control: laparoscopy usual care (n=33) Follow-up: 30 days	N=75 Colorectal conditions (%): rectal cancer (100) Age (mean): 66	Sequence generation: NA, not randomized Allocation concealment: NA, grouped according to surgeon's preference Blinding: NR

Author, year Country Funding Source	Inclusion/Exclusion Criteria	Intervention (n) Control (n) Follow-up	Demographics	Risk of Bias
and fast track vs usual care)	different operation performed than originally scheduled	Compliance: NR	Gender (% male): 44 (fast track 52% vs 33% usual care, P=.001 across groups) BMI: 28 Comorbidity status (%): ASA I (52), ASA II (36), ASA III (12)	Incomplete outcome data: no Selective outcome reporting: no *Risk of bias:* high
Wang 2012[35] China No funding indicated 2 X 2 study (open vs laparoscopic and fast track vs usual care)	Inclusion: no disease of immune system, no pre-operative radiotherapy or chemotherapy, no history of operation on abdominal and distant metastases; ASA score I–III, and self-care function prior to hospitalization Exclusion: association with other organ resection, conversion from laparoscopic operation to laparotomy, inability to place an epidural catheter, inability to infuse drugs, need for a stoma, and emergency operation	Intervention: laparoscopy combined with fast track (n=42) Control: laparoscopy usual care (n=42) Follow-up: 30 days Compliance: NR	N=84, data for 80 Colorectal conditions (%): colon cancer 100 Procedures (%): right hemicolectomy (39), left hemicolectomy (34), sigmoid colectomy (28) Age (median): 56 (both groups) Gender (% male): 66 BMI: 22 Comorbidity status (%): ASA I (39), ASA II (48), ASA3 (14)	Sequence generation: NR Allocation concealment: adequate Blinding: NR Incomplete outcome data: 5% (n=4) excluded from analyses Selective outcome reporting: no *Risk of bias:* unclear
Wang 2012[44] China Social Development Fund	Inclusion: no previous abdominal surgery, no preoperative chemotherapy or radiotherapy, absence of distant metastases, ASA physical status I=III Exclusion: age < 18 years, cannot take care of themselves at home, undergone conversion to laparotomy, epidural catheter could not be inserted or did not work, anastomosis performed below 12cm from the anus, or patients receiving a stoma	Intervention: fast-track rehabilitation (n=54) Control: usual care (n=54) Follow-up: 30 days Compliance: study team made rounds 3 times daily to direct care but no compliance data reported	N=107 (data for 99) Colorectal condition (s): adenocarcinoma of colon Procedures (%):right hemicolectomy (34), left hemicolectomy (26), sigmoid colectomy (39) Age (median): 54 (fast track), 53 (usual care)	Sequence generation: unclear Allocation concealment: unclear Blinding: no; groups separated into different wards; outcomes observed by all members of study team and consensus reached Incomplete outcome data: 7% (n=8, unavailable PCA pump,

Author, year Country Funding Source	Inclusion/Exclusion Criteria	Intervention (n) Control (n) Follow-up	Demographics	Risk of Bias
			Gender (% male): 60 BMI: median 22 (both groups) Comorbidity status (%): ASA I (28), ASA II (52), ASA III (20)	conversion to laparotomy, stoma, metaptosis to pelvic floor); not included in analyses Selective outcome reporting: no *Risk of bias:* unclear
Wang 2012[46] China No funding indicated	Inclusion: age > 65 years, diagnoses of colorectal cancer, undergoing laparoscopic colorectal resection Exclusion: distant metastasis involving pelvic invasion, the urethra, or iliac vessels; or were unable to undergo surgery because of poor cardiopulmonary function	Intervention: fast-track rehabilitation (n=40) Control: usual care (n=38) Follow-up: 3-44 months Compliance: NR	N=78 Colorectal conditions (%): colon cancer (68), rectal cancer (32) Procedures (%): right hemicolectomy (17), left hemicolectomy (4), sigmoid colectomy (29), anterior resection (25) Age (median): 71 (fast track), 72 (usual care) Gender (% male): 54 BMI: NR Comorbidity status (%): ASA I (28), ASA II (55), ASA III (17)	Sequence generation: adequate Allocation concealment: unclear Blinding: NR Incomplete outcome data: no Selective outcome reporting: no *Risk of bias:* medium
Vlug 2011[34] *LAFA-study* The Netherlands (multisite) Industry 2 X 2 study (open vs laparoscopic	Inclusion: ages 40-80 years; ASA I, II, or III; elective segmental colectomy for histologically confirmed adenocarcinoma or adenoma; without evidence of metastatic disease Exclusion: prior midline laparotomy, unavailability of a laparoscopic surgeon, emergency surgery, or a planned stoma	Intervention: laparoscopy combined with fast track (n=106) Control: laparoscopy usual care (n=110) Follow-up: 30 days Compliance: 11.2 of the 15 components successfully	N=216 (data for 209) Colorectal conditions (%): colon cancer and benign disease 100 Procedures (%): right colectomy (47), left colectomy (53) Age (mean): 67	Sequence generation: NR Allocation concealment: adequate Blinding: patients and medical staff blinded for surgical approach until day of discharge)

Author, year Country Funding Source	Inclusion/Exclusion Criteria	Intervention (n) Control (n) Follow-up	Demographics	Risk of Bias
and fast track vs usual care)		applied per patient; 6.0 components of fast track were successfully applied per patient in the usual care group	Gender (% male): 58 BMI: 26 Comorbidity status (%) ASA I/II (81), III (19)Comorbidity (%): 69	Incomplete outcome data: 3% (n=7) excluded from analyses (3 protocol violation, 2 withdrew consent) Selective outcome reporting: no *Risk of bias:* medium
Mixed Open and Laparoscopic Surgery Studies				
Forsmo 2016[50] Norway Funding: Internal (University Hospital)	Inclusion: age >18 years, scheduled for elective open or laparoscopic colorectal surgery for malignant or benign disease; also included rectal cancer patients who had pelvic radiation Exclusion: multivisceral resection planned, ASA IV, pregnancy, emergency operation, impaired mental capacity making consent difficult, inability to adapt to ERAS criteria NOTE: operating surgeon decided which surgical approach should be used	Intervention: enhanced recovery after surgery (n=162) Control: standard care (n=162) Follow-up: 30 days Compliance: significant differences between groups for a) preoperative counseling (ERAS 100%), b) carbohydrate drink (night before and 2 hr before surgery (ERAS 100%), c) laxative (ERAS 100%), d) intravenous anesthesia (ERAS 99%), e) earlier and increased oral intake and decreased intravenous fluid (ERAS group), f) earlier and increased mobilization (ERAS group), g) laxative POD1 (ERAS 80%, standard 3%), h) post-op oral opiates (ERAS 40%, standard 54%),	N=324 (data for 307) Colorectal conditions (%): colon (46), rectal (54) (overall 79% malignant) Procedures (%): right (25), left or sigmoid (21), low anterior resection (30), abdominoperineal (20), proctocolectomy (5) Age (median): 65 (ERAS), 66 (usual care) Gender (% male): 54 BMI: NR Comorbidity status (%): ASA I (21), ASA II (63), ASA III (15)	Sequence generation: adequate Allocation concealment: adequate Blinding: none Incomplete outcome data: 5% excluded after randomization (protocol violation, emergency procedure, different hospital) Selective outcome reporting: no *Risk of bias:* low

Author, year Country Funding Source	Inclusion/Exclusion Criteria	Intervention (n) Control (n) Follow-up	Demographics	Risk of Bias
		i) post-op nasogastric tube (ERAS 3%, standard 12%), j) urine catheter removal (medians: ERAS POD2, standard POD4), k) thoracic epidural removal (medians: ERAS POD2, standard POD4)		

ASA=American Society of Anesthesiologists score; BMI= body mass index; ERAS=enhanced recovery after surgery; NR=not reported; POSSUM=Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity; POD=post-operative day; TME=total mesorectal excision

Table 2. Final Health Outcomes, Part A

Author Year Population	Length of stay, days mean (SD)		Length of stay (total[a]), mean (SD)		Overall morbidity % (n/N)		Overall mortality (note timepoint) % (n/N)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
Open Surgery Studies								
Feng 2016[23] Colorectal cancer	Post-operative 7.5 (2.2) (n=116) P=..001[b]	Post-operative 8.6 (2.8) (n=114)	NR	NR	Surgical complications 6 (7/116) P=.03	Surgical complications 15 (17/114)	NR	NR
Pappalardo 2016[31] Rectal cancer	Dischargeable[c] POD4 68% (17/25) POD5 20% (5/25) POD6 12% (3/25) P<.05 (overall)	Dischargeable[c] POD4 16% (4/25) POD5 20% (5/25) POD6 32% (8/25) POD7 or longer 28% (7/25)	NR	NR	NR	NR	0 (0/25)	0 (0/25)
Jia 2014[27] Colorectal cancer (elderly)	9.0 (1.8) (n=117) P<.001	13.2 (1.3) (n=116)	NR	NR	NR	NR	Perioperative 0 (0/117)	Perioperative 0 (0/116)
Nanavati 2014[30] Gastrointestinal surgery (3% cancer)	4.7 (1.3) (n=30) P=.000	7.3 (1.4) (n=30)	NR	NR	NR	NR	30 day 0 (0/30)	30 day 0 (0/30)
Gouvas 2012[25] *CCT* Rectal cancer	Median 7 (range 4-13) P=.001	Median 8 (range 7-23)	Median 7 (range 4-25) P=.104	Median 8 (range 7-25)	Overall morbidity (related to complications) 39 (14/36) P=.18[b]	Overall morbidity (related to complications) 56 (25/45)	30 day 3 (1/36) P=NS	30 day 0 (0/45)
Ren 2011[32] Colorectal cancer	5.7 (1.6) (n=299) P<.001	6.6 (2.4) (n=298)	NR	NR	Post-op complications 9.7 (29/299) P=.90	Post-op complications 9.4 (28/298)	30 day 0 (0/299)	30 day 0 (0/298)

Author Year Population	Length of stay, days mean (SD)		Length of stay (total[a]), mean (SD)		Overall morbidity % (n/N)		Overall mortality (note timepoint) % (n/N)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
Wang 2012[35] Colon cancer	NR	NR	Post-operative 6.5 (4.1) (n=41) P<.05	Post-operative 7.4 (4.2) (n=42)	Overall complications 17 (7/41) P=NS	Overall complications 24 (10/42)	30 day 0 (0/41) P=NS	30 day 2 (1/42)
Yang 2012[37] Colorectal cancer	6.0 (1.0) (n=32) P<.05	11.7 (3.8) (n=30)	NR	NR	Total infectious complications 6 (2/32) Total non-infectious complications 13 (4/32) Overall P=.09[b]	Total infectious complications 27 (8/30) Total non-infectious complications 13 (4/30)	NR	NR
Vlug 2011[34] Colon cancer and benign disease	Postoperative Median 6 (IQR 4.5-10) P=.032	Postoperative Median 7 (IQR 6-10.5)	Postoperative Median 7 (IQR 5-11) P=NS	Postoperative Median 7 (IQR 6-13)	Overall morbidity (related to complications) 46 (43/93) P=NS	Overall morbidity (related to complications) 41 (41/98)	30 day 4 (4/93) P=NS	30 day 2 (2/98)
Wang 2011[36] Colorectal cancer	Postoperative 5.1 (3.1) (n=106) P=.001	Postoperative 7.6 (4.8) (n=104)	NR	NR	Patients with complications 19 (20/106) P=.02	Patients with complications 38 (39/104)	2 (2/106) P=.57	1 (1/104)
Ionescu 2009[26] Rectosigmoid (58%) or colon (42%) cancer	6.4 (3.4) (n=48) P=.001	9.2 (2.7) (n=48)	NR	NR	NR	NR	NR	NR
Muller 2009[29] Colon surgery (87% malignant) with primary anastomosis	Median LOS 5 (2-30) (n=76) P<.0001	Median LOS 9 (6-30) (n=75)	NR	NR	Total complications 21 (16/76) P=.001	Total complications 49 (37/75)	NR	NR

Author Year Population	Length of stay, days mean (SD)		Length of stay (total[a]), mean (SD)		Overall morbidity % (n/N)		Overall mortality (note timepoint) % (n/N)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
Šerclová 2009[33] Intestinal resection (78% Crohn's disease, 7% cancer)	7.4 (1.3) (n=51) P<.001	10.4 (3.1) (n=52)	NR	NR	Total complications 22 (11/51) P=.003	Total complications 48 (25/52)	0 (0/51)	0 (0/52)
Khoo 2007[28] Colon (67%) or rectal (33%) cancer	Median 5 (range 3-37) P<.001 Rectal cancer 5.5 (4-37) Colon cancer 4 (3-13)	Median 7 (range 4-63) Rectal cancer 8.5 (4-63) Colon cancer 7 (5-35)	Median 5 (range 3-37) P<.001	Median 7 (range 4-63)	NR	NR	At day 14 0 (0/35)	At day 14 6 (2/35)
Gatt 2005[24] Colon surgery (69% malignant)	Median 5 (IQR 4-9) P=.03	Median 7.5 (IQR 6-10)	NR	NR	Total complications of surgery 47 (9/19) P=.08	Total complications of surgery 75 (15/20)	At day 30 5 (1/19) P=.49[b]	At day 30 0 (0/20)
Anderson 2003[22] Colon surgery (72% malignant)	4.0 (1.8) (n=14) Median 3 (IQR 2-7) P=.002 for both	7.0 (2.1) (n=11) Median 7 (IQR 4-10)	NR	NR	NR	NR	At day 30 0 (0/14) P=NS	At day 30 9 (1/11)
Laparoscopic Studies								
Ota 2017[42] CCT Colorectal cancer NOTE: 97% (ERAS) and 91% (control) had laparoscopic surgery	Postoperative Median 8.5 (5-41) P<.001 Met discharge criteria POD3 (1-39) P<.001	Postoperative Median 14 (7-46) Met discharge criteria POD10 (7-56) P<.001	NR	NR	NR	NR	0 (0/159)	0 (0/161)
Scioscia 2017[43] Bowel endometriosis	Median 3 (3-12) P<.001	Median 7 (4-33)	NR	NR	NR	NR	NR	NR

Author Year Population	Length of stay, days mean (SD)		Length of stay (total[a]), mean (SD)		Overall morbidity % (n/N)		Overall mortality (note timepoint) % (n/N)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
Mari 2016[40] Colorectal cancer (75%) or diverticular disease (25%)	Day of discharge 5.0 (2.6) P<.05	Day of discharge 7.2 (3.0)	NR	NR	Patients with complications 17 (12/70) P=NS	Patients with complications 21 (15/70)	0 (0/70)	0 (0/70)
Wang 2015[45] CCT Colon cancer	Postoperative 6.1 (1.7) P<.001	Postoperative 8.7 (2.8)	NR	NR	Total morbidity 17.5% (10/57) P=.24	Total morbidity 26.7% (16/60)	0 (0/57)	0 (0/60)
Feng 2014[38] Rectal cancer	Postoperative 5.1 (1.4) (n=57) P<.001	Postoperative 7.0 (2.3) (n=59)	All patients admitted 2-3 days before operation		Total complications 3 (2/59) P=.03	Total complications 17 (10/57)	0 (0/57)	0 (0/59)
Mari 2014[41] Colon cancer (69%) or diverticular disease (31%)	Day of discharge 4.7 (2.4) (n=25) P<.005	Day of discharge 7.7 (2.4) (n=25)	NR	NR	No major complications in either group		0 (0/25)	0 (0/25)
Gouvas 2012[25] *CCT* Rectal cancer	Median 4 (range 3-12) P<.001	Median 8 (range 3-18)	Median 4 (range 3-31) P<.001	Median 9 (range 3-22)	Overall morbidity (related to complications) 21 (9/42) P=.008 [b]	Overall morbidity (related to complications) 52 (17/33)	At day 30 2 (1/42) P=NS	At day 30 0 (0/33)
Wang 2012[35] Colon cancer	NR	NR	Postoperative 5.2 (3.9) (n=40) P<.05	Postoperative 6.3 (4.7) (n=40)	Complications, overall 8 (3/40) P=.48[b]	Complications, overall 15 (6/40)	At day 30 3 (1/40) P=NS	At day 30 0 (0/40)
Wang 2012[44] Adenocarcinoma of the colon	NR	NR	Postoperative, median 4 (2-12) P<.01	Postoperative, median 5 (3-48)	Patients with 1 or more complications 12 (6/49) P=.30	Patients with 1 or more complications 20 (10/50)	2 (1/49) on POD3 P=.31	0 (0/50)

Author Year Population	Length of stay, days mean (SD)		Length of stay (total[a]), mean (SD)		Overall morbidity % (n/N)		Overall mortality (note timepoint) % (n/N)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
Wang 2012[46] Colorectal cancer (elderly)	5.5 (5-6) P<.001 (n=40)	7.0 (6-8) (n=38)	NR	NR	Overall complications 5 (2/40) P=.045	Overall complications 21 (8/38)	1 death from hepatic metastasis after right hemicolectomy; 2 deaths from myocardial infarction Groups not reported; no significant difference between groups	
Vlug 2011[34] Colon cancer and benign disease	Postoperative Median 5 (IQR 4-7) P=.020	Postoperative Median 6 (IQR 4-8.5)	Postoperative Median 5 (IQR 4-8) P=.026*	Postoperative Median 6 (IQR 4.5-9.5)	Overall morbidity (related to complications) 34 (34/100) P=NS	Overall morbidity (related to complications) 34 (37/109)	At day 30 2 (2/100) P=NS	At day 30 2 (2/109)
Mixed Open and Laparoscopic Surgery Studies								
Forsmo 2016[50] Colorectal cancer and benign disease	Postoperative Median 5 (IQR 2-50) P<.001	Postoperative Median 7 (IQR 2-48)	Postoperative Median 5 (IQR 2-50) P=.001	Postoperative Median 8 (IQR 2-48)	Overall morbidity 42 (65/154) P=.69 Patients with 1 or more major complications 11 (17/154) P=.33	Overall morbidity 44 (68/153) Patients with 1 or more major complications 8 (12/153)	< 30 days 2 (3/154) P=.08	< 30 days 0 (0/153)

ASA= American Society of Anesthesiologists Index; IQR= interquartile range; NR=not reported; NS=not statistically significant; POD=Postoperative day

[a] Initial and readmission

[b] Calculated (t-test or Fisher's exact test)

[c] Defined as meeting discharge criteria: normal oral feeding, complete canalization, abdominal drain and vesical catheter removed, no fever, no need for intravenous therapy; NOTE: one patient in traditional care group not accounted for by study authors

Table 3. Final Health Outcomes, Part B

Author Year Population	Readmission rate % (n/N)		Ileus % (n/N)		Pain score, Clinically meaningful change (note score and define)		Quality of life, Clinically meaningful change (note score and define)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
Open Surgery Studies								
Feng 2016[23] Colorectal cancer	NR	NR	1 (1/116) P=.62	2 (2/114)	NR	NR	NR	NR
Pappalardo 2016[31] Rectal cancer	NR	NR	NR	NR	NR	NR	NR	NR
Jia 2014[27] Colorectal cancer (elderly)	NR	NR	NR	NR	NR	NR	NR	NR
Nanavati 2014[30] Gastrointestinal surgery (3% cancer)	3 (1/30) for leak P=NS	3 (1/30) for leak	3 (1/30) P=NS	10 (3/30)	NR	NR	NR	NR
Gouvas 2012[25] *CCT* Rectal cancer	Not reported by group, rates ranged from 9.5 to 15% P=NS between all groups		8 (3/36) P=.045[a]	27 (12/45)	NR	NR	NR	NR
Ren 2011[32] Colorectal cancer	NR	NR	NR	NR	NR	NR	NR	NR
Wang 2012[35] Colon cancer	7 (3/41) P=NS	5 (2/42)	NR	NR	NR	NR	NR	NR
Yang 2012[37] Colorectal cancer	0 (0/32)	0 (0/30)	NR	NR	NR	NR	NR	NR
Vlug 2011[34] Colon cancer and benign disease	8 (7/93) P=NS	7 (7/98)	Mechanical ileus requiring reoperation n=2 Prolonged postoperative	Mechanical ileus requiring reoperation n=5 Prolonged postoperative	NR	NR	NR	NR

Author Year Population	Readmission rate % (n/N)		Ileus % (n/N)		Pain score, Clinically meaningful change (note score and define)		Quality of life, Clinically meaningful change (note score and define)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
			(5 days) ileus n=5	(5 days) ileus n=5				
Wang 2011[36] Colorectal cancer	4 (4/106) P=NS	9 (9/110)	NR	NR	NR	NR	NR	NR
Ionescu 2009[26] Rectosigmoid (58%) or colon (42%) cancer	0 (0/48)	0 (0/48)	NR	NR	NR	NR	NR	NR
Muller 2009[29] Colon surgery (87% malignant) with primary anastomosis	4 (3/76) P=NS[a]	3 (2/75)	Postoperative Ileus 4 (3/76) P=.72[a]	Postoperative Ileus 5 (4/75)	NR	NR	NR	NR
Šerclová 2009[33] Intestinal resection (78% Crohn's disease, 7% cancer)	0 (0/51)	0 (0/52)	NR	NR	VAS pain score (0-10) Clinically important difference in pain defined as 1 (standard deviation 0.5 to 1.5) Clinically significant lower pain for FT group vs non-FT group for postoperative days 0-5		NR	NR
Khoo 2007[28] Colon (67%) or rectal (33%) cancer	9 (3/35) P=.61[a]	3 (1/35)	NR	NR	NR	NR	NR	NR
Gatt 2005[24] Colon surgery (69% malignant)	5 (1/19) P=.17	20 (4/20)	16 (3/19) P=NS[a]	15 (3/20)	NR	NR	NR	NR
Anderson 2003[22] Colon surgery (72% malignant)	0 (0/19)	0 (0/20)	7 (1/14) P=NS	9 (1/11)	NR	NR	NR	NR

Author Year Population	Readmission rate % (n/N)		Ileus % (n/N)		Pain score, Clinically meaningful change (note score and define)		Quality of life, Clinically meaningful change (note score and define)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
Laparoscopic Studies								
Ota 2017[42] CCT Colorectal cancer NOTE: 97% (ERAS) and 91% (control) had laparoscopic surgery	1 (2/159) P=.16	0 (0/161)	6 (10/159) P=.79	6 (9/161)	NR	NR	NR	NR
Scioscia 2017[43] Bowel endometriosis	18 (11/62) P=.69	16 (26/162)	NR	NR	NR	NR	NR	NR
Mari 2016[40] Colorectal cancer (75%) or diverticular disease (25%)	NR	NR	3 (2/70) P=NS	6 (4/70)	NR	NR	NR	NR
Wang 2015[45] CCT Colon cancer	NR	NR	5.2 (3/57) P=NS	8.3 (5/60)	Pain Scale QLQ-C30[b,c] Change from pre-op to POD3: 24.6 P=.82 POD28: 7.9 P=.05	Pain Scale QLQ-C30[b,c] Change from pre-op to POD3: 22.2 POD28: 11.1	Global Quality of Life (QLQ-C30)[b,c] Change from pre-op to POD3: -10.9 P=.000 POD28: 0.5 P=.11	Global Quality of Life (QLQ-C30)[b,c] Change[s] from pre-op to POD3: -18.7 POD28: -1.8
Feng 2014[38] Rectal cancer	0 (0/57) P=NS	1.7 (1/59) for rectovaginal fistula	0 (0/57) P=NS	1.7 (1/59)	NR	NR	NR	NR
Mari 2014[41] Colon cancer (69%) or diverticular disease (31%)	0 (0/25)	0 (0/25)	NR	NR	NR	NR	NR	NR
Gouvas 2012[25] *CCT*	Not reported by group, rates ranged from 9.5 to 15%		7 (3/42) P=.17[a]	18 (6/33)	NR	NR	NR	NR

Author Year Population	Readmission rate % (n/N)		Ileus % (n/N)		Pain score, Clinically meaningful change (note score and define)		Quality of life, Clinically meaningful change (note score and define)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
Rectal cancer	P=NS between all groups							
Wang 2012[35] Colon cancer	3 (1/40) P=NS	8 (3/40)	NR	NR	NR	NR	NR	NR
Wang 2012[44] Adenocarcinoma of the colon	4 (2/49) P=.66	6 (3/50)	NR	NR	NR	NR	NR	NR
Wang 2012[46] Colorectal cancer (elderly)	NR	NR	NR	NR	NR	NR	NR	NR
Vlug 2011[34] Colon cancer and benign disease	6 (6/100) P=NS[a]	6 (7/109)	Mechanical ileus requiring reoperation n=3 Prolonged postoperative ileus n=7	Mechanical ileus requiring reoperation n=0 Prolonged postoperative ileus n=8	NR	NR	NR	NR
Mixed Open and Laparoscopic Surgery Studies								
Forsmo 2016[50] Colorectal cancer and benign disease	19 (29/154) P=.23	13 (21/153)	Mechanical, requiring reoperation 0 (0/154) P=.32 Prolonged postoperative 3 (4/154) P=.35	Mechanical, requiring reoperation 1 (1/153) Prolonged postoperative 5 (7/153)	NR	NR	NR	NR

NR=not reported; NS=not statistically significant; POD=post-operative day

[a] Calculated (Fisher's exact test)

[b] QLQ-C30=European Organization for Research and Treatment of Cancer Quality of Life tool (cancer-specific); QLQ-CR29=colonic cancer specific module; higher scores for function and quality of life indicate higher function and higher quality of life

[c] Change of 5-10 points (on 0-100 scale) denotes clinically significant change of "little better (or worse)"; change of 10-20 points denotes "moderate better (or worse)"; change of >20 points denotes "very much better (or worse)"

Table 4. Intermediate Outcomes

Author Year Population	Gastrointestinal function (define), days Mean (SD)		IV fluid administration		Mobilization, days Mean (SD)		Pain scale score (define) % (n/N)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
Open Surgery Studies								
Feng 2016[23] Colorectal cancer	Flatus 3.7 (1.1) P=.049 Stool passage 4.8 (1.6) P=.04 Oral intake 3.3 (1.3) P=.03	Flatus 4.3 (1.5) Stool passage 5.8 (2.1) Oral intake 5.3 (1.6)	NR	NR	First ambulation 3.7 (1.7) P=.02	First ambulation 5.4 (2.1)	NR	NR
Pappalardo 2016[31] Rectal cancer	Bowel movement 52 hours P<.05	Bowel movement 19 to 33 hours later than ERAS group	NR	NR	Mobilization POD1 100 (25/25) Ambulate POD2 100 (25/25)	Mobilization POD2 68% (17/25) POD3 32% (8/25) Ambulate subsequent day for 100%	NR	NR
Jia 2014[27] Colorectal cancer (elderly)	Flatus, hours 48.5 (9.6) (n=117) P<.001	Flatus, hours 77.7 (7.2) (n=116)	NR	NR	NR	NR	NR	NR
Nanavati 2014[30] Gastrointestinal surgery (3% cancer)	Flatus 2.8 (n=30) Stool passage 4.0 P<.05 for both	Flatus 4.0 (n=30) Stool passage 6.2	NR	NR	NR	NR	NR	NR
Gouvas 2012[25] *CCT* Rectal cancer	First bowel movement Median 4 (range 1-7) P<.001	First bowel movement Median 6 (range 1-12)	NR	NR	NR	NR	NR	NR
Ren 2011[32]	Flatus, hours 53.7 (17.1)	Flatus, hours 63.1 (20.0)	NR	NR	NR	NR	NR	NR

Author Year Population	Gastrointestinal function (define), days Mean (SD)		IV fluid administration		Mobilization, days Mean (SD)		Pain scale score (define) % (n/N)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
Colorectal cancer	(n=299) Bowel movement, hours 73.7 (23.7) P<.001 for both	(n=298) Bowel movement, hours 88.8 (29.5)						
Wang 2012[35] Colon cancer	NR	NR	NR	NR	NR	NR	NR	NR
Yang 2012[37] Colorectal cancer	Flatus 2 (1) (n=32) Defecation 3.8 (1.6) Soft Diet 4.0 (2.0) P<.05 for all	Flatus 4 (2) (n=30) Defecation 6.4 (2.5) Soft Diet 8.2 (2.2)	NR	NR	NR	NR	NR	NR
Vlug 2011[34] Colon cancer and benign disease	Medians Tolerate solid food 1 (IQR 1–3) Flatus 1 (IQR 1–3) Stool passage 3 (IQR 2–4) *Overall dis-charge criteria (including components above and mobilization) achieved significantly earlier in ERAS group versus usual care*	Medians Tolerate solid food 3 (IQR 2–5) Flatus 2 (IQR 1–3) Stool passage 4 (IQR 3–6)	NR	NR	Mobilization, median minutes POD1 120 (60-215) Mobilization as pre-operative, median days 4 (IQR 3–7)	Mobilization, median minutes POD1 20 (0-60) Mobilization as pre-operative, median days 6 (IQR 5–8)	SF-36 Bodily Pain score returned to baseline at 4 weeks with no significant differences across groups	
Wang 2011[36]	Flatus 2.1 (2.0)	Flatus 3.2 (2.5)	NR	NR	Walk on surgery day	Walk on surgery day	NR	NR

Author Year Population	Gastrointestinal function (define), days Mean (SD)		IV fluid administration		Mobilization, days Mean (SD)		Pain scale score (define) % (n/N)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
Colorectal cancer	(n=106) P=.001	(n=104)			35% (11/106) P=.001 Walk on day 1 53% (56/106) P=.000 Walk on day 2 85% (90/106) P=.001	0% (0/104) Walk on day 1 23% (24/104) Walk on day 2 59% (61/104)		
Ionescu 2009[26] Rectosigmoid (58%) or colon (42%) cancer	Bowel function, hours 43.7 (14.9) (n=48) P=.042 Solid Food intake, hours 42.2 (12.7) P=.01 Fluid intake, hours 10.9 (8.1) P=.001	Bowel function, hours 52.02 (23.7) (n=48) Solid Food intake, hours 64.3 (23.3) Fluid intake, hours 23.5 (16.9)	NR	NR	Complete Mobilization, hours 19.6 (8.6) P=.001	Complete Mobilization, hours 37.1 (23.9)	NR	NR
Muller 2009[29] Colon surgery (87% malignant) with primary anastomosis	NR	NR	NR	NR	NR	NR	NR	NR
Šerclová 2009[33] Intestinal resection (78% Crohn's disease, 7% cancer)	Bowel Movement 1.3 (0.8) (n=51) Stool 2.1 (1.1) P<.001 for both Semi-solid and solid diet on Day 5 100 (51/51)	Bowel Movement 3.1 (1.0) (n=52) Stool 3.9 (1.1) Semi-solid and solid diet on Day 5 20 (10/52)	NR	NR	Day 0 64% could walk Day 1 54% walked 44% used treadmill 2% rehabilitated in sitting position only	Day 0 0% could walk Day 1 14% walked 2% used treadmill 68% rehabilitated in sitting position only	Mean daily VAS values (post-op day 0 to 5) 1.6, 1.0, 0.6, 0.3, 0, 0	Mean daily VAS values (post-op day 0 to 5) 3.2, 2.4, 1.8, 1.6, 1.2, 0.8

Author Year Population	Gastrointestinal function (define), days Mean (SD)		IV fluid administration		Mobilization, days Mean (SD)		Pain scale score (define) % (n/N)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
	P<.001					16% rehabilitated in bed		
Khoo 2007[28] Colon (67%) or rectal (33%) cancer	Tolerate solid diet Median 1 (range 0-6) Stool passage/ stoma functioning 3 (range 1-5) P<.001 for both	Tolerate solid diet Median 4 (range 2-9) Stool passage/ stoma functioning 5 (range 0-23)	Median over 47 hours peri-operatively 3000 mL	Median over 47 hours peri-operatively 6263 mL	Median 2 (range 1–10) P<.001	Median 4 (range 2–32)	NR	NR
Gatt 2005[24] Colon surgery (69% malignant)	Ability to tolerate diet of 3 light meals a day Median, hours approx. 50 P=.04	Ability to tolerate diet of 3 light meals a day Median, hours approx. 90	Duration of intravenous fluids from the time of surgery Median, hours approx. 35 P=.007	Duration of intravenous fluids from the time of surgery Median, hours approx. 68	No differences between the groups in time to be able to walk to toilet unaided (P=.79)		No differences between the groups in pain scores	
Anderson 2003[22] Colon surgery (72% malignant)	Ability to tolerate diet of 3 light meals a day Median, hours 48 (IQR 33-55) P<.001	Ability to tolerate diet of 3 light meals a day Median, hours 76 (IQR 70-110)	Discontinuation of supplemental intravenous fluids Median, hours 26 (IQR 24-37) P<.001	Discontinuation of supplemental intravenous fluids Median, hours 57 (IQR 42-105)	Walk to toilet unaided Median, hours 46 (IQR 37-54) P=.04	Walk to toilet unaided Median, hours 69 (IQR 44-121)	Post-op day 1 median pain scores at rest, on movement, and on coughing all significantly higher in usual care group versus intervention group Post-op day 7 pain on coughing remained significantly higher in usual care group	
Laparoscopic Studies								
Ota 2017[42] CCT Colorectal cancer NOTE: 97% (ERAS) and 91% (control) had laparoscopic surgery	Flatus Median 1 (1-5) P<.001 Bowel movement 2 (1-6) P<.001	Flatus Median 2 (1-5) Bowel movement 3 (1-7)	IV fluid until POD Median 1 (1-11) P<.001	IV fluid until POD Median 5 (3-35)	NR	NR	NR	NR

Author Year Population	Gastrointestinal function (define), days Mean (SD)		IV fluid administration		Mobilization, days Mean (SD)		Pain scale score (define) % (n/N)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
	Oral food 1 (1-31) P<.001	Oral food 3 (1-9)						
Scioscia 2017[43] Bowel endometriosis	NR	NR	NR	NR	NR	NR	NR	NR
Mari 2016[40] Colorectal cancer (75%) or diverticular disease (25%)	Flatus 1.6 (0.7) P<.05 Bowel movement P=NS (data NR) Solid diet 1.5 (0.9) P<.05	Flatus 2.1 (0.8) Bowel movement (data NR) Solid diet 3.0 (0.5)	NR	NR	Walk ≥100 m 1.5 (0.7) P<.05	Walk ≥100 m 2.6 (0.9)	NR	NR
Wang 2015[45] CCT Colon cancer	Flatus, hours 60.9 (11.1) P=.000 Bowel movement, hours 75.1 (14.9) P=.002	Flatus, hours 74.2 (16.3) Bowel movement, hours 85.5 (19.4)	NR	NR	First time out of bed, hours 15.3 (3.6) P=.000	First time out of bed, hours 42.5 (14.7)	NR	NR
Feng 2014[38] Rectal cancer	Flatus, hours 53.4 (23.6) P=.001 First defecation, hours 65.2 (22.2) P=.000 All (n=57)	Flatus, hours 67.9 (20.1) First defecation, hours 87.0 (24.9) All (n=59)	NR	NR	NR	NR	Pain (VAS) POD1 4.3 (1.0) P=.02 POD3 2.7 (1.2) P=.03 POD5 2.3 (1.5) P=.11	Pain (VAS) POD1 3.4 (1.0) POD3 1.8 (0.9) POD5 1.6 (1.2)
Mari 2014[41]	First bowel movement 0.3 (0.65)	First bowel movement 1.7 (0.5)	NR	NR	Walk at least 60-meters 1.3 (0.8)	Walk at least 60-meters 3.6 (0.5)	Pain, based on VAS pain scale Higher pain perception in immediate postoperative time in	

Author Year Population	Gastrointestinal function (define), days Mean (SD)		IV fluid administration		Mobilization, days Mean (SD)		Pain scale score (define) % (n/N)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
Colon cancer (69%) or diverticular disease (31%)	(n=25) Stool passage 1.6 (1.0) Flatus 0.9 (0.8) Solid diet 1.2 (0.4) All P<.005	(n=25) Stool passage 5 (1.8) Flatus 2.1 (0.9) Solid diet 3.8 (1.0)			(n=25) P<.005	(n=25)	ERAS group (P<.05) but non-significant after 5 hours; From day 1, ERAS patients referred less pain as compared with control patients P=NS	
Gouvas 2012[25] *CCT* Rectal cancer	First bowel movement Median 2 (range 0-6) P<.001	First bowel movement Median 5 (range 2-12)	NR	NR	NR	NR	NR	NR
Wang 2012[35] Colon cancer	NR	NR	NR	NR	NR	NR	NR	NR
Wang 2012[44] Adenocarcinoma of the colon	Flatus, median 2 (1-6) P=.017 Semi-liquid diet 1 (1-3) P<.001 Normal diet 3 (2-5) P<.001 All (n=49)	Flatus, median 3 (1-7) Semi-liquid diet 2 (1-5) Normal diet 4 (3-7) All (n=50)	NR	NR	Autonomic mobilization 1 (1-3) P<.001	Autonomic mobilization 2 (1-3)	NR	NR
Wang 2012[46] Colorectal cancer (elderly)	Flatus, median hours 31 (26-40) P=.001 Bowel movement, median hours 55 (48-63) P=.009 Fluid diet, median hours 12 (11-16)	Flatus, median hours 38 (32-51) Bowel movement, median hours 64 (51-71) Fluid diet, median hours 47 (35-50)	NR	NR	Ambulation, median hours 12 (10-14) P<.001 (n=40)	Ambulation, median hours 19 (16-24) (n=38)	NR	NR

Author Year Population	Gastrointestinal function (define), days Mean (SD)		IV fluid administration		Mobilization, days Mean (SD)		Pain scale score (define) % (n/N)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
	P<.001 All (n=40)	All (n=38)						
Vlug 2011[34] Colon cancer and benign disease	Medians Tolerate solid food 1 (IQR 1-2) Flatus 1 (IQR 1-2) Stool passage 2 (IQR 1-4) *Overall dis-charge criteria (including components above and mobilization) achieved significantly earlier in ERAS group versus usual care*	Medians Tolerate solid food 2 (IQR 1-3) Flatus 2 (IQR 1–3) Stool passage 3 (IQR 2-4)	NR	NR	Mobilization, median minutes POD1 120 (50-240) Mobilization as pre-operative, median days 3 (IQR 2-5)	Mobilization, median minutes POD1 30 (15-60) Mobilization as pre-operative, Median days 5 (IQR 4-7)	NR	NR
Mixed Open and Laparoscopic Surgery Studies								
Forsmo 2016[50] Colorectal cancer and benign disease	Flatus, median 1 (0-4) Bowel movement, median 1 (1-6) Both P<.001 Tolerate solid food, median 2 (0-9) P=.61	Flatus, median 1 (1-14) Bowel movement, median 2 (1-14) Both P<.001 Tolerate solid food, median 1 (0-12)	IV fluid, first 24 hrs (including intraoperative), L (median) 3.9 (1.9-9.0) P=.001 First 7 days 5.6 (1.9-19.2) P<.001	IV fluid, first 24 hrs (including intraoperative), L (median) 4.4 (1.8-9.5) First 7 days 7.8 (2.8-30.1)	NR	NR	NR	NR

IQR=interquartile range; NR=not reported; NS=not statistically significant; POD=post-operative day; VAS= Visual Analogue Scale

Table 5. Harms Associated with Enhanced Recovery, Part A

Author Year Population	Surgical complications (define) % (n/N)		Need for reoperation % (n/N)		Bleeding % (n/N)		General or gastrointestinal complications % (n/N)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
Open Surgery Studies								
Feng 2016[23] Colorectal cancer	Anastomotic leakage 1 (1/116) P=.37 Wound infection 1 (1/116) P=.37	Anastomotic leakage 3 (3/114) Wound infection 3 (3/114)	NR	NR	Anastomotic bleeding 1 (1/116) P=.62	Anastomotic bleeding 2 (2/114)	NR	NR
Pappalardo 2016[31] Rectal cancer	Anastomotic leakage 12 (3/25) (1 major) P=NS	Anastomotic leakage 8 (2/25) (1 major)	NR	NR	NR	NR	NR	NR
Jia 2014[27] Colorectal cancer (elderly)	Infection of incision 5 (6/117) P=.57 Anastomotic leakage 3 (3/117) P=1.0	Infection of incision 7 (8/116) Anastomotic leakage 2 (2/116)	NR	NR	NR	NR	Intestinal obstruction 3 (4/117) P=.74	Intestinal obstruction 5 (6/116)
Nanavati 2014[30] Gastrointestinal surgery (3% cancer)	Anastomotic leakage 0 (0/30) P=NS Wound infection 3 (1/30) Wound dehiscence 3 (1/30) Total 13 (4/30) P=NS	Anastomotic leakage 3 (1/30) Wound infection 0 (0/30) Wound dehiscence 0 (0/30) Total 17 (5/30)	0 (0/130)	3 (1/30) for anastomotic leak	NR	NR	NR	NR

Author Year Population	Surgical complications (define) % (n/N)		Need for reoperation % (n/N)		Bleeding % (n/N)		General or gastrointestinal complications % (n/N)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
Gouvas 2012[25] *CCT* Rectal cancer	Leak 11 (4/36) Wound complications 31 (11/36) P=NS for both	Leak 7 (3/45) Wound complications 38 (17/45)	Not reported by group, rates ranged from 4 to 15% P=NS between all groups		8 (3/36) P=.21[a]	20 (9/45)	Obstruction 3 (1/36) P=NS	Obstruction 2 (1/45)
Ren 2011[32] Colorectal cancer	Wound infection 2 (5/299) Anastomotic Leaks 2 (5/299) Intestinal Perforation 0 (1/299) P=NS for all	Wound infection 2 (5/298) Anastomotic Leaks 2 (5/298) Pancreatic Leakage 0 (1/298)	NR	NR	NR	NR	Intestinal obstruction 2 (6/299) P=NS Gastric retention 3 (10/299) P=.30[a] Diarrhea 0 (1/299)	Intestinal Obstruction 2 (7/298) Gastric retention 2 (5/298)
Wang 2012[35] Colon cancer	"Surgical"[b] 7 (3/41) P=NS	"Surgical"[b] 7 (3/42)	NR	NR	NR	NR	"General"[b] 10 (4/41) P=NS	"General"[b] 17 (7/42)
Yang 2012[37] Colorectal cancer	Surgical site infection 3 (1/32) P=.61 Anastomotic leaks 0 (0/32)	Surgical site infection 7 (2/30) Anastomotic leaks 0 (0/30)	NR	NR	NR	NR	Dysbiosis 3 (1/32) P=.10[a]	Dysbiosis 17 (5/30)

Author Year Population	Surgical complications (define) % (n/N)		Need for reoperation % (n/N)		Bleeding % (n/N)		General or gastrointestinal complications % (n/N)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
Vlug 2011[34] Colon cancer and benign disease	Major complications (including non-surgical) 20 (18/93) P=NS Including: Anastomotic leakage n=8 (2 fatal) Iatrogenic bowel perforation n=2 Dehiscence n=6 Wound infection 16 total	Major complications (including non-surgical) 21 (21/98) Including: Anastomotic leakage n=7 Iatrogenic bowel perforation n=1 Dehiscence n=3 Wound infection 10 total	14 (13/93) P=NS	18 (18/98)	NR	NR	Minor complications (including surgical) 26 (25/93) P=NS	Minor complications (including surgical) 19 (20/98)
Wang 2011[36] Colorectal cancer	Anastomotic leakage 4 (4/106) Wound infection 4 (4/106) P=NS for both	Anastomotic leakage 2 (2/104) Wound infection 7 (7/104)	2 (2/106) for bowel obstruction	5 (5/104) for bowel obstruction	NR	NR	Bowel obstruction 2 (2/106) P=.28 Re-insertion of nasogastric tube 4 (4/106) P<.05	Bowel obstruction 5 (5/104) Re-insertion of nasogastric tube 11 (12/104)
Ionescu 2009[26] Rectosigmoid (58%) or colon (42%) cancer	Anastomotic leak 2 (1/48) Wound infection 8 (4/48) P=NS for both	Anastomotic leak 2 (1/48) Wound infection 10 (5/48)	0 (0/48) for anastomotic leak P=NS[a]	2 (1/48) for anastomotic leak	NR	NR	Post-operative nausea and vomiting 35 (17/48) P=.54	Post-operative nausea and vomiting 43 (21/48)

Author Year Population	Surgical complications (define) % (n/N)		Need for reoperation % (n/N)		Bleeding % (n/N)		General or gastrointestinal complications % (n/N)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
Muller 2009[29] Colon surgery (87% malignant) with primary anastomosis	Wound infection 5 (4/76) P=.37[a] Anastomotic leaks 1 (1/76) P=.62[a]	Wound infection 9 (7/75) Anastomotic leaks 3 (2/75)	NR	NR	Postoperative bleeding 1 (1/76) P=.62[a]	Postoperative bleeding 3 (2/75)	"Other events" 0 (0/76) P=.12[a]	"Other events" 4 (3/75)
Šerclová 2009[33] Intestinal resection (78% Crohn's disease, 7% cancer)	>1 complication 0 (0/51) P=.50[a] Wound complications 8 (4/51) P=.003	>1 complication 4 (2/52) Wound complications 33 (17/52)	NR	NR	NR	NR	Vomiting Day of surgery 8% POD1 16% POD2 2%* POD3 2% POD4 2% *P<.05 (P=NS all other days)	Vomiting Day of surgery 14% POD1 12% POD2 16% POD3 10% POD4 8%
Khoo 2007[28] Colon (67%) or rectal (33%) cancer	Anastomotic leakage 3 (1/35) P=.61[a]	Anastomotic leakage 9 (3/35)	NR	NR	NR	NR	Nasogastric tube reinsertion 9 (3/35) P=NS[a]	Nasogastric tube reinsertion 11 (4/35)
Gatt 2005[24] Colon surgery (69% malignant)	Wound infection 0 (0/19) P=.11[a]	Wound infection 20 (4/20)	NR	NR	NR	NR	Diarrhea/ nausea 5 (1/19) P=NS[a]	Diarrhea/ nausea 10 (2/20)
Anderson 2003[22] Colon surgery (72% malignant)	Wound infection 7 (1/14) P=NS[a]	Wound infection 0 (0/11)	NR	NR	NR	NR	NR	NR

Author Year Population	Surgical complications (define) % (n/N)		Need for reoperation % (n/N)		Bleeding % (n/N)		General or gastrointestinal complications % (n/N)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
Laparoscopic Studies								
Ota 2017[42] CCT Colorectal cancer NOTE: 97% (ERAS) and 91% (control) had laparoscopic surgery	Surgical complications (total) 17 (27/159) P=NS Surgical site infection 3 (5/159) P=1.0 Intraperitoneal infection 0 (0/159) P=.25 Anastomotic leakage 3 (4/159) P=.99	Surgical complications (total) 16 (26/161) Surgical site infection 4 (6/161) Intraperitoneal infection 2 (3/161) Anastomotic leakage 3 (4/161)	1 (2/159) P=.16	4 (6/161)	Anastomotic bleeding 5 (8/159) P=.02 Intraperitoneal bleeding 0 (0/159) P=.08	Anastomotic bleeding 1 (1/161) Intraperitoneal bleeding 2 (3/161)	NR	NR
Scioscia 2017[43] Bowel endometriosis	NR	NR	For severe complications 6.5 (4/62) P=.20	For severe complications 8.5 (14/162)	Need for transfusion 3.2 (2/62) P=.73	Need for transfusion 5.5 (9/162)	NR	NR
Mari 2016[40] Colorectal cancer (75%) or diverticular disease (25%)	Wound infection 3 (2/70) Anastomotic fistula 3 (2/70) P=NS for both	Wound infection 1 (1/70) Anastomotic fistula 4 (3/70)	NR	NR	Proctorrhagia 1 (1/70) P=NS	Proctorrhagia 4 (3/70)	Vomiting 7 (5/70) P=NS	Vomiting 3 (2/70)
Wang 2015[45] CCT Colon cancer	Wound infection 3.5 (2/57) Anastomotic leakage 1.8 (1/57) P=NS[a] for b oth	Wound infection 3.3 (2/60) Anastomotic leakage 3.3 (2/60)	NR	NR	NR	NR	Gastric retention 1.8 (1/57) P=NS[a]	Gastric retention 3.3 (2/60)

Author Year Population	Surgical complications (define) % (n/N)		Need for reoperation % (n/N)		Bleeding % (n/N)		General or gastrointestinal complications % (n/N)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
Feng 2014[38] Rectal cancer	Change to open surgery due to difficulty in tumor resection (4/57) Incision Infection 0 (0/57) Anastomotic leakage 0 (0/57) Abdominal infection 0 (0/57) All P=NS	Change to open surgery due to difficulty in tumor resection (3/59) Incision Infection 1.7 (1/59) Anastomotic leakage 6.8 (4/59) Abdominal infection 0 (0/59)	0 (0/57) P=NS	1.7 (1/59) for anastomotic leak	NR	NR	Rectovaginal fistula 0 (0/57) P=NS	Rectovaginal fistula 1.7 (1/59)
Mari 2014[41] Colon cancer (69%) or diverticular disease (31%)	No anastomotic leaks	No anastomotic leaks	NR	NR	NR	NR	NR	NR
Gouvas 2012[25] *CCT* Rectal cancer	Leak 10 (4/42) Wound complications 7 (3/42) P=NS for both	Leak 15 (5/33) Wound complications 12 (4/33)	Not reported by group, rates ranged from 4 to 15% P=NS between all groups		0 (0/42)	0 (0/33)	Obstruction 0 (0/42)	Obstruction 3 (1/33)
Wang 2012[35] Colon cancer	"Surgical"[b] 3 (1/40) P=NS	"Surgical"[b] 5 (2/40)	NR	NR	NR	NR	"General"[b] 5 (2/40) P=NS	"General"[b] 10 (4/40)
Wang 2012[44] Adenocarcinoma of the colon	Anastomotic leakage 0 (0/49) Wound infection 6 (3/49) P=NS for both	Anastomotic leakage 2 (1/50) Wound infection 4 (2/50)	None	None	NR	NR	Obstruction 0 (0/49)	Obstruction 2 (1/50)

Author Year Population	Surgical complications (define) % (n/N)		Need for reoperation % (n/N)		Bleeding % (n/N)		General or gastrointestinal complications % (n/N)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
Wang 2012[46] Colorectal cancer (elderly)	Incision infection 3 (1/40) P=.35 (n=40) Leakage 0 (0/40)	Incision infection 8 (3/38) (n=38) Leakage 0 (0/38)	NR	NR	NR	NR	Obstruction 0 (0/40)	Obstruction 5 (2/38)
Vlug 2011[34] Colon cancer and benign disease	Anastomotic leakage n=7 Wound infection 6 total	Anastomotic leakage n=6 (1 fatal) Iatrogenic bowel perforation n=2 (1 patient died) Dehiscence n=3 Wound infection 8 total	10 (10/100) P=NS	10 (11/109)	NR	NR	NR	NR
Mixed Open and Laparoscopic Surgery Studies								
Forsmo 2016[50] Colorectal cancer and benign disease	Anastomotic leakage[c] Colon: 5 (3/59) P=.45 Rectum: 12 (7/58) P=.17 Wound infection Abdominal: 7 (10/154) P=.51 Perineal: 25 (8/154) P=.81 Abdominal wall dehiscence 3 (5/154) P=.99	Anastomotic leakage[c] Colon: 3 (2/77) Rectum: 4 (2/45) Wound infection Abdominal: 9 (13/153) Perineal: 32 (9/153) Abdominal wall dehiscence 3 (5/153)	11 (17/154) P=.24	7 (11/153)	NR	NR	NR	NR

NR=not reported; NS=not statistically significant

[a] Calculated (Fisher's exact test)

[b] Surgical complications includes wound complications, anastomotic leak, and bowel obstruction requiring re-operation; General complications includes cardiovascular, pulmonary, thromboembolic, urinary and other complications
[c] In patients with an anastomosis

Table 6. Harms Associated with Enhanced Recovery, Part B

Author Year	Foley catheter re-insertion/other renal or urologic complications % (n/N)		Aspiration pneumonia or pulmonary infection % (n/N)		Vascular or cardiovascular complications % (n/N)		Miscellaneous complications % (n/N)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
Open Surgery Studies								
Feng 2016[23] Colorectal cancer	Urinary retention 2 (2/116) P=.68	Urinary retention 3 (3/114)	Pulmonary infection 1 (1/116) P=.21	Pulmonary infection 4 (4/114)	NR	NR	NR	NR
Pappalardo 2016[31] Rectal cancer	Urinary complications 0 (0/25)	Urinary complications 0 (0/25)	NR	NR	Vascular complications 0 (0/25)	Vascular complications 0 (0/25)	Pulmonary complications (not specified) 0 (0/25)	Pulmonary complications 0 (0/25)
Jia 2014[27] Colorectal cancer (elderly)	UTI 4 (5/117) P=.05	UTI 11 (13/116)	Pulmonary infection 5 (6/117) P=.006	Pulmonary infection 16 (19/116)	Heart failure 3 (4/117) P=.02 DVT 3 (4/117) P=.34	Heart failure 11 (13/116) DVT 6 (7/116)	Post-op delirium[a] 3 (4/117) P=.008	Post-op delirium[a] 13 (15/116)
Nanavati 2014[30] Gastrointestinal surgery (3% cancer)	NR	NR	NR	NR	NR	NR	NR	NR
Gouvas 2012[25] *CCT* Rectal cancer	Urinary retention 11 (4/36) P=NS	Urinary retention 20 (9/45)	Chest infection 17 (6/36) P=.004 [b]	Chest infection 49 (22/45)	DVT 3 (1/36) Pulmonary embolism 3 (1/36)	DVT 16 (7/45) Pulmonary embolism 4 (2/45)	NR	NR
Ren 2011[32] Colorectal cancer	NR	NR	NR	NR	Cardiovascular and cerebro-vascular complication 0 (1/299)	Cardiovascular and cerebro-vascular complication 2 (5/298)	NR	NR
Wang 2012[35] Colon cancer	NR	NR	NR	NR	NR	NR	NR	NR

Author Year	Foley catheter re-insertion/other renal or urologic complications % (n/N)		Aspiration pneumonia or pulmonary infection % (n/N)		Vascular or cardiovascular complications % (n/N)		Miscellaneous complications % (n/N)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
Yang 2012[37] Colorectal cancer	Urine distension 3 (1/32) P=NS	Urine distension 3 (1/30)	Pneumonia 0 (0/32) P=.48	Pneumonia 3 (1/30)	Arrhythmia 0 (0/32) P=NS	Arrhythmia 3 (1/30)	Stress ulcer 0 (0/32) P=NS	Stress ulcer 3 (1/30)
Vlug 2011[34] Colon cancer and benign disease	Urine retention n=6 complications	Urine retention n=1 complication	NR	NR	None reported	CVA n=2 complications (1 fatal)	Other infectious complications n=11 Respiratory n=2 complications (1 fatal)	Other infectious complications n=14 Respiratory n=4 complications
Wang 2011[36] Colorectal cancer	Catheter re-insertion 4 (4/106) P=.06[b] Urinary retention 5 (5/106) P=.01[b] Urinary tract complication 2 (2/106) P=NS	Catheter re-insertion 11 (12/104) Urinary retention 15 (16/104) Urinary tract complication 5 (5/104)	NR	NR	Cardiac complication 2 (2/106) Thrombo-embolic complication 1 (1/106) P=NS[b] for both	Cardiac complication 5 (5/104) Thrombo-embolic complication 3 (3/104)	Pulmonary complication (not specified) 3 (3/106) P=.13[b]	Pulmonary complication 8 (8/104)
Ionescu 2009[26] Rectosigmoid (58%) or colon (42%) cancer	UTI 0 (0/48) Hematuria 2 (1/48) P=NS for both	UTI 6 (3/48) Hematuria 0 (0/48)	NR	NR	Pulmonary embolism 0 (0/48) P=NS	Pulmonary embolism 2 (1/48)	Postoperative hernia 0 (0/48) P=NS	Postoperative hernia 2 (1/48)
Muller 2009[29] Colon surgery (87% malignant) with primary anastomosis	Urinary infection/ retention 4 (3/76) P=.49[b]	Urinary infection/ retention 7 (5/75)	Pneumonia or respiratory events 1 (1/76)	Pneumonia or respiratory events 5 (4/75)	Cardiovascular events 4 (3/76) P=.08[b]	Cardiovascular events 12 (9/75)	NR	NR

Author Year	Foley catheter re-insertion/other renal or urologic complications % (n/N)		Aspiration pneumonia or pulmonary infection % (n/N)		Vascular or cardiovascular complications % (n/N)		Miscellaneous complications % (n/N)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
Šerclová 2009[33] Intestinal resection (78% Crohn's disease, 7% cancer)	NR	NR	NR	NR	NR	NR	NR	NR
Khoo 2007[28] Colon (67%) or rectal (33%) cancer	Re-insertion due to urinary retention 11 (4/35) P=.11[b] UTI 3 (1/35) P=NS	Re-insertion due to urinary retention 0 (0/35) UTI 6 (2/35)	NR	NR	Cardio-respiratory compromise 0 (0/35) P=.11[b]	Cardio-respiratory compromise 11 (4/35)	Pressure sores 0 (0/35)	Pressure sores 9 (3/35)
Gatt 2005[24] Colon surgery (69% malignant)	UTI 0 (0/19) P=.49[b]	UTI 10 (2/20)	Chest infection 5 (1/19) P=NS	Chest infection 0 (0/20)	DVT 10 (2/19) P=.23[b]	DVT 0 (0/20)	NR	NR
Anderson 2003[22] Colon surgery (72% malignant)	UTI 7 (1/14) P=.56[b]	UTI 18 (2/11)	NR	NR	Atrial fibrillation 0 (0/14)	Atrial fibrillation 9 (1/11)	Respiratory depression related to patient-controlled analgesia 0 (0/14)	Respiratory depression related to patient-controlled analgesia 9 (1/11)
Laparoscopic Studies								
Ota 2017[42] CCT Colorectal cancer NOTE: 97% (ERAS) and 91% (control) had laparoscopic surgery	Hepatorenal complication 0 (0/159) P=.32 UTI 0 (0/159)	Hepatorenal complication 1 (1/161) UTI 0 (0/161	NR	NR	Cardiovascular complication 0 (0/159) P=.32 DVT 0 (0/159)	Cardiovascular complication 1 (1/161) DVT 0 (0/161)	Respiratory complication (not specified) 0 (0/159) P=.32 Delirium 0 (0/159) P=.25	Respiratory complication 1 (1/161) Delirium 2 (3/161)
Scioscia 2017[43] Bowel endometriosis	NR	NR	NR	NR	NR	NR	Pyrexia 14.5 (9/62) P=.83	Pyrexia 12.7 (21/162)

Author Year	Foley catheter re-insertion/other renal or urologic complications % (n/N)		Aspiration pneumonia or pulmonary infection % (n/N)		Vascular or cardiovascular complications % (n/N)		Miscellaneous complications % (n/N)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
Mari 2016[40] Colorectal cancer (75%) or diverticular disease (25%)	Urinary retention 1 (1/70) P=NS	Urinary retention 4 (3/70)	Pneumonia 4 (3/70) P=NS	Pneumonia 7 (5/70)	Atrial fibrillation 0 (0/70) P=NS	Atrial fibrillation 1 (1/70)		
Wang 2015[45] CCT Colon cancer	NR	NR	Pulmonary infection 1.8 (1/57) P=.62[b]	Pulmonary infection 5.0 (3/60)	Cardiovascular events 3.5 (2/57) P=NS[b]	Cardiovascular events 3.3 (2/60)	NR	NR
Feng 2014[38] Rectal cancer	Urinary retention 1.8 (1/57) Urinary infection 0 (0/57) P=NS for both	Urinary retention 3.4 (2/59) Urinary infection 0 (0/59)	Pneumonia 1.8 (1/57) P=NS	Pneumonia 1.7 (1/59)	DVT 0 (0/57)	DVT 0 (0/59)	NR	NR
Mari 2014[41] Colon cancer (69%) or diverticular disease (31%)	NR	NR	NR	NR	NR	NR	Respiratory distress 4 (1/25) P=NS[b]	Respiratory distress 0 (0/25)
Gouvas 2012[25] *CCT* Rectal cancer	Urinary retention 5 (2/42) P=.01[b]	Urinary retention 24 (8/33)	Chest infection 10 (4/42) P=.20[b]	Chest infection 21 (7/33)	DVT 2 (1/42) P=NS	DVT 9 (3/33)	NR	NR
Wang 2012[35] Colon cancer	NR	NR	NR	NR	NR	NR	NR	NR
Wang 2012[44] Adenocarcinoma of the colon	Catheter reinsertion 8 (4/49) UTI 2 (1/49) P=NS for both	Catheter reinsertion 14 (7/50) UTI 2 (1/50)	NR	NR	Cardiac complication 0 (0/49) P=.49[b] Thrombo-embolic complication 0 (0/49) P=NS[b]	Cardiac complication 4 (2/50) Thrombo-embolic complication 2 (1/50)	Pulmonary complication (not specified) 2 (1/49) P=NS[b]	Pulmonary complication 4 (2/50)

Author Year	Foley catheter re-insertion/other renal or urologic complications % (n/N)		Aspiration pneumonia or pulmonary infection % (n/N)		Vascular or cardiovascular complications % (n/N)		Miscellaneous complications % (n/N)	
	ERAS	Control	ERAS	Control	ERAS	Control	ERAS	Control
Wang 2012[46] Colorectal cancer (elderly)	NR	NR	Intrapulmonary infection 3 (1/40) P=.35	Intrapulmonary infection 8 (3/38)	NR	NR	NR	NR
Vlug 2011[34] Colon cancer and benign disease	Urine retention n=4 complications	Urine retention n=6 complications	NR	NR	CVA n=1 complication (fatal)	CVA n=0	Other infectious complications n=8 Respiratory n=2 complications (1 fatal)	Other infectious complications n=9 Respiratory n=2 complications
Mixed Open and Laparoscopic Surgery Studies								
Forsmo 2016[50] Colorectal cancer and benign disease	Renal failure 5 (8/154) P=.79 Urinary retention 6 (9/154) P=.20 UTI 7 (11/154) P=.31	Renal failure 5 (7/153) Urinary retention 10 (15/153) UTI 10 (16/153)	Pneumonia 5 (7/154) P=.79 Pleural effusion requiring drainage 3 (5/154) P=.47	Pneumonia 5 (8/153) Pleural effusion requiring drainage 2 (3/153)	Cardiac arrhythmia 1 (2/154) P=.65 Pulmonary embolism 1 (2/154) P=.16	Cardiac arrhythmia 2 (3/153) Pulmonary embolism 0 (0/153)	Respiratory complications requiring ICU (not specified) 1 (2/154) P=.16 Post-operative confusion 2 (3/154) P=.99 Intra-abdominal infection 7 (11/154) P=.22	Respiratory complications requiring ICU 0 (0/153) Post-operative confusion 2 (3/153) Intra-abdominal infection 4 (6/153)

CVA=cerebral vascular accident; DVT=deep vein thrombosis; ICU=intensive care unit; UTI=urinary tract infection; NR=not reported; NS=not statistically significant

[a] Based on Delirium Rating Scale-Revised-98, Delirium was defined as the total score ≧18

[b] Calculated (Fisher's exact test)

APPENDIX E. ERAS AND USUAL CARE COMPONENTS

Table 1. ERAS and Standard Care Protocol Components - Open Surgery Studies (SEE Appendix E Table 2 for Gouvas 2012, Wang 2012 J Gast Surg, and Vlug 2011)

Author, Year: Feng 2016[23]	Reason for Surgery: Colorectal Cancer		
Phases	**ERAS Components**	**ERAS Protocol**	**Standard Care Protocol**
PREADMISSION	Smoking/alcohol cessation		
	Nutritional screening/support		
	Medical optimization of chronic disease		
PREOPERATIVE	Structured information/patient and caretaker engagement	ü	
	Bowel preparation (no routine use of mechanical bowel prep)	ü	
	Pre-operative fasting (clear fluids to 2 hours and solids to 6 hours before surgery)	ü	
	Carbohydrate treatment	ü	
	Thrombosis prophylaxis		
	Infection prophylaxis and/or skin preparation with chlorhexidine-alcohol	ü	
	Nausea and vomiting prophylaxis		
	Pre-anesthetic sedative medication (no routine use)		
INTRAOPERATIVE	Minimal invasive surgical techniques		
	Standardized anesthesia protocol – may use thoracic epidural blocks with local anesthetics and low-dose opioids for open surgery and spinal analgesia or patient-controlled morphine as alternative to thoracic epidural for laparoscopic surgery	ü	
	Maintain fluid balance; vasopressors for blood pressure control		
	Restrictive use of surgical site drains	ü	
	Remove nasogastric tubes before reversal of anesthesia (and no routine use)		
	Control of body temperature	ü	
POSTOPERATIVE	Early mobilization	ü	
	Early intake of oral fluids and solids	ü	
	Early removal of urinary catheters and intravenous fluids	ü	
	Chewing gum, laxatives, peripheral opioid-blocking agents		
	Protein and energy-rich nutritional supplements	ü	
	Glucose control		
	Multimodal approach to opioid-sparing pain control – consider thoracic epidural analgesia (open surgery) or spinal analgesia (laparoscopic surgery); also NSAIDS and paracetamol	ü	
	Multimodal approach to control of nausea and vomiting		
	Prepare for early discharge		

Author, Year: Pappalardo 2016[31] (Standard Protocol Not Specified)	Reason for Surgery: Rectal Cancer

Phases	ERAS Components	ERAS Protocol	Standard Care Protocol
PREADMISSION	Smoking/alcohol cessation		
	Nutritional screening/support		
	Medical optimization of chronic disease		
PREOPERATIVE	Structured information/patient and caretaker engagement		
	Bowel preparation (no routine use of mechanical bowel prep)		
	Pre-operative fasting (clear fluids to 2 hours and solids to 6 hours before surgery)		
	Carbohydrate treatment		
	Thrombosis prophylaxis	**ü**	
	Infection prophylaxis including skin preparation with chlorhexidine-alcohol	**ü**	
	Nausea and vomiting prophylaxis		
	Pre-anesthetic sedative medication (no routine use)		
	Minimal invasive surgical techniques		
INTRAOPERATIVE	Standardized anesthesia protocol – may use thoracic epidural blocks with local anesthetics and low-dose opioids for open surgery and spinal analgesia or patient-controlled morphine as alternative to thoracic epidural for laparoscopic surgery	**ü (epidural)**	
	Maintain fluid balance; vasopressors for blood pressure control		
	Restrictive use of surgical site drains		
	Remove nasogastric tubes before reversal of anesthesia		
	Control of body temperature		
POSTOPERATIVE	Early mobilization		
	Early intake of oral fluids and solids		
	Early removal of urinary catheters and intravenous fluids		
	Chewing gum, laxatives, peripheral opioid-blocking agents		
	Protein and energy-rich nutritional supplements		
	Glucose control		
	Multimodal approach to opioid-sparing pain control – consider thoracic epidural analgesia (open surgery) or spinal analgesia (laparoscopic surgery); also NSAIDS and paracetamol	**ü**	
	Multimodal approach to control of nausea and vomiting		
	Prepare for early discharge		

Author, Year: Jia 2014[27]	Reason for Surgery: Colon (49%) or Rectal (51%) Cancer		
Phases	**ERAS Components**	**ERAS Protocol**	**Standard Care Protocol**
PREADMISSION	Smoking/alcohol cessation		
	Nutritional screening/support		
	Medical optimization of chronic disease		
PREOPERATIVE	Structured information/patient and caretaker engagement		
	Bowel preparation (no routine use of mechanical bowel prep)	ü	
	Pre-operative fasting (clear fluids to 2 hours and solids to 6 hours before surgery)		ü
	Carbohydrate treatment	ü	
	Thrombosis prophylaxis		
	Infection prophylaxis and/or skin preparation with chlorhexidine-alcohol		
	Nausea and vomiting prophylaxis		
	Pre-anesthetic sedative medication (no routine use)		
	Minimal invasive surgical techniques		
	Standardized anesthesia protocol – may use thoracic epidural blocks with local anesthetics and low-dose opioids for open surgery and spinal analgesia or patient-controlled morphine as alternative to thoracic epidural for laparoscopic surgery	ü	
INTRAOPERATIVE	Maintain fluid balance; vasopressors for blood pressure control		
	Restrictive use of surgical site drains	ü	
	Remove nasogastric tubes before reversal of anesthesia (and no routine use)	ü	
	Control of body temperature		
POSTOPERATIVE	Early mobilization	ü	
	Early intake of oral fluids and solids	ü	
	Early removal of urinary catheters and intravenous fluids	ü	
	Chewing gum, laxatives, peripheral opioid-blocking agents		
	Protein and energy-rich nutritional supplements		
	Glucose control		
	Multimodal approach to opioid-sparing pain control – consider thoracic epidural analgesia (open surgery) or spinal analgesia (laparoscopic surgery); also NSAIDS and paracetamol	ü	
	Multimodal approach to control of nausea and vomiting		
	Prepare for early discharge		

Author, Year: Nanavati 2014[30]	**Reason for Surgery: Colorectal Procedures (42% Ileostomal Closure, 17% Colostoma Closure); 7% Laparoscopic**

Phases	ERAS Components	ERAS Protocol	Standard Care Protocol
PREADMISSION	Smoking/alcohol cessation		
	Nutritional screening/support		
	Medical optimization of chronic disease		
PREOPERATIVE	Structured information/patient and caretaker engagement		
	Bowel preparation (no routine use of mechanical bowel prep)	ü	
	Pre-operative fasting (clear fluids to 2 hours and solids to 6 hours before surgery)		
	Carbohydrate treatment	ü	
	Thrombosis prophylaxis		
	Infection prophylaxis and/or skin preparation with chlorhexidine-alcohol	ü	
	Nausea and vomiting prophylaxis	ü	
	Pre-anesthetic sedative medication (no routine use)		
	Minimal invasive surgical techniques	ü	
INTRAOPERATIVE	Standardized anesthesia protocol – may use thoracic epidural blocks with local anesthetics and low-dose opioids for open surgery and spinal analgesia or patient-controlled morphine as alternative to thoracic epidural for laparoscopic surgery		
	Maintain fluid balance; vasopressors for blood pressure control	ü	
	Restrictive use of surgical site drains	ü	
	Remove nasogastric tubes before reversal of anesthesia (and no routine use)	ü	ü
	Control of body temperature		
POSTOPERATIVE	Early mobilization	ü	
	Early intake of oral fluids and solids	ü	
	Early removal of urinary catheters and intravenous fluids	ü	
	Chewing gum, laxatives, peripheral opioid-blocking agents		
	Protein and energy-rich nutritional supplements		
	Glucose control		
	Multimodal approach to opioid-sparing pain control – consider thoracic epidural analgesia (open surgery) or spinal analgesia (laparoscopic surgery); also NSAIDS and paracetamol		
	Multimodal approach to control of nausea and vomiting		
	Prepare for early discharge		

Author, Year: Ren 2012[32]	Reason for Surgery: Colorectal Cancer		
Phases	**ERAS Components**	**ERAS Protocol**	**Standard Care Protocol**
PREADMISSION	Smoking/alcohol cessation		
	Nutritional screening/support		
	Medical optimization of chronic disease		
PREOPERATIVE	Structured information/patient and caretaker engagement		
	Bowel preparation (no routine use of mechanical bowel prep)	ü	
	Pre-operative fasting (clear fluids to 2 hours and solids to 6 hours before surgery)	ü	
	Carbohydrate treatment	ü	
	Thrombosis prophylaxis		
	Infection prophylaxis and/or skin preparation with chlorhexidine-alcohol	ü	
	Nausea and vomiting prophylaxis	ü	ü
	Pre-anesthetic sedative medication (no routine use)		
INTRAOPERATIVE	Minimal invasive surgical techniques		
	Standardized anesthesia protocol – may use thoracic epidural blocks with local anesthetics and low-dose opioids for open surgery and spinal analgesia or patient-controlled morphine as alternative to thoracic epidural for laparoscopic surgery		
	Maintain fluid balance; vasopressors for blood pressure control	ü	
	Restrictive use of surgical site drains		
	Remove nasogastric tubes before reversal of anesthesia (and no routine use)	ü	
	Control of body temperature	ü	
	Early mobilization	ü	
	Early intake of oral fluids and solids	ü	
	Early removal of urinary catheters and intravenous fluids	**ü (early removal)**	**ü (early removal)**
POSTOPERATIVE	Chewing gum, laxatives, peripheral opioid-blocking agents	ü	
	Protein and energy-rich nutritional supplements	ü	
	Glucose control		
	Multimodal approach to opioid-sparing pain control – consider thoracic epidural analgesia (open surgery) or spinal analgesia (laparoscopic surgery); also NSAIDS and paracetamol	ü	
	Multimodal approach to control of nausea and vomiting		
	Prepare for early discharge		

Author, Year: Yang 2012[37]	Reason for Surgery: Colorectal Cancer		
Phases	**ERAS Components**	**ERAS Protocol**	**Standard Care Protocol**
PREADMISSION	Smoking/alcohol cessation		
	Nutritional screening/support		
	Medical optimization of chronic disease		
PREOPERATIVE	Structured information/patient and caretaker engagement		
	Bowel preparation (no routine use of mechanical bowel prep)		
	Pre-operative fasting (clear fluids to 2 hours and solids to 6 hours before surgery)	ü	
	Carbohydrate treatment	ü	
	Thrombosis prophylaxis		
	Infection prophylaxis and/or skin preparation with chlorhexidine-alcohol	ü	ü
	Nausea and vomiting prophylaxis		
	Pre-anesthetic sedative medication (no routine use)		
	Minimal invasive surgical techniques		
	Standardized anesthesia protocol – may use thoracic epidural blocks with local anesthetics and low-dose opioids for open surgery and spinal analgesia or patient-controlled morphine as alternative to thoracic epidural for laparoscopic surgery	**ü (avoid long-acting opiods)**	**ü (avoid long-acting opiods)**
INTRAOPERATIVE	Maintain fluid balance; vasopressors for blood pressure control	**ü (fluid restriction)**	**ü (fluid restriction)**
	Restrictive use of surgical site drains	ü	ü
	Remove nasogastric tubes before reversal of anesthesia (and no routine use)	ü	
	Control of body temperature	ü	ü
POSTOPERATIVE	Early mobilization	ü	
	Early intake of oral fluids and solids	ü	
	Early removal of urinary catheters and intravenous fluids	ü	
	Chewing gum, laxatives, peripheral opioid-blocking agents		
	Protein and energy-rich nutritional supplements	ü	
	Glucose control	ü	
	Multimodal approach to opioid-sparing pain control – consider thoracic epidural analgesia (open surgery) or spinal analgesia (laparoscopic surgery); also NSAIDS and paracetamol	ü	ü
	Multimodal approach to control of nausea and vomiting		
	Prepare for early discharge		

Author, Year: Wang 2011[36]	Reason for Surgery: Colon (65%) or Rectal (35%) Cancer		
Phases	**ERAS Components**	**ERAS Protocol**	**Standard Care Protocol**
PREADMISSION	Smoking/alcohol cessation		
	Nutritional screening/support		
	Medical optimization of chronic disease		
PREOPERATIVE	Structured information/patient and caretaker engagement	ü	
	Bowel preparation (no routine use of mechanical bowel prep)	ü	
	Pre-operative fasting (clear fluids to 2 hours and solids to 6 hours before surgery)	ü	
	Carbohydrate treatment	ü	
	Thrombosis prophylaxis		
	Infection prophylaxis and/or skin preparation with chlorhexidine-alcohol		
	Nausea and vomiting prophylaxis		
	Pre-anesthetic sedative medication (no routine use)	ü	
	Minimal invasive surgical techniques	ü	
	Standardized anesthesia protocol – may use thoracic epidural blocks with local anesthetics and low-dose opioids for open surgery and spinal analgesia or patient-controlled morphine as alternative to thoracic epidural for laparoscopic surgery		
INTRAOPERATIVE	Maintain fluid balance; vasopressors for blood pressure control		
	Restrictive use of surgical site drains	ü	
	Remove nasogastric tubes before reversal of anesthesia (and no routine use)	ü	
	Control of body temperature		
POSTOPERATIVE	Early mobilization	ü	
	Early intake of oral fluids and solids	ü	
	Early removal of urinary catheters and intravenous fluids	ü	
	Chewing gum, laxatives, peripheral opioid-blocking agents		
	Protein and energy-rich nutritional supplements		
	Glucose control		
	Multimodal approach to opioid-sparing pain control – consider thoracic epidural analgesia (open surgery) or spinal analgesia (laparoscopic surgery); also NSAIDS and paracetamol	ü	
	Multimodal approach to control of nausea and vomiting		
	Prepare for early discharge		

Author, Year: Ionescu 2009[26]	Reason for Surgery: Rectosigmoid (58%) or Colon (42%) Cancer		
Phases	**ERAS Components**	**ERAS Protocol**	**Standard Care Protocol**
PREADMISSION	Smoking/alcohol cessation		
	Nutritional screening/support		
	Medical optimization of chronic disease		
PREOPERATIVE	Structured information/patient and caretaker engagement	ü	
	Bowel preparation (no routine use of mechanical bowel prep)	ü	
	Pre-operative fasting (clear fluids to 2 hours and solids to 6 hours before surgery)	ü	
	Carbohydrate treatment	ü	
	Thrombosis prophylaxis		
	Infection prophylaxis and/or skin preparation with chlorhexidine-alcohol		
	Nausea and vomiting prophylaxis		
	Pre-anesthetic sedative medication (no routine use)		
	Minimal invasive surgical techniques		
INTRAOPERATIVE	Standardized anesthesia protocol – may use thoracic epidural blocks with local anesthetics and low-dose opioids for open surgery and spinal analgesia or patient-controlled morphine as alternative to thoracic epidural for laparoscopic surgery	ü	ü
	Maintain fluid balance; vasopressors for blood pressure control		
	Restrictive use of surgical site drains		
	Remove nasogastric tubes before reversal of anesthesia (and no routine use)	ü	
	Control of body temperature		
POSTOPERATIVE	Early mobilization	ü	ü
	Early intake of oral fluids and solids	ü	
	Early removal of urinary catheters and intravenous fluids	ü	
	Chewing gum, laxatives, peripheral opioid-blocking agents		
	Protein and energy-rich nutritional supplements		
	Glucose control		
	Multimodal approach to opioid-sparing pain control – consider thoracic epidural analgesia (open surgery) or spinal analgesia (laparoscopic surgery); also NSAIDS and paracetamol	ü	ü
	Multimodal approach to control of nausea and vomiting		
	Prepare for early discharge	ü	ü

Author, Year: Muller 2009[29]	**Reason for Surgery: 87% Colon Cancer**		
Phases	**ERAS Components**	**ERAS Protocol**	**Standard Care Protocol**
PREADMISSION	Smoking/alcohol cessation		
	Nutritional screening/support		
	Medical optimization of chronic disease		
PREOPERATIVE	Structured information/patient and caretaker engagement		
	Bowel preparation (no routine use of mechanical bowel prep)	ü	ü
	Pre-operative fasting (clear fluids to 2 hours and solids to 6 hours before surgery)	**ü (4 hrs)**	**ü (4 hrs)**
	Carbohydrate treatment		
	Thrombosis prophylaxis	ü	ü
	Infection prophylaxis and/or skin preparation with chlorhexidine-alcohol	ü	ü
	Nausea and vomiting prophylaxis		
	Pre-anesthetic sedative medication (no routine use)		
INTRAOPERATIVE	Minimal invasive surgical techniques		
	Standardized anesthesia protocol – may use thoracic epidural blocks with local anesthetics and low-dose opioids for open surgery and spinal analgesia or patient-controlled morphine as alternative to thoracic epidural for laparoscopic surgery	ü	ü
	Maintain fluid balance; vasopressors for blood pressure control	ü	ü
	Restrictive use of surgical site drains	ü	ü
	Remove nasogastric tubes before reversal of anesthesia (and no routine use)	ü	ü
	Control of body temperature		
	Early mobilization	ü	ü
	Early intake of oral fluids and solids	ü	
	Early removal of urinary catheters and intravenous fluids	ü	
	Chewing gum, laxatives, peripheral opioid-blocking agents		
POSTOPERATIVE	Protein and energy-rich nutritional supplements	ü	
	Glucose control		
	Multimodal approach to opioid-sparing pain control – consider thoracic epidural analgesia (open surgery) or spinal analgesia (laparoscopic surgery); also NSAIDS and paracetamol	ü	ü
	Multimodal approach to control of nausea and vomiting		
	Prepare for early discharge		

Author, Year: Šerclová 2009[33]	**Reason for Surgery: 78% Crohn's, 9% Ulcerative Colitis, 7% Cancer, 6% Other, only ASA I-II, average age 35**

Phases	ERAS Components	ERAS Protocol	Standard Care Protocol
PREADMISSION	Smoking/alcohol cessation		
	Nutritional screening/support		
	Medical optimization of chronic disease		
PREOPERATIVE	Structured information/patient and caretaker engagement	ü	
	Bowel preparation (no routine use of mechanical bowel prep)	ü	
	Pre-operative fasting (clear fluids to 2 hours and solids to 6 hours before surgery)	ü	
	Carbohydrate treatment	ü	
	Thrombosis prophylaxis		
	Infection prophylaxis and/or skin preparation with chlorhexidine-alcohol		
	Nausea and vomiting prophylaxis		
	Pre-anesthetic sedative medication (no routine use)		
	Minimal invasive surgical techniques		
INTRAOPERATIVE	Standardized anesthesia protocol – may use thoracic epidural blocks with local anesthetics and low-dose opioids for open surgery and spinal analgesia or patient-controlled morphine as alternative to thoracic epidural for laparoscopic surgery		
	Maintain fluid balance; vasopressors for blood pressure control		
	Restrictive use of surgical site drains	ü	
	Remove nasogastric tubes before reversal of anesthesia (and no routine use)	ü	
	Control of body temperature		
POSTOPERATIVE	Early mobilization	ü	
	Early intake of oral fluids and solids	ü	
	Early removal of urinary catheters and intravenous fluids	ü	
	Chewing gum, laxatives, peripheral opioid-blocking agents		
	Protein and energy-rich nutritional supplements		
	Glucose control		
	Multimodal approach to opioid-sparing pain control – consider thoracic epidural analgesia (open surgery) or spinal analgesia (laparoscopic surgery); also NSAIDS and paracetamol	ü	
	Multimodal approach to control of nausea and vomiting		
	Prepare for early discharge		

Author, Year: Khoo 2007[28]	Reason for Surgery: Colon (67%) and Rectal (33%) Cancer		
Phases	**ERAS Components**	**ERAS Protocol**	**Standard Care Protocol**
PREADMISSION	Smoking/alcohol cessation		
	Nutritional screening/support		
	Medical optimization of chronic disease		
PREOPERATIVE	Structured information/patient and caretaker engagement		
	Bowel preparation (no routine use of mechanical bowel prep)		
	Pre-operative fasting (clear fluids to 2 hours and solids to 6 hours before surgery)	**ü (3 hrs)**	**ü (3 hrs)**
	Carbohydrate treatment		
	Thrombosis prophylaxis		
	Infection prophylaxis and/or skin preparation with chlorhexidine-alcohol		
	Nausea and vomiting prophylaxis	**ü**	
	Pre-anesthetic sedative medication (no routine use)		
INTRAOPERATIVE	Minimal invasive surgical techniques		
	Standardized anesthesia protocol – may use thoracic epidural blocks with local anesthetics and low-dose opioids for open surgery and spinal analgesia or patient-controlled morphine as alternative to thoracic epidural for laparoscopic surgery	**ü**	**ü**
	Maintain fluid balance; vasopressors for blood pressure control	**ü**	
	Restrictive use of surgical site drains		
POSTOPERATIVE	Remove nasogastric tubes before reversal of anesthesia (and no routine use)	**ü**	
	Control of body temperature		
	Early mobilization	**ü**	
	Early intake of oral fluids and solids	**ü**	
	Early removal of urinary catheters and intravenous fluids	**ü**	
	Chewing gum, laxatives, peripheral opioid-blocking agents	**ü**	
	Protein and energy-rich nutritional supplements	**ü**	
	Glucose control		
	Multimodal approach to opioid-sparing pain control – consider thoracic epidural analgesia (open surgery) or spinal analgesia (laparoscopic surgery); also NSAIDS and paracetamol	**ü**	
	Multimodal approach to control of nausea and vomiting		
	Prepare for early discharge		

Author, Year: Gatt 2005[24]	**Reason for Surgery: 69% Colon Cancer, 31% Other (Colon)**

Phases	ERAS Components	ERAS Protocol	Standard Care Protocol
PREADMISSION	Smoking/alcohol cessation		
	Nutritional screening/support		
	Medical optimization of chronic disease		
PREOPERATIVE	Structured information/patient and caretaker engagement	ü	
	Bowel preparation (no routine use of mechanical bowel prep)	ü	
	Pre-operative fasting (clear fluids to 2 hours and solids to 6 hours before surgery)	ü **(3 hrs)**	
	Carbohydrate treatment	ü	
	Thrombosis prophylaxis		
	Infection prophylaxis and/or skin preparation with chlorhexidine-alcohol		
	Nausea and vomiting prophylaxis		
	Pre-anesthetic sedative medication (no routine use)		
INTRAOPERATIVE	Minimal invasive surgical techniques		
	Standardized anesthesia protocol – may use thoracic epidural blocks with local anesthetics and low-dose opioids for open surgery and spinal analgesia or patient-controlled morphine as alternative to thoracic epidural for laparoscopic surgery	ü	ü
	Maintain fluid balance; vasopressors for blood pressure control		
	Restrictive use of surgical site drains	ü	
	Remove nasogastric tubes before reversal of anesthesia (and no routine use)	ü	
	Control of body temperature		
	Early mobilization	ü	
	Early intake of oral fluids and solids	ü	
	Early removal of urinary catheters and intravenous fluids		
	Chewing gum, laxatives, peripheral opioid-blocking agents		
POSTOPERATIVE	Protein and energy-rich nutritional supplements		
	Glucose control		
	Multimodal approach to opioid-sparing pain control – consider thoracic epidural analgesia (open surgery) or spinal analgesia (laparoscopic surgery); also NSAIDS and paracetamol	ü	ü
	Multimodal approach to control of nausea and vomiting		
	Prepare for early discharge		

Author, Year: Anderson 2003[22]	Reason for Surgery: 72% Colon Cancer; 28% Other (Colon)

Phases	ERAS Components	ERAS Protocol	Standard Care Protocol
PREADMISSION	Smoking/alcohol cessation		
	Nutritional screening/support		
	Medical optimization of chronic disease		
PREOPERATIVE	Structured information/patient and caretaker engagement	ü	
	Bowel preparation (no routine use of mechanical bowel prep)	ü	
	Pre-operative fasting (clear fluids to 2 hours and solids to 6 hours before surgery)	ü	
	Carbohydrate treatment	ü	
	Thrombosis prophylaxis		
	Infection prophylaxis and/or skin preparation with chlorhexidine-alcohol	ü	ü
	Nausea and vomiting prophylaxis		
	Pre-anesthetic sedative medication (no routine use)		
INTRAOPERATIVE	Minimal invasive surgical techniques		
	Standardized anesthesia protocol – may use thoracic epidural blocks with local anesthetics and low-dose opioids for open surgery and spinal analgesia or patient-controlled morphine as alternative to thoracic epidural for laparoscopic surgery	ü	
	Maintain fluid balance; vasopressors for blood pressure control		
	Restrictive use of surgical site drains	ü	
	Remove nasogastric tubes before reversal of anesthesia (and no routine use)	ü	
	Control of body temperature		
	Early mobilization		
	Early intake of oral fluids and solids	ü	
	Early removal of urinary catheters and intravenous fluids		
	Chewing gum, laxatives, peripheral opioid-blocking agents		
POSTOPERATIVE	Protein and energy-rich nutritional supplements		
	Glucose control		
	Multimodal approach to opioid-sparing pain control – consider thoracic epidural analgesia (open surgery) or spinal analgesia (laparoscopic surgery); also NSAIDS and paracetamol	ü	
	Multimodal approach to control of nausea and vomiting		
	Prepare for early discharge		

Table 2. ERAS and Standard Care Protocol Components – Laparoscopic Surgery Studies

Author, Year: Ota 2017[42] (Standard Care at surgeon's discretion; many components [*] implemented)	**Reason for Surgery: Colon or Rectosigmoid Cancer (90% Laparoscopic Surgery)**		
Phases	**ERAS Components**	**ERAS Protocol**	**Standard Care Protocol**
PREADMISSION	Smoking/alcohol cessation		
	Nutritional screening/support		
	Medical optimization of chronic disease		
PREOPERATIVE	Structured information/patient and caretaker engagement	ü	
	Bowel preparation (no routine use of mechanical bowel prep)	ü[a]	
	Pre-operative fasting (clear fluids to 2 hours and solids to 6 hours before surgery)		
	Carbohydrate treatment	ü	
INTRAOPERATIVE	Thrombosis prophylaxis	ü	
	Infection prophylaxis and/or skin preparation with chlorhexidine-alcohol	ü	*
	Nausea and vomiting prophylaxis		
	Pre-anesthetic sedative medication (no routine use)		
	Minimal invasive surgical techniques	**ü (>90%) laparoscopic)**	**ü (>90% laparoscopic)**
	Standardized anesthesia protocol – may use thoracic epidural blocks with local anesthetics and low-dose opioids for open surgery and spinal analgesia or patient-controlled morphine as alternative to thoracic epidural for laparoscopic surgery	**ü (epidural anesthesia)**	*** (epidural anesthesia)**
	Maintain fluid balance; vasopressors for blood pressure control	ü	*
	Restrictive use of surgical site drains	ü	*
POSTOPERATIVE	Remove nasogastric tubes before reversal of anesthesia (and no routine use)	ü	*
	Control of body temperature		
	Early mobilization	ü	*
	Early intake of oral fluids and solids	ü	
	Early removal of urinary catheters and intravenous fluids	ü	
	Chewing gum, laxatives, peripheral opioid-blocking agents	**ü (gum, laxative)**	*** (laxative)**
	Protein and energy-rich nutritional supplements	ü	
	Glucose control		
	Multimodal approach to opioid-sparing pain control – consider thoracic epidural analgesia (open surgery) or	ü	

	spinal analgesia (laparoscopic surgery); also NSAIDS and paracetamol		
	Multimodal approach to control of nausea and vomiting		
	Prepare for early discharge		

[a] not used for right hemicolectomy or transverse colectomy

Author, Year: Scioscia 2017[43]	**Reason for Surgery: Bowel Endometriosis**		
Phases	**ERAS Components**	**ERAS Protocol**	**Standard Care Protocol**
PREADMISSION	Smoking/alcohol cessation		
	Nutritional screening/support		
	Medical optimization of chronic disease		
PREOPERATIVE	Structured information/patient and caretaker engagement		
	Bowel preparation (no routine use of mechanical bowel prep)	**ü (low residue diet)**	
	Pre-operative fasting (clear fluids to 2 hours and solids to 6 hours before surgery)		
	Carbohydrate treatment		
	Thrombosis prophylaxis		
	Infection prophylaxis and/or skin preparation with chlorhexidine-alcohol		
	Nausea and vomiting prophylaxis		
	Pre-anesthetic sedative medication (no routine use)		
INTRAOPERATIVE	Minimal invasive surgical techniques	**ü (laparoscopic)**	**ü (laparoscopic)**
	Standardized anesthesia protocol – may use thoracic epidural blocks with local anesthetics and low-dose opioids for open surgery and spinal analgesia or patient-controlled morphine as alternative to thoracic epidural for laparoscopic surgery		
	Maintain fluid balance; vasopressors for blood pressure control		
	Restrictive use of surgical site drains		
	Remove nasogastric tubes before reversal of anesthesia (and no routine use)	**ü**	
	Control of body temperature		
	Early mobilization	**ü**	
	Early intake of oral fluids and solids	**ü**	
	Early removal of urinary catheters and intravenous fluids		
	Chewing gum, laxatives, peripheral opioid-blocking agents		
POSTOPERATIVE	Protein and energy-rich nutritional supplements		
	Glucose control		
	Multimodal approach to opioid-sparing pain control – consider thoracic epidural analgesia (open surgery) or spinal analgesia (laparoscopic surgery); also NSAIDS and paracetamol		
	Multimodal approach to control of nausea and vomiting		
	Prepare for early discharge		

Author, Year: Mari 2016[40]	**Reason for Surgery: Major Colorectal Surgery (75% Cancer, 25% Diverticular Disease)**		
Phases	**ERAS Components**	**ERAS Protocol**	**Standard Care Protocol**
PREADMISSION	Smoking/alcohol cessation		
	Nutritional screening/support		
	Medical optimization of chronic disease		
PREOPERATIVE	Structured information/patient and caretaker engagement		
	Bowel preparation (no routine use of mechanical bowel prep)	ü	
	Pre-operative fasting (clear fluids to 2 hours and solids to 6 hours before surgery)	ü	
	Carbohydrate treatment		
	Thrombosis prophylaxis		
	Infection prophylaxis and/or skin preparation with chlorhexidine-alcohol		
	Nausea and vomiting prophylaxis		
	Pre-anesthetic sedative medication (no routine use)		
	Minimal invasive surgical techniques	ü (laparoscopic)	ü (laparoscopic)
INTRAOPERATIVE	Standardized anesthesia protocol – may use thoracic epidural blocks with local anesthetics and low-dose opioids for open surgery and spinal analgesia or patient-controlled morphine as alternative to thoracic epidural for laparoscopic surgery		
	Maintain fluid balance; vasopressors for blood pressure control	ü	
	Restrictive use of surgical site drains	ü	
	Remove nasogastric tubes before reversal of anesthesia (and no routine use)	ü	
	Control of body temperature		
POSTOPERATIVE	Early mobilization	ü	
	Early intake of oral fluids and solids	ü	
	Early removal of urinary catheters and intravenous fluids		
	Chewing gum, laxatives, peripheral opioid-blocking agents		
	Protein and energy-rich nutritional supplements		
	Glucose control		
	Multimodal approach to opioid-sparing pain control – consider thoracic epidural analgesia (open surgery) or spinal analgesia (laparoscopic surgery); also NSAIDS and paracetamol	ü	
	Multimodal approach to control of nausea and vomiting		
	Prepare for early discharge		

Author, Year: Wang 2015[45] (same protocol as Ren 2012[32] except minimally invasive)	**Reason for Surgery: Colon Cancer**		
Phases	**ERAS Components**	**ERAS Protocol**	**Standard Care Protocol**
PREADMISSION	Smoking/alcohol cessation		
	Nutritional screening/support		
	Medical optimization of chronic disease		
PREOPERATIVE	Structured information/patient and caretaker engagement		
	Bowel preparation (no routine use of mechanical bowel prep)	ü	
	Pre-operative fasting (clear fluids to 2 hours and solids to 6 hours before surgery)	ü	
	Carbohydrate treatment	ü	
	Thrombosis prophylaxis		
	Infection prophylaxis and/or skin preparation with chlorhexidine-alcohol	ü	
	Nausea and vomiting prophylaxis	ü	ü
	Pre-anesthetic sedative medication (no routine use)		
	Minimal invasive surgical techniques	ü	ü
INTRAOPERATIVE	Standardized anesthesia protocol – may use thoracic epidural blocks with local anesthetics and low-dose opioids for open surgery and spinal analgesia or patient-controlled morphine as alternative to thoracic epidural for laparoscopic surgery		
	Maintain fluid balance; vasopressors for blood pressure control	ü	
	Restrictive use of surgical site drains		
	Remove nasogastric tubes before reversal of anesthesia (and no routine use)	ü	
	Control of body temperature	ü	
POSTOPERATIVE	Early mobilization	ü	
	Early intake of oral fluids and solids	ü	
	Early removal of urinary catheters and intravenous fluids	**ü (early removal)**	**ü (early removal)**
	Chewing gum, laxatives, peripheral opioid-blocking agents	ü	
	Protein and energy-rich nutritional supplements	ü	
	Glucose control		
	Multimodal approach to opioid-sparing pain control – consider thoracic epidural analgesia (open surgery) or spinal analgesia (laparoscopic surgery); also NSAIDS and paracetamol	ü	
	Multimodal approach to control of nausea and vomiting		
	Prepare for early discharge		

Author, Year: Feng 2014[38]	**Reason for Surgery: Rectal Cancer**		
Phases	**ERAS Components**	**ERAS Protocol**	**Standard Care Protocol**
PREADMISSION	Smoking/alcohol cessation		
	Nutritional screening/support		
	Medical optimization of chronic disease		
PREOPERATIVE	Structured information/patient and caretaker engagement		
	Bowel preparation (no routine use of mechanical bowel prep)	ü	
	Pre-operative fasting (clear fluids to 2 hours and solids to 6 hours before surgery)		
	Carbohydrate treatment	ü	
	Thrombosis prophylaxis		
	Infection prophylaxis and/or skin preparation with chlorhexidine-alcohol		
	Nausea and vomiting prophylaxis		
	Pre-anesthetic sedative medication (no routine use)		
INTRAOPERATIVE	Minimal invasive surgical techniques	ü	ü
	Standardized anesthesia protocol – may use thoracic epidural blocks with local anesthetics and low-dose opioids for open surgery and spinal analgesia or patient-controlled morphine as alternative to thoracic epidural for laparoscopic surgery	ü	ü
	Maintain fluid balance; vasopressors for blood pressure control		
	Restrictive use of surgical site drains	ü	
	Remove nasogastric tubes before reversal of anesthesia (and no routine use)		
	Control of body temperature	ü	
	Early mobilization	ü	
	Early intake of oral fluids and solids	ü	
	Early removal of urinary catheters and intravenous fluids	ü	
	Chewing gum, laxatives, peripheral opioid-blocking agents		
POSTOPERATIVE	Protein and energy-rich nutritional supplements	ü	
	Glucose control		
	Multimodal approach to opioid-sparing pain control – consider thoracic epidural analgesia (open surgery) or spinal analgesia (laparoscopic surgery); also NSAIDS and paracetamol	ü	
	Multimodal approach to control of nausea and vomiting		
	Prepare for early discharge		

Author, Year: Mari 2014[41]	**Reason for Surgery: 69% Colon Cancer, 31% Diverticular Disease**

Phases	ERAS Components	ERAS Protocol	Standard Care Protocol
PREADMISSION	Smoking/alcohol cessation		
	Nutritional screening/support		
	Medical optimization of chronic disease		
PREOPERATIVE	Structured information/patient and caretaker engagement		
	Bowel preparation (no routine use of mechanical bowel prep)		
	Pre-operative fasting (clear fluids to 2 hours and solids to 6 hours before surgery)		
	Carbohydrate treatment	ü	
	Thrombosis prophylaxis		
	Infection prophylaxis and/or skin preparation with chlorhexidine-alcohol	ü	ü
	Nausea and vomiting prophylaxis		
	Pre-anesthetic sedative medication (no routine use)		
	Minimal invasive surgical techniques	ü	ü
INTRAOPERATIVE	Standardized anesthesia protocol – may use thoracic epidural blocks with local anesthetics and low-dose opioids for open surgery and spinal analgesia or patient-controlled morphine as alternative to thoracic epidural for laparoscopic surgery	ü	
	Maintain fluid balance; vasopressors for blood pressure control	ü	
	Restrictive use of surgical site drains		
	Remove nasogastric tubes before reversal of anesthesia (and no routine use)	ü	
	Control of body temperature	ü	ü
POSTOPERATIVE	Early mobilization	ü	
	Early intake of oral fluids and solids	ü	
	Early removal of urinary catheters and intravenous fluids	ü	
	Chewing gum, laxatives, peripheral opioid-blocking agents		
	Protein and energy-rich nutritional supplements	ü	
	Glucose control		
	Multimodal approach to opioid-sparing pain control – consider thoracic epidural analgesia (open surgery) or spinal analgesia (laparoscopic surgery); also NSAIDS and paracetamol	ü	ü
	Multimodal approach to control of nausea and vomiting		
	Prepare for early discharge		

Author, Year: Gouvas 2012[25]	**Reason for Surgery (Open and Laparoscopic): Rectal Cancer**		
Phases	**ERAS Components**	**ERAS Protocol**	**Standard Care Protocol**
PREADMISSION	Smoking/alcohol cessation		
	Nutritional screening/support		
	Medical optimization of chronic disease		
PREOPERATIVE	Structured information/patient and caretaker engagement	ü	
	Bowel preparation (no routine use of mechanical bowel prep)		
	Pre-operative fasting (clear fluids to 2 hours and solids to 6 hours before surgery)	ü	
	Carbohydrate treatment	ü	
	Thrombosis prophylaxis		
	Infection prophylaxis and/or skin preparation with chlorhexidine-alcohol		
	Nausea and vomiting prophylaxis		
	Pre-anesthetic sedative medication (no routine use)		
INTRAOPERATIVE	Minimal invasive surgical techniques **(laparoscopic arms only)**	ü	ü
	Standardized anesthesia protocol – may use thoracic epidural blocks with local anesthetics and low-dose opioids for open surgery and spinal analgesia or patient-controlled morphine as alternative to thoracic epidural for laparoscopic surgery	ü	ü
	Maintain fluid balance; vasopressors for blood pressure control	ü	
	Restrictive use of surgical site drains		
	Remove nasogastric tubes before reversal of anesthesia (and no routine use)	ü **(removal)**	
	Control of body temperature	ü	
	Early mobilization	ü	
	Early intake of oral fluids and solids	ü	
	Early removal of urinary catheters and intravenous fluids		
	Chewing gum, laxatives, peripheral opioid-blocking agents		
POSTOPERATIVE	Protein and energy-rich nutritional supplements	ü	
	Glucose control		
	Multimodal approach to opioid-sparing pain control – consider thoracic epidural analgesia (open surgery) or spinal analgesia (laparoscopic surgery); also NSAIDS and paracetamol	ü	
	Multimodal approach to control of nausea and vomiting		
	Prepare for early discharge	ü	

Author, Year: Wang 2012[35] and Wang 2012[44]	Reason for Surgery: Colon Cancer NOTE: Wang 2012[35] – Open and Laparoscopic

Phases	ERAS Components	ERAS Protocol	Standard Care Protocol
PREADMISSION	Smoking/alcohol cessation		
	Nutritional screening/support		
	Medical optimization of chronic disease		
PREOPERATIVE	Structured information/patient and caretaker engagement	ü	
	Bowel preparation (no routine use of mechanical bowel prep)	ü	
	Pre-operative fasting (clear fluids to 2 hours and solids to 6 hours before surgery)	ü	
	Carbohydrate treatment	ü	
	Thrombosis prophylaxis		
	Infection prophylaxis and/or skin preparation with chlorhexidine-alcohol		
	Nausea and vomiting prophylaxis		
	Pre-anesthetic sedative medication (no routine use)		
	Minimal invasive surgical techniques (laparoscopic arms only)	ü	ü
INTRAOPERATIVE	Standardized anesthesia protocol – may use thoracic epidural blocks with local anesthetics and low-dose opioids for open surgery and spinal analgesia or patient-controlled morphine as alternative to thoracic epidural for laparoscopic surgery	ü	
	Maintain fluid balance; vasopressors for blood pressure control	ü	
	Restrictive use of surgical site drains	ü	
	Remove nasogastric tubes before reversal of anesthesia (and no routine use)	ü	
	Control of body temperature		
POSTOPERATIVE	Early mobilization	ü	
	Early intake of oral fluids and solids	ü	
	Early removal of urinary catheters and intravenous fluids	ü	
	Chewing gum, laxatives, peripheral opioid-blocking agents		
	Protein and energy-rich nutritional supplements		
	Glucose control		
	Multimodal approach to opioid-sparing pain control – consider thoracic epidural analgesia (open surgery) or spinal analgesia (laparoscopic surgery); also NSAIDS and paracetamol	ü	
	Multimodal approach to control of nausea and vomiting		
	Prepare for early discharge		

Author, Year: Wang 2012[46]	Reason for Surgery: Colorectal Cancer		
Phases	**ERAS Components**	**ERAS Protocol**	**Standard Care Protocol**
PREADMISSION	Smoking/alcohol cessation		
	Nutritional screening/support		
	Medical optimization of chronic disease		
PREOPERATIVE	Structured information/patient and caretaker engagement		
	Bowel preparation (no routine use of mechanical bowel prep)	ü	
	Pre-operative fasting (clear fluids to 2 hours and solids to 6 hours before surgery)		
	Carbohydrate treatment	ü	
	Thrombosis prophylaxis		
	Infection prophylaxis and/or skin preparation with chlorhexidine-alcohol		ü
	Nausea and vomiting prophylaxis		
	Pre-anesthetic sedative medication (no routine use)		
INTRAOPERATIVE	Minimal invasive surgical techniques	ü	ü
	Standardized anesthesia protocol – may use thoracic epidural blocks with local anesthetics and low-dose opioids for open surgery and spinal analgesia or patient-controlled morphine as alternative to thoracic epidural for laparoscopic surgery	ü	
	Maintain fluid balance; vasopressors for blood pressure control	ü	
	Restrictive use of surgical site drains		
	Remove nasogastric tubes before reversal of anesthesia (and no routine use)	ü (removal)	
	Control of body temperature		
	Early mobilization	ü	
	Early intake of oral fluids and solids	ü	
	Early removal of urinary catheters and intravenous fluids	ü	
	Chewing gum, laxatives, peripheral opioid-blocking agents	ü	
POSTOPERATIVE	Protein and energy-rich nutritional supplements		
	Glucose control		
	Multimodal approach to opioid-sparing pain control – consider thoracic epidural analgesia (open surgery) or spinal analgesia (laparoscopic surgery); also NSAIDS and paracetamol		
	Multimodal approach to control of nausea and vomiting		
	Prepare for early discharge		

Author, Year: Vlug 2011[34]	Reason for Surgery (Open and Laparoscopic): Colon Cancer		
Phases	**ERAS Components**	**ERAS Protocol**	**Standard Care Protocol**
PREADMISSION	Smoking/alcohol cessation		
	Nutritional screening/support		
	Medical optimization of chronic disease		
PREOPERATIVE	Structured information/patient and caretaker engagement	ü	
	Bowel preparation (no routine use of mechanical bowel prep)	ü	ü
	Pre-operative fasting (clear fluids to 2 hours and solids to 6 hours before surgery)	ü	
	Carbohydrate treatment	ü	
	Thrombosis prophylaxis		
	Infection prophylaxis and/or skin preparation with chlorhexidine-alcohol		
	Nausea and vomiting prophylaxis	ü	
	Pre-anesthetic sedative medication (no routine use)	ü	
	Minimal invasive surgical techniques (laparoscopic arms only)	ü	ü
	Standardized anesthesia protocol – may use thoracic epidural blocks with local anesthetics and low-dose opioids for open surgery and spinal analgesia or patient-controlled morphine as alternative to thoracic epidural for laparoscopic surgery	**ü (and general anesthesia)**	**ü (and general anesthesia)**
INTRAOPERATIVE	Maintain fluid balance; vasopressors for blood pressure control	ü	
	Restrictive use of surgical site drains	ü	ü
	Remove nasogastric tubes before reversal of anesthesia (and no routine use)	ü	ü
	Control of body temperature	ü	ü
POSTOPERATIVE	Early mobilization	ü	
	Early intake of oral fluids and solids	ü	
	Early removal of urinary catheters and intravenous fluids	ü	
	Chewing gum, laxatives, peripheral opioid-blocking agents	ü	
	Protein and energy-rich nutritional supplements	ü	
	Glucose control		
	Multimodal approach to opioid-sparing pain control – consider thoracic epidural analgesia (open surgery) or spinal analgesia (laparoscopic surgery); also NSAIDS and paracetamol	ü	ü
	Multimodal approach to control of nausea and vomiting		

Table 3. ERAS and Standard Care Protocol Components - Open and Laparoscopic Surgery Studies

Author, Year: Forsmo 2016[50]	**Reason for Surgery: Colorectal Surgery (Malignant [79%] or Benign [21%]) (Open [60%] or Laparoscopic [40%] Surgery)**		
Phases	**ERAS Components**	**ERAS Protocol**	**Standard Care Protocol**
PREADMISSION	Smoking/alcohol cessation		
	Nutritional screening/support		
	Medical optimization of chronic disease		
	Structured information/patient and caretaker engagement	**ü**	
PREOPERATIVE	Bowel preparation (no routine use of mechanical bowel prep)		
	Pre-operative fasting (clear fluids to 2 hours and solids to 6 hours before surgery)	**ü**	**ü (fluids to 2 hrs)**
	Carbohydrate treatment	**ü**	
	Thrombosis prophylaxis	**ü**	**ü**
	Infection prophylaxis and/or skin preparation with chlorhexidine-alcohol	**ü**	**ü**
INTRAOPERATIVE	Nausea and vomiting prophylaxis		
	Pre-anesthetic sedative medication (no routine use)	**ü**	
	Minimal invasive surgical techniques		
	Standardized anesthesia protocol – may use thoracic epidural blocks with local anesthetics and low-dose opioids for open surgery and spinal analgesia or patient-controlled morphine as alternative to thoracic epidural for laparoscopic surgery	**unclear**	**unclear**
	Maintain fluid balance; vasopressors for blood pressure control	**ü**	
	Restrictive use of surgical site drains	**ü (no drain for colon resection)**	**ü (no drain for colon resection)**
	Remove nasogastric tubes before reversal of anesthesia (and no routine use)	**ü**	**ü**
	Control of body temperature	**ü**	**ü**
POSTOPERATIVE	Early mobilization	**ü (enforced)**	**ü**
	Early intake of oral fluids and solids	**ü (enforced)**	**ü**
	Early removal of urinary catheters and intravenous fluids	**ü**	
	Chewing gum, laxatives, peripheral opioid-blocking agents	**ü**	
	Protein and energy-rich nutritional supplements		
	Glucose control		
	Multimodal approach to opioid-sparing pain control – consider thoracic epidural analgesia (open surgery) or spinal analgesia (laparoscopic surgery); also NSAIDS and paracetamol	**ü**	
	Multimodal approach to control of nausea and vomiting		
	Prepare for early discharge		

APPENDIX F. EVIDENCE PROFILE FOR ERAS COMPARED TO CONTROL FOR COLORECTAL SURGERIES

Quality assessment							№ of patients		Effect		Quality
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**ERAS**	**Control**	**Relative (95% CI)**	**Absolute (95% CI)**	
Length of stay											
21	randomized trials	serious [a]	serious [b]	not serious	not serious	strong association	1463	1470	-	MD **2.4 days lower** (3.1 lower to 1.8 lower)	⊕⊕⊕◯ MODERATE
Mortality											
22	randomized trials	serious [a]	not serious	not serious	serious [c]	none	16/1619 (1.0%)	9/1636 (0.6%)	**OR 1.79** (0.81 to 3.95)	**4 more per 1,000** (from 1 fewer to 16 more)	⊕⊕◯◯ LOW
Perioperative morbidity											
19	randomized trials	serious [a]	not serious	not serious	not serious	none	299/1456 (20.5%)	426/1463 (29.1%)	**RR 0.66** (0.54 to 0.80)	**99 fewer per 1,000** (from 58 fewer to 134 fewer)	⊕⊕⊕◯ MODERATE
Readmissions											
19	randomized trials	serious [a]	not serious	not serious	serious [d]	none	73/1196 (6.1%)	84/1319 (6.4%)	**RR 1.11** (0.82 to 1.50)	**7 more per 1,000** (from 11 fewer to 32 more)	⊕⊕◯◯ LOW
Surgical site infection											
17	randomized trials	serious [a]	not serious	not serious	serious [d]	none	50/1443 (3.5%)	69/1437 (4.8%)	**RR 0.75** (0.52 to 1.07)	**12 fewer per 1,000** (from 3 more to 23 fewer)	⊕⊕◯◯ LOW

CI: Confidence interval; **MD:** Mean difference; **RR:** Risk ratio; **OR:** Odds ratio

Explanations

a. Mostly moderate, high, or unclear RoB

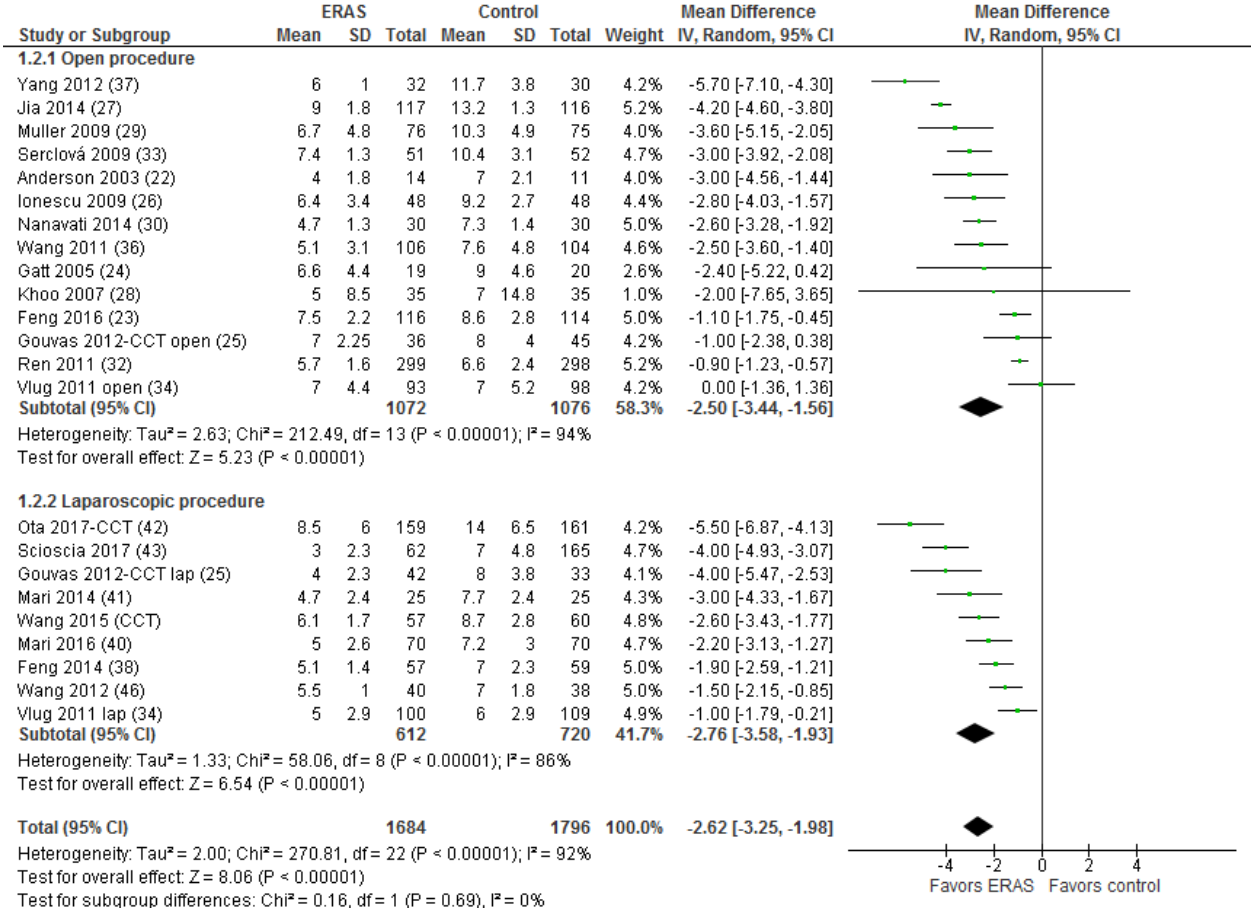
b. I-square indicated substantial statistical heterogeneity

c. Wide confidence intervals and very few events

d. Wide confidence intervals

APPENDIX G. POOLED ANALYSES BY PROCEDURE AND COLORECTAL CONDITION

Figure 1. Length of Stay by Procedure[a]



[a]Excludes Forsmo 2016[50] (mixed open and laparoscopic surgery)

Figure 2. Length of Stay by Condition

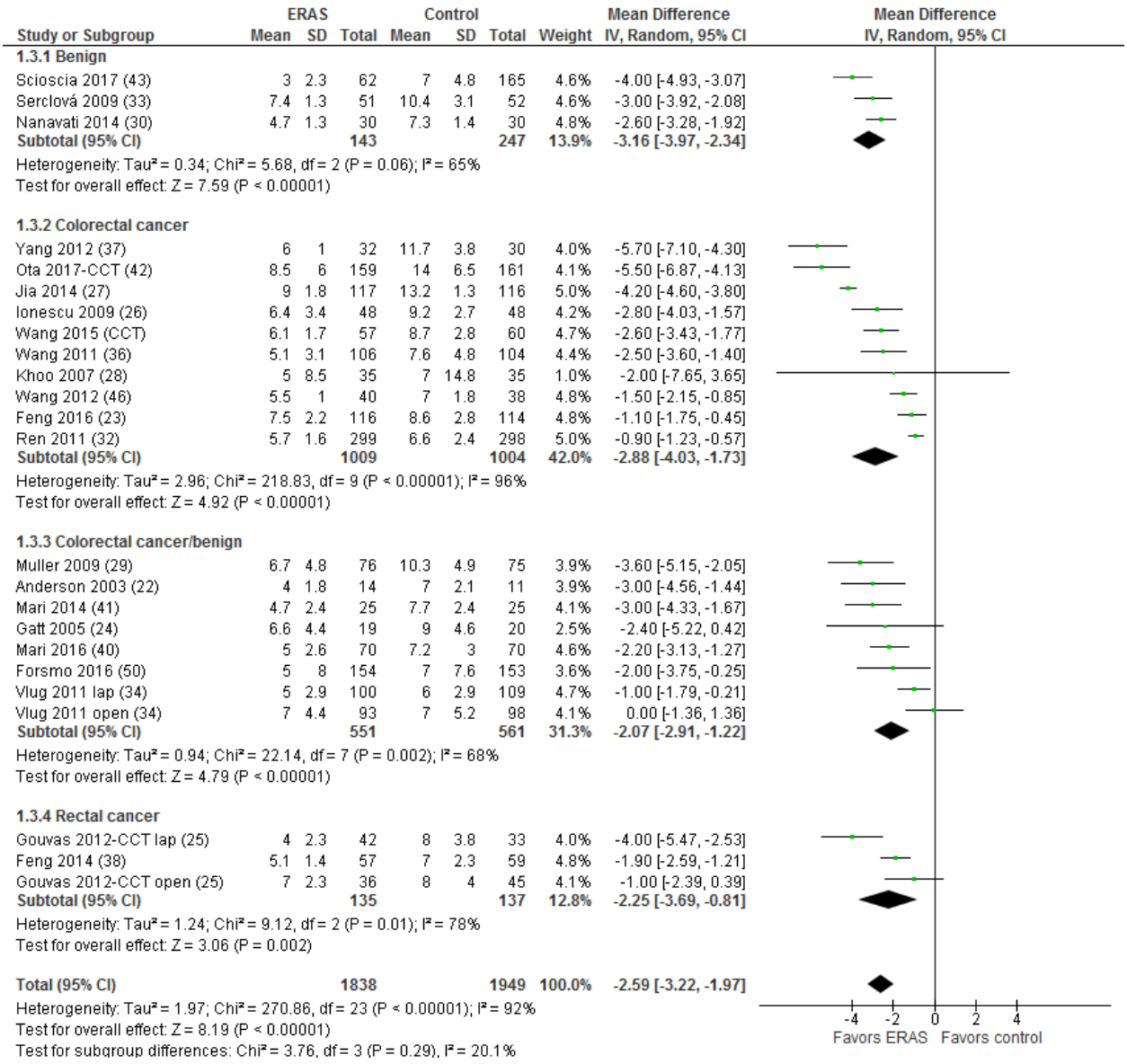
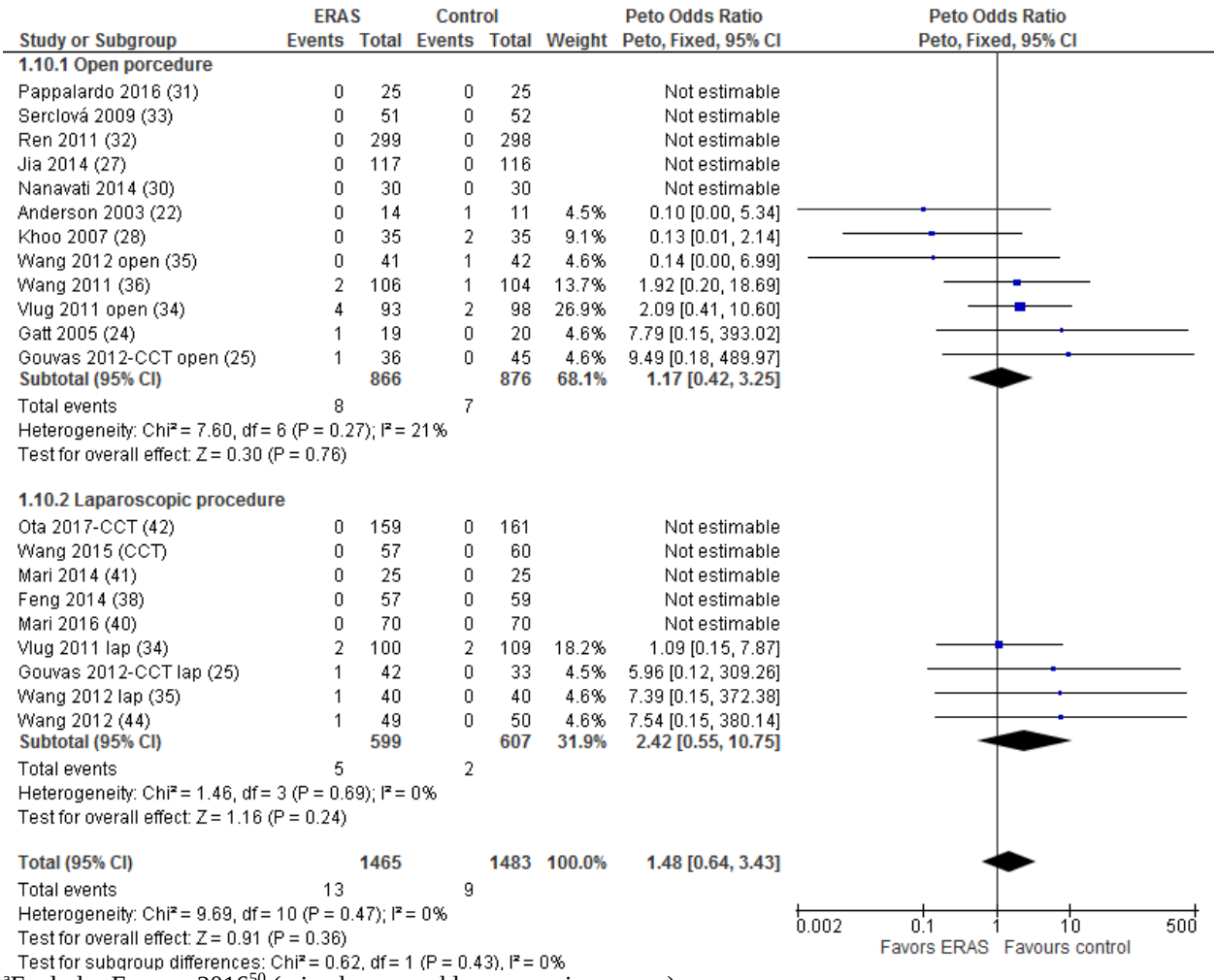


Figure 3. Mortality by Procedure[a]



[a]Excludes Forsmo 2016[50] (mixed open and laparoscopic surgery)

Figure 4. Mortality by Condition

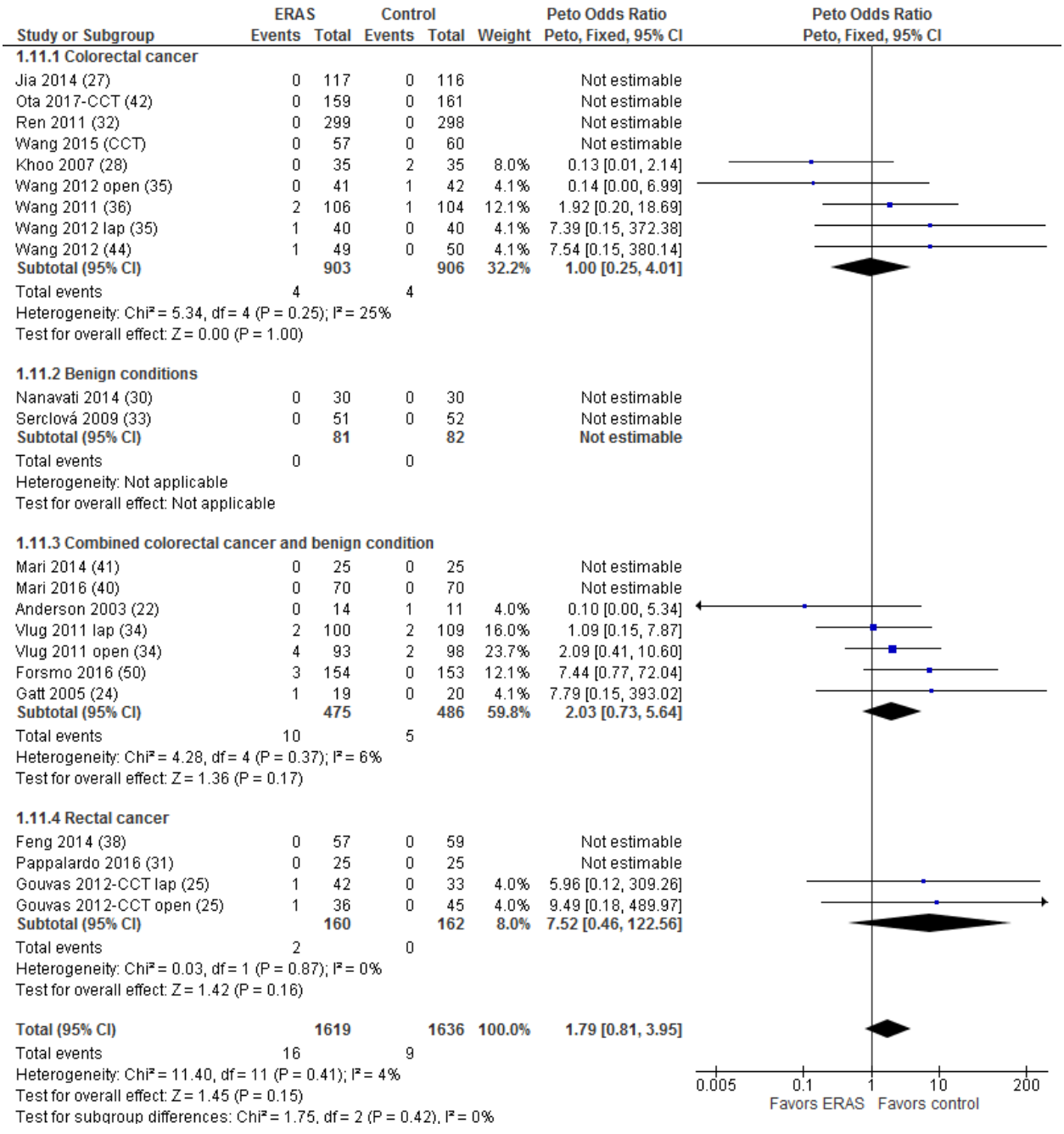
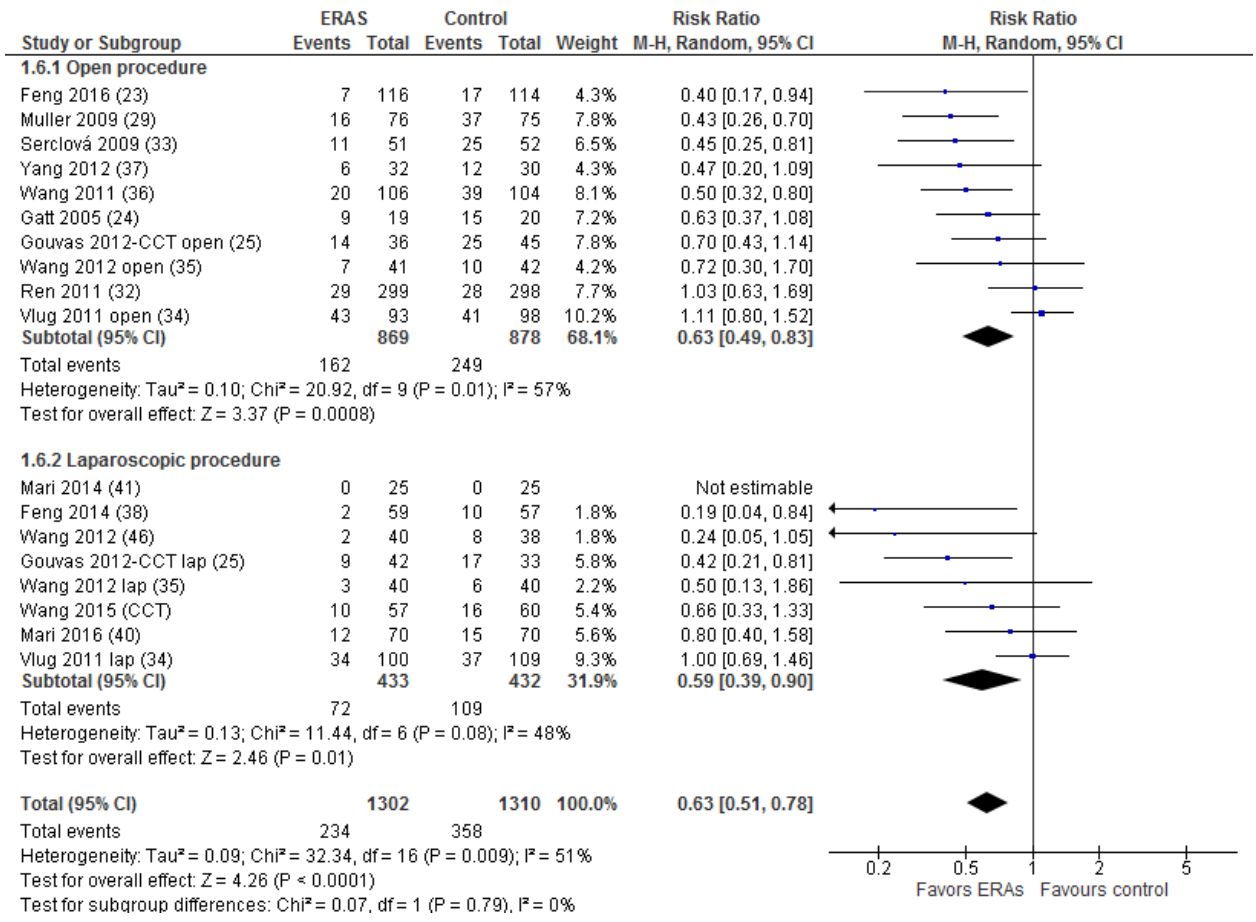


Figure 5. Morbidity by Procedure[a]



[a]Excludes Forsmo 2016[50] (mixed open and laparoscopic surgery)

Figure 6. Morbidity by Condition

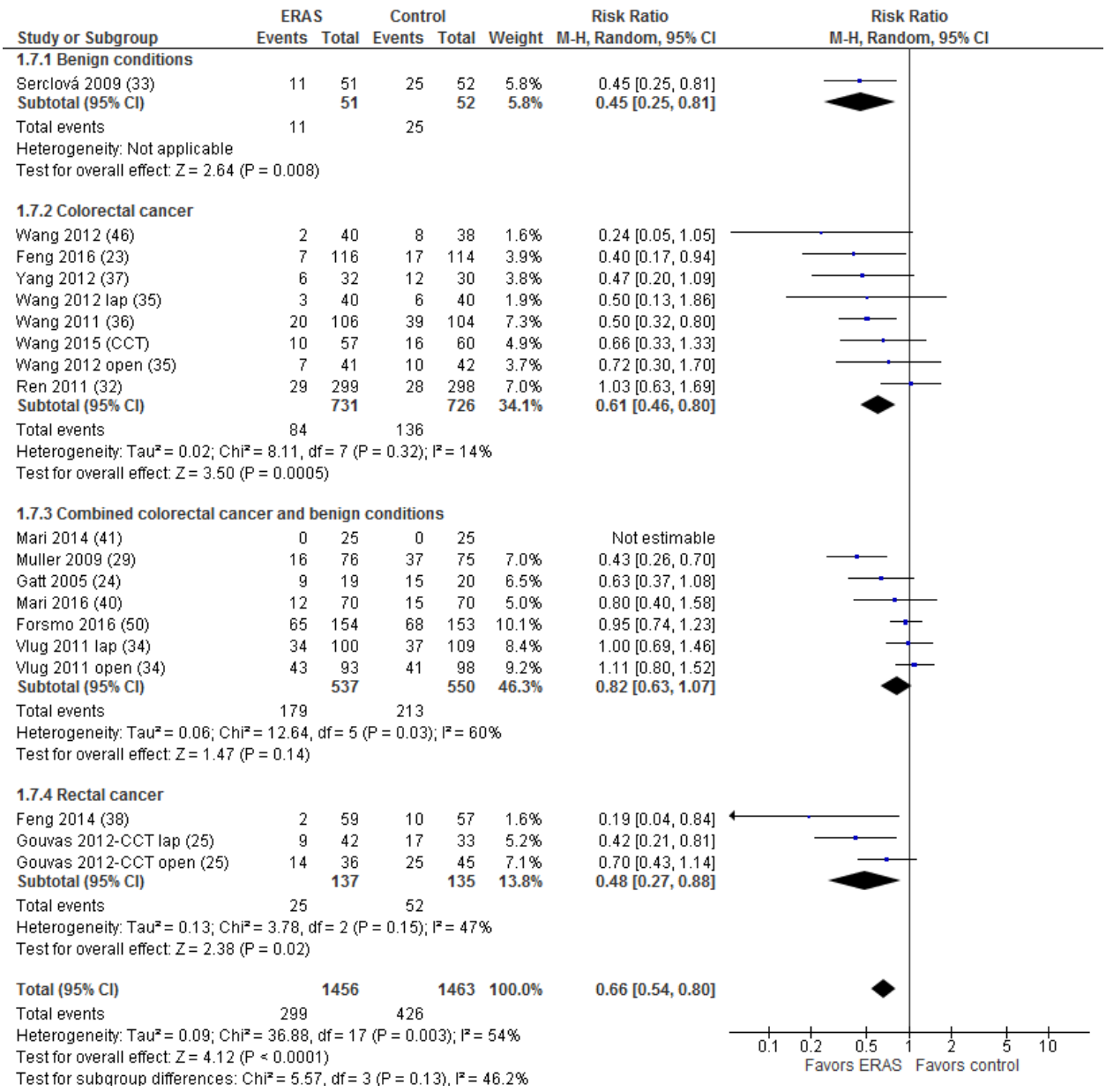
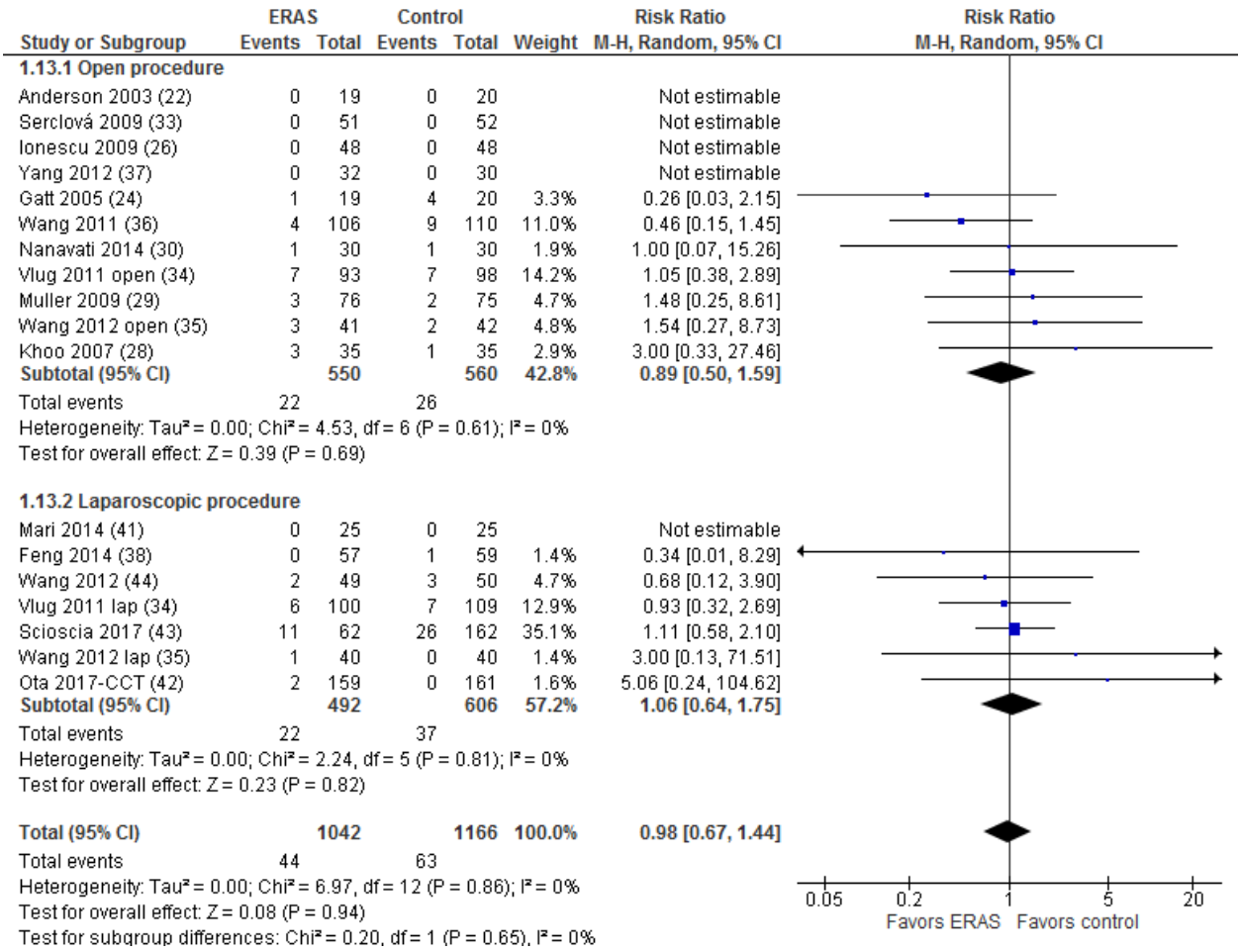


Figure 7. Readmissions by Procedure[a]



[a]Excludes Forsmo 2016[50] (mixed open and laparoscopic surgery)

Figure 8. Readmissions by Condition

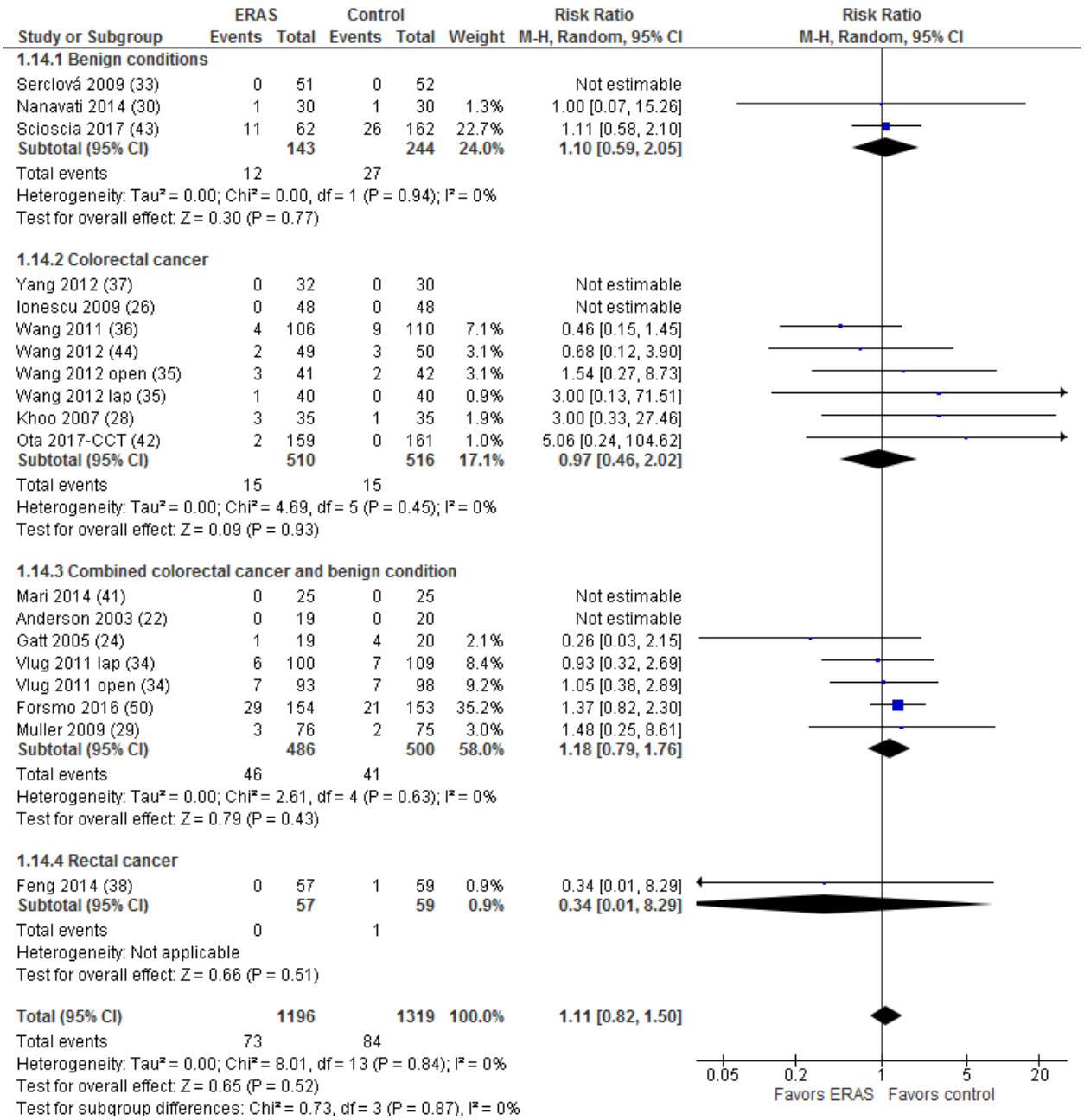
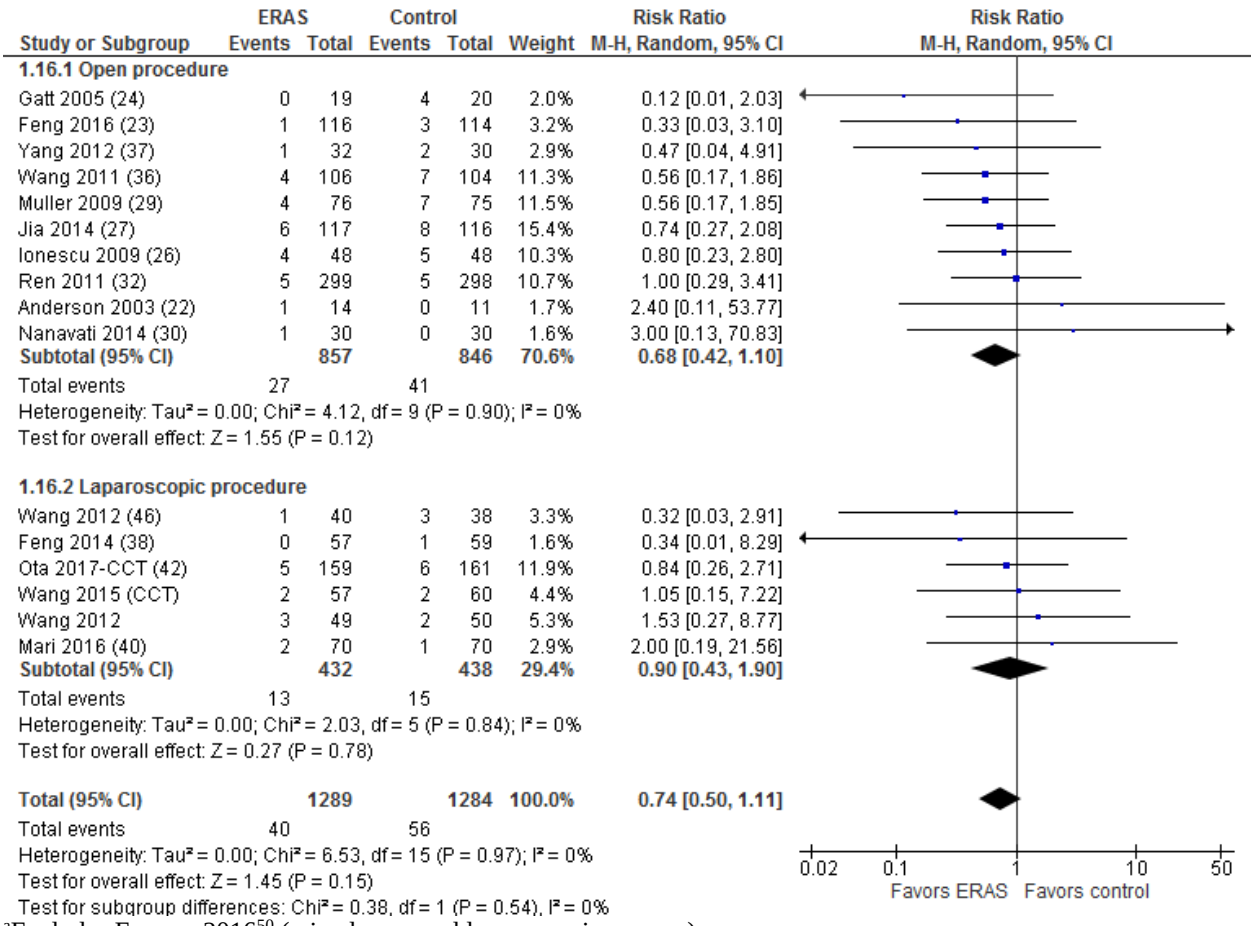


Figure 9. Surgical Site Infections by Procedure[a]



[a]Excludes Forsmo 2016[50] (mixed open and laparoscopic surgery)

Figure 10. Surgical Site Infections by Condition