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Enhanced Recovery Protocols for Adults Undergoing Colorectal Surgery: A Systematic Review and Meta-analysis

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BACKGROUND: Enhanced surgical recovery protocols are designed to reduce hospital length of stay and health care costs.

OBJECTIVE: This study aims to systematically review and summarize evidence from randomized and controlled clinical trials comparing enhanced recovery protocols versus usual care in adults undergoing elective colorectal surgery with emphasis on recent trials, protocol components, and subgroups for surgical approach and colorectal condition.

DATA SOURCES: MEDLINE from 2011 to July 2017; reference lists of existing systematic reviews and included studies were reviewed to identify all eligible trials published before 2011.

STUDY SELECTION: English language trials comparing a protocol of preadmission, preoperative, intraoperative, and postoperative components with usual care in adults undergoing elective colorectal surgery were selected.

INTERVENTION: The enhanced recovery protocol for colorectal surgery was investigated.

MAIN OUTCOME MEASURES: Length of stay, perioperative morbidity, mortality, readmission within 30 days, and surgical site infection were the primary outcomes measured.

RESULTS: Twenty-five trials of open or laparoscopic surgery for cancer or noncancer conditions were included. Enhanced recovery protocols consisted of 4 to 18 components. Few studies fully described the various components. Length of stay (mean reduction, 2.6 days; 95% CI, –3.2 to –2.0) and risk of overall perioperative morbidity (risk ratio, 0.66; 95% CI, 0.54–0.80) were lower in enhanced recovery protocol groups than in usual care groups (moderate-quality evidence). All-cause mortality (rare), readmissions, and surgical site infection rates were similar between protocol groups (low-quality evidence).

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In predefined subgroup analyses, findings did not vary by surgical approach (open vs laparoscopic) or colorectal condition.

LIMITATIONS: Protocols varied across studies and little information was provided regarding compliance with, or implementation of, specific protocol components.

CONCLUSIONS: Enhanced recovery protocols for adults undergoing colorectal surgery improve patient outcomes with no increase in adverse events. Evidence was insufficient regarding which components, or component combinations, are key to improving patient outcomes. PROSPERO registration number: CRD42017067991.

KEY WORDS: Colorectal surgery; Enhanced recovery; Patient outcomes; Systematic review.

Enhanced recovery protocols, also referred to as enhanced recovery after surgery, enhanced recovery programs, or fast-track rehabilitation, are multimodal perioperative management pathways designed to enhance early recovery after surgery and improve patient outcomes. Enhanced recovery protocols are associated with earlier hospital discharge and reduced health care costs without increased complications or hospital readmissions in comparison with standard care.[1–3] Most protocols consist of elements targeting preadmission education or management and perioperative, intraoperative, and postoperative care. Although there are guidelines for implementing an enhanced recovery protocol for colorectal surgery,[2,4] variation in the number and definition of protocol components, as well as variation in the criteria for adherence, contributes to difficulties in determining which components are most important for improving patient outcomes.

Although not limited to colorectal surgery, the largest body of evidence for the comparative effectiveness of enhanced recovery protocols is available for elective colorectal surgery in adults.[2] Accordingly, on nomination of this topic to the Department of Veterans Affairs (VA) Evidence-based Synthesis Program, we followed an a priori protocol completing a comprehensive systematic review of randomized controlled trials (RCTs) and controlled clinical trials (CCTs) evaluating the comparative effectiveness and harms of enhanced recovery protocols versus usual care (as defined by the study authors) in elective colorectal surgery in adults. We build on existing systematic reviews on this topic by including recent trials and reporting results by type of surgery (open or laparoscopic), colorectal condition (cancer or noncancer), and adherence to an enhanced recovery protocol. We assessed quality of evidence for critical, patient-important outcomes. The topic was nominated with the intent to guide potential standardized protocols for enhanced recovery after surgery within the Veterans Health Administration (VHA).

MATERIALS AND METHODS

Our protocol was prospectively registered in PROSPERO (CRD42017067991).

Data Sources

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 for enhanced recovery protocols (eg, fast track, multimodal, accelerated, enhanced) and terms for colorectal surgery (both open and laparoscopic) (Supplemental Table 1, http://links.lww.com/DCR/A677). We also searched reference lists of existing systematic reviews and included studies to identify all eligible trials published before 2011.

Study Selection

Identified abstracts were independently reviewed by 2 researchers. Full-text review of potentially eligible studies was completed by 1 researcher with input from other investigators. We included RCTs or concurrent CCTs comparing a protocol of preadmission, preoperative, intraoperative, and postoperative components with a usual care protocol (as defined by study authors) in adults undergoing any elective colorectal surgery. We excluded studies that compared laparoscopic and open surgery within an enhanced recovery protocol, studies with historical controls, trials of a single component of enhanced recovery, and studies that included only postoperative care components (often referred to as "postoperative rehabilitation" or "controlled rehabilitation").

Data Extraction and Synthesis

For studies that met inclusion criteria, we used structured forms to extract data on patient characteristics, study setting, components of care included in the enhanced recovery and usual care protocols, and patient outcomes. Data were extracted by 1 author and verified by another. We categorized outcomes of interest as health-related outcomes (eg, length of stay, overall morbidity, mortality, readmission rate, ileus, clinically important difference in pain scores, and clinically meaningful changes in quality of life), intermediate outcomes (eg, return of bowel function, intravenous fluid administration, early patient mobilization, and pain scale scores), and harms (eg, surgical site infection, anastomotic leakage, cardiovascular or respiratory complications, urinary tract infection, need for reoperation, bleeding, and Foley catheter reinsertion and complications). Our analysis included overall comparative effectiveness and harms of enhanced recovery versus usual

care and prespecified subgroup analyses to assess whether effectiveness and harms varied by surgical approach (open or laparoscopic), colorectal condition (colorectal cancer, rectal cancer, colorectal cancer or benign conditions, or benign conditions alone), or fidelity to an enhanced recovery protocol.

We assessed risk of bias using a modified Cochrane approach considering sequence generation, allocation, blinding, incomplete outcome reporting, and selective outcome reporting. We rated risk of bias of each study as high, medium, low, or unclear.[5]

Data for critical outcomes (length of stay, mortality, morbidity, readmissions, and surgical site infections) were pooled and analyzed using DerSimonian and Laird random-effects models in Cochrane Collaboration Review Manager software.[6] We calculated weighted mean differences for length of stay and risk ratios (RRs) for overall morbidity, all-cause mortality, readmissions, and surgical site infections. Peto ORs were applied when events were rare, such as mortality. Heterogeneity between studies was assessed by using the I^2 test, with values greater than 50% considered substantial.[7] 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 et al.[8]

Quality of evidence for critical outcomes was evaluated using GRADE methodology (GRADEpro 2015 accessed at www.gradepro.org). The following domains were considered: 1) risk of bias; 2) consistency; 3) directness; and 4) precision. The quality of evidence was rated as high (ie, high confidence that the true effect lies close to that of the estimate of the effect) to very low (ie, very little confidence in the effect estimate and that the true effect is likely to be substantially different from the estimate of effect) on a per outcome basis.

RESULTS

After removing duplicate citations, we reviewed 1789 abstracts and 160 full-text articles (Fig. 1). After excluding 139 articles, we included 21. From existing systematic reviews, we identified 6 additional trials published before the dates of our literature search resulting in inclusion of 27 articles reporting results from 25 trials.[9–35]

Overview of Included Studies

Among the 25 trials, 13 RCTs of open surgery compared an enhanced recovery protocol with a usual care protocol,[9–11,13–20,23,24] 8 (6 RCTs, 2 CCTs) compared protocols in patients undergoing laparoscopic surgery,[25–33] and 3 (2 RCTs, 1 CCT) included 4 groups of patients providing

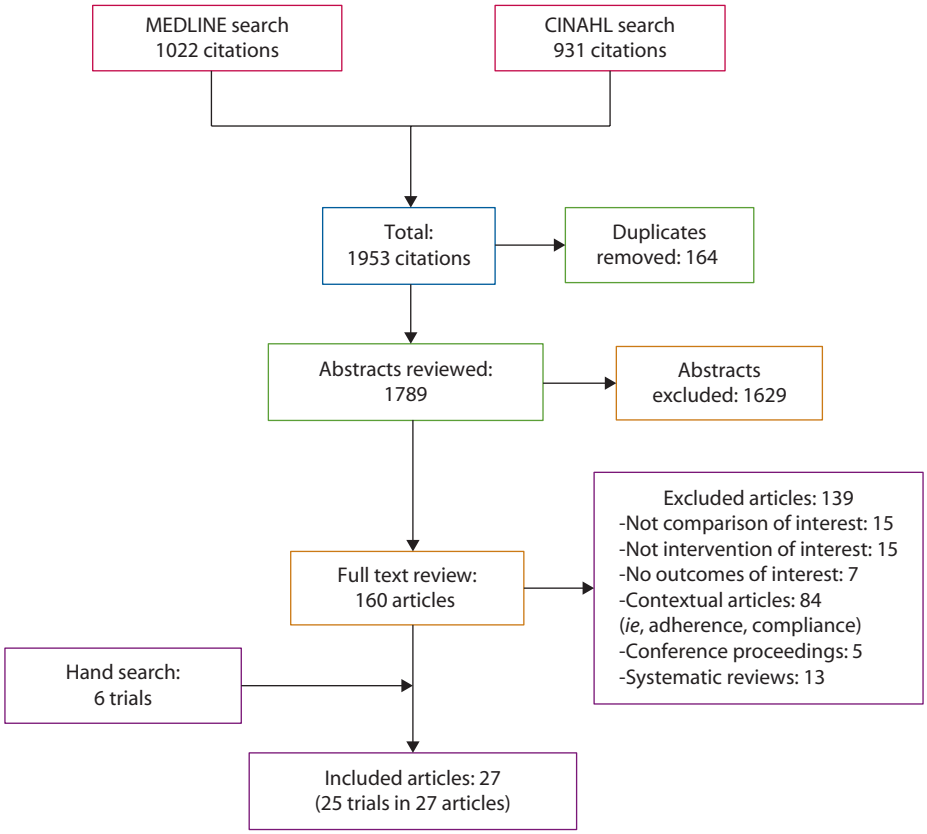


FIGURE 1. Literature flow chart.

comparisons of enhanced recovery and usual care for both open and laparoscopic surgery.[12,21,22] One additional RCT included both open and laparoscopic surgery with the surgeon deciding the surgical approach.[34,35] None of the trials was conducted in the United States. There were 10 trials from China,[10,14,19,22,25,31–33] 10 from Europe,[12,13,16,18,20,21,27,28,30,35] 3 from the United Kingdom,[9,11,15] 1 from Japan,[29] and 1 from India.[17] There were 12 trials of patients with colorectal cancer,[10,13-15,19,22-24,29,31-33] 7 trials of patients with either colorectal cancer or benign conditions,[9,11,16,21,27,28,35] 3 trials of patients with rectal cancer,[12,18,25] and 3 trials of patients with noncancerous colorectal conditions.[17,20,30] We rated 5 studies at low risk of bias, 8 studies at medium risk of bias, 4 studies at high risk of bias, and 7 studies at unclear risk of bias because methods of sequence generation, allocation concealment, and blinding were often not reported. Additional study characteristics and risk of bias assessments are reported in Supplemental Table 2 (http://links.lww.com/DCR/A678).

Enhanced Recovery Protocols

For each study, we charted the enhanced recovery protocol components specified for the enhanced recovery group and for the usual care group using protocols published by the Enhanced Recovery After Surgery (ERAS) Society (Table 1) as a guide.[2,4] The ERAS protocol includes 26 components: 3 preadmission, 8 preoperative, 6 intraoperative, and 9 postoperative. Overall, enhanced recovery group protocols included between 4 and 17 enhanced recovery components, whereas standard care group protocols included between 0 and 10 components. No study included preadmission components (Table 1). The most common preoperative components in the enhanced recovery protocols were carbohydrate treatment, no routine use of bowel preparation, and preoperative fasting. The most common intraoperative components were early removal of nasogastric tubes, standardized anesthesia protocols, and restrictive use of surgical site drains. Postoperatively, the most common components were early mobilization, early intake of oral fluids and solids, and a multimodal approach to opioid-sparing pain control. In the standard care protocols, the most commonly included enhanced recovery components were standardized anesthesia protocols, infection prophylaxis, and multimodal approach to pain control. Authors rarely described specific component implementation or what defined successful adherence to a specific component. Charting of the components highlighted the variation in enhanced recovery protocols im-

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 preparation)	16	2
	Preoperative 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
	Preanesthetic sedative medication (no routine use)	3	0
Intraoperative	Minimally 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
Postoperative	Early mobilization	22	4
	Early intake of oral fluids and solids	23	1
	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

ERAS = enhanced recovery after surgery; Lap = laparoscopic surgery; NSAID = nonsteroidal anti-inflammatory drug.

plemented; in practice, there is not a single ERAS protocol, and many items included in the ERAS Society protocol are absent from the implemented protocols.

Outcomes

Outcomes are summarized in Supplemental Table 3 (http://links.lww.com/DCR/A679) (with complete data available in the full evidence report (http://www.hsrd.research.va.gov/publications/esp/eras.cfm).

Length of stay (Fig. 2A) and overall perioperative morbidity (Fig. 2B) were significantly reduced in the enhanced recovery protocol groups compared with the usual care protocol groups. In pooled analyses, the mean reduction in length of stay was 2.6 days (95%CI, –3.2 to –2.0). We found considerable statistical heterogeneity across studies for length of stay ($I^2 = 92\%$) that was not explained in exploratory analyses by study design or long length of stay in the control group. The RR for experiencing complications was 0.66 (95%CI, 0.54–0.80), an absolute difference of 99 fewer complications per 1000 participants with enhanced recovery (Table 2). Quality of evidence was moderate for both length of stay and perioperative morbidity (Table 2).

All-cause mortality, reported to 30 days postsurgery in most studies, was rare and did not differ significantly between the enhanced recovery and usual care protocol groups (Peto OR, 1.79; 95% CI, 0.81–3.95) (Fig. 2C). Readmissions, also typically reported to 30 days postsurgery, were similar (pooled RR, 1.10; 95% CI, 0.81–1.50) (Fig. 2D). Quality of evidence was low for both mortality and readmissions (Table 2). The incidence of ileus was not significantly different between enhanced recovery and usual care protocol groups.

Among the intermediate outcomes, return of GI function (time to flatus and/or first bowel movement and time to oral intake of solid foods) was significantly shorter following surgery with an enhanced recovery protocol than with a usual care protocol. Pain and quality of life were infrequently reported.

Surgical site infection rates did not differ significantly between protocol groups (Fig. 2E). The pooled RR was 0.75 (95% CI, 0.52–1.07). Quality of evidence was low (Table 2). Other harms, including bleeding events, anastomotic leakage, need for reoperation, urinary tract infection, and cardiovascular complications also did not differ between groups.

Based on predefined subgroup analysis for critical outcomes (length of stay, all-cause mortality, overall morbidity, readmissions, and surgical site infections), the effect of enhanced recovery versus usual care protocols did not vary by surgical approach (open vs laparoscopic) nor clinical indication (cancerous or noncancerous) (for all subgroup difference $p > 0.05$) (Table 3 and Supplemental Figure 1a–1j, http://links.lww.com/DCR/A680). As with the overall analysis, length of stay was significantly shorter and overall morbidity was significantly lower in all enhanced recovery groups with 1 exception. Morbidity was similar between the enhanced recovery and usual care protocols in the subset of studies enrolling patients undergoing colorectal surgery for either colorectal cancer or benign conditions (RR, 0.82; 95% CI, 0.63–1.07) (Supplemental Digital Content 2, Figure 1f).

Few studies reported a measure of adherence to the enhanced recovery protocol components. Four trials addressed adherence,[16,21,29,35] but only one reported on the association of adherence and critical outcomes.[29] With the use of a trend analysis, increased adherence (defined as the percentage of protocol components fulfilled) was significantly associated with shorter length of stay but not overall rate of complications.

We also performed a sensitivity analysis based on included ERAS components[2,4] in the trial protocols. We identified 11 studies that had minimal overlap between enhanced recovery and usual care protocols and included 2 multidisciplinary components (intraoperative standardized anesthesia protocol and postoperative multimodal approach to opioid-sparing pain control).[9,10,14,15,19,20,22,23,27,31,33] We found that the pooled effect on length of stay and overall morbidity did not vary by differentiation of enhanced recovery protocols versus usual care protocols.

DISCUSSION

Our systematic review of 25 RCTs and concurrent CCTs adds new information to prior reviews and found that enhanced recovery protocols significantly reduced length of stay and overall perioperative morbidity compared with usual care protocols (moderate-quality evidence). Outcomes were consistent across surgical approach (ie, open and laparoscopic) and clinical indication (ie, colorectal cancer, rectal cancer, mix of colorectal cancer and benign conditions, or benign conditions alone). Mortality, hospital readmissions, and surgical site infections were similar in the 2 protocol groups (low-quality evidence) with consistent findings across surgical approach and clinical indication.

Strengths of our review include an a priori protocol, searching of multiple databases, documenting enhanced recovery and standard care protocols for each included study, a focus on patient-centered health outcomes, and use of GRADE methodology on a per outcome basis. Our review included only English language publications. Other limitations are limitations of the available literature. None of the studies were conducted in the United States. Although protocol components were outlined in the studies, little detail was provided. It was unclear if, and to what extent, there was compliance with the protocol, and there is likely a wide range of degrees of application of the various components making it difficult to know what exactly was done. Only 1

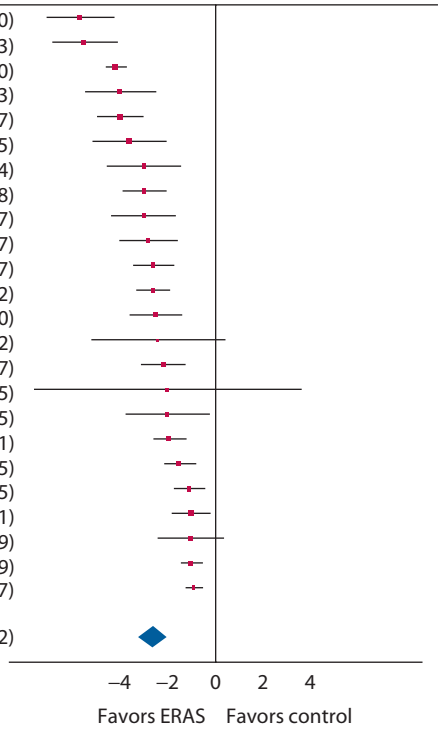
A

Length of stay

Study or subgroup	ERAS Mean	ERAS SD	ERAS Total	Control Mean	Control SD	Control Total	Weight	Mean difference IV, random, 95% CI
Yang 2012 (24)	6	1	32	11.7	3.8	30	4.0%	−5.70 (−7.10 to −4.30)
Ota 2017 (29)	8.5	6	159	14	6.5	161	4.0%	−5.50 (−6.87 to −4.13)
Jia 2014 (14)	9	1.8	117	13.2	1.3	116	5.0%	−4.20 (−4.60 to −3.80)
Gouvas 2012 lap (12)	4	2.3	42	8	3.8	33	3.9%	−4.00 (−5.47 to −2.53)
Scioscia 2017 (30)	3	2.3	62	7	4.8	165	4.5%	−4.00 (−4.93 to −3.07)
Muller 2009 (16)	6.7	4.8	76	10.3	4.9	75	3.8%	−3.60 (−5.15 to −2.05)
Anderson 2003 (9)	4	1.8	14	7	2.1	11	3.8%	−3.00 (−4.56 to −1.44)
Serclova 2009 (20)	7.4	1.3	51	10.4	3.1	52	4.5%	−3.00 (−3.92 to −2.08)
Mari 2014 (28)	4.7	2.4	25	7.7	2.4	25	4.1%	−3.00 (−4.33 to −1.67)
Ionescu 2009 (13)	6.4	3.4	48	9.2	2.7	48	4.2%	−2.80 (−4.03 to −1.57)
Wang 2015 (32)	6.1	1.7	57	8.7	2.8	60	4.6%	−2.60 (−3.43 to −1.77)
Nanavati 2014 (17)	4.7	1.3	30	7.3	1.4	30	4.8%	−2.60 (−3.28 to −1.92)
Wang 2011 (23)	5.1	3.1	106	7.6	4.8	104	4.4%	−2.50 (−3.60 to −1.40)
Gatt 2005 (11)	6.6	4.4	19	9	4.6	20	2.4%	−2.40 (−5.22 to 0.42)
Mari 2016 (27)	5	2.6	70	7.2	3	70	4.5%	−2.20 (−3.13 to −1.27)
Khoo 2007 (15)	5	8.5	35	7	14.8	35	0.9%	−2.00 (−7.65 to 3.65)
Forsmo 2016 (35)	5	8	154	7	7.6	153	3.6%	−2.00 (−3.75 to −0.25)
Feng 2014 (25)	5.1	1.4	57	7	2.3	59	4.8%	−1.90 (−2.59 to −1.21)
Wang 2012 (33)	5.5	1	40	7	1.8	38	4.8%	−1.50 (−2.15 to −0.85)
Feng 2016 (10)	7.5	2.2	116	8.6	2.8	114	4.8%	−1.10 (−1.75 to −0.45)
Vlug 2011 lap (21)	5	2.9	100	6	2.9	109	4.7%	−1.00 (−1.79 to −0.21)
Gouvas 2012 open (12)	7	2.3	36	8	4	45	4.0%	−1.00 (−2.39 to 0.39)
Vlug 2011 open (21)	6	1.6	93	7	1.3	98	5.0%	−1.00 (−1.41 to −0.59)
Ren 2011 (19)	5.7	1.6	299	6.6	2.4	298	5.0%	−0.90 (−1.23 to −0.57)
Total {95% CI)			1838			1949	100.0%	−2.62 (−3.22 to −2.02)

Heterogeneity: $Tau^2 = 1.86$; $Chi^2 = 292.54$, df = 23 ($p < 0.00001$); $I^2 = 92\%$

Test for overall effect: Z = 8.51 ($p < 0.00001$)



B

Morbidity

Study or subgroup	ERAS Events	ERAS Total	Control Events	Control Total	Weight	Risk ratio M-H, random, 95% CI
Mari 2014 (28)	0	25	0	25		Not estimable
Feng 2014 (25)	2	57	10	59	1.6%	0.21 (0.05–0.90)
Wang 2012 (33)	2	40	8	38	1.6%	0.24 (0.05–1.05)
Feng 2016 (10)	7	116	17	114	3.8%	0.40 (0.17–0.94)
Gouvas 2012 lap (12)	9	42	17	33	5.2%	0.42 (0.21–0.81)
Muller 2009 (16)	16	76	37	75	7.0%	0.43 (0.26–0.70)
Serclova 2009 (20)	11	51	25	52	5.8%	0.45 (0.25–0.81)
Yang 2012 (24)	6	32	12	30	3.8%	0.47 (0.20–1.09)
Wang 2012 lap (22)	3	40	6	40	1.9%	0.50 (0.13–1.86)
Wang 2011 (23)	20	106	39	104	7.3%	0.50 (0.32–0.80)
Gatt 2005 (11)	9	19	15	20	6.5%	0.63 (0.37–1.08)
Wang 2015 (32)	10	57	16	60	4.8%	0.66 (0.33–1.33)
Gouvas 2012 open (12)	14	36	25	45	7.1%	0.70 (0.43–1.14)
Wang 2012 open (22)	7	41	10	42	3.7%	0.72 (0.30–1.70)
Mari 2016 (27)	12	70	15	70	5.0%	0.80 (0.40–1.58)
Forsmo 2016 (35)	65	154	68	153	10.2%	0.95 (0.74–1.23)
Vlug 2011 lap (21)	34	100	37	109	8.5%	1.00 (0.69–1.46)
Ren 2011 (19)	29	299	28	298	7.0%	1.03 (0.63–1.69)
Vlug 2011 open (21)	43	93	41	98	9.3%	1.11 (0.80–1.52)
Total (95% CI)		1454		1465	100.0%	0.66 (0.54–0.80)
Total events	299		426			

Heterogeneity: $Tau^2 = 0.08$; $Chi^2 = 36.54$, df = 17 (F = 0.004); $I^2 = 53\%$

Test for overall effect: Z = 4.12 ($p < 0.0001$)

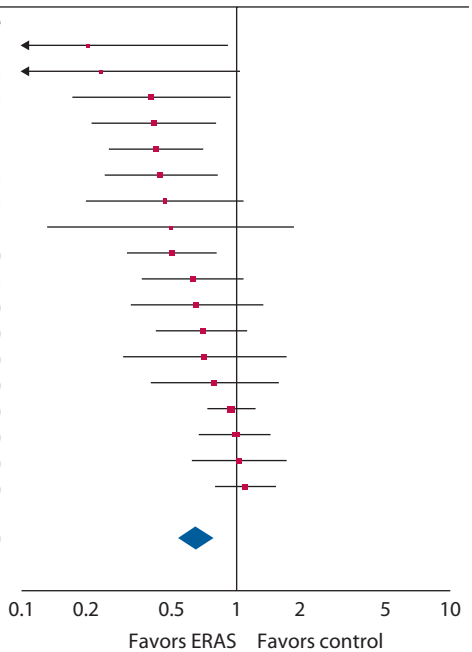


FIGURE 2. Pooled analyses for length of stay (mean difference between groups) (A), morbidity (risk ratio) (B), mortality (odds ratio) (C), readmissions (risk ratio) (D), and surgical site infections (risk ratio) (E). ERAS = enhanced recovery after surgery; M-H = Mantel-Haenszel.

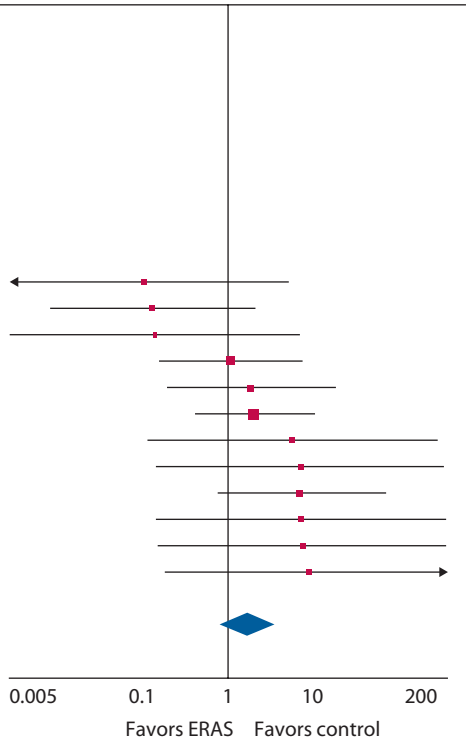
C

Mortality

Study or subgroup	ERAS Events	ERAS Total	Control Events	Control Total	Weight	Peto odds ratio Peto, fixed, 95% CI
Ren 2011 (19)	0	299	0	298		Not estimable
Mari 2014 (28)	0	25	0	25		Not estimable
Pappalardo 2016 (18)	0	25	0	25		Not estimable
Feng 2014 (25)	0	57	0	59		Not estimable
Ota 2017 (29)	0	159	0	161		Not estimable
Nanavati 2014 (17)	0	30	0	30		Not estimable
Serclova 2009 (20)	0	51	0	52		Not estimable
Wang 2015 (32)	0	57	0	60		Not estimable
Mari 2016 (27)	0	70	0	70		Not estimable
Jia 2014 (14)	0	117	0	116		Not estimable
Anderson 2003 (9)	0	14	1	11	4.0%	0.10 (0.00–5.34)
Khoo 2007 (15)	0	35	2	35	8.0%	0.13 (0.01–2.14)
Wang 2012 open (22)	0	41	1	42	4.1%	0.14 (0.00–6.99)
Vlug 2011 lap (21)	2	100	2	109	16.0%	1.09 (0.15–7.87)
Wang 2011 (23)	2	106	1	104	12.1%	1.92 (0.20–18.69)
Vlug 2011 open (21)	4	93	2	98	23.7%	2.09 (0.41–10.60)
Gouvas 2012 lap (12)	1	42	0	33	4.0%	5.96 (0.12–309.26)
Wang 2012 lap (22)	1	40	0	40	4.1%	7.39 (0.15–372.38)
Forsmo 2016 (35)	3	154	0	153	12.1%	7.44 (0.77–72.04)
Wang 2012 (33)	1	49	0	50	4.1%	7.54 (0.15–380.14)
Gatt 2005 (11)	1	19	0	20	4.1%	7.79 (0.15–393.02)
Gouvas 2012 open (12)	1	36	0	45	4.0%	9.49 (0.18–489.97)
Total (95% CI)		1619		1636	100.0%	1.79 (0.81–3.95)
Total events	16		9			

Heterogeneity: $Chi^2 = 11.40$, df = 11 ($p = 0.41$); $I^2 = 4\%$

Test for overall effect: Z = 1.45 ($p = 0.15$)



D

Readmissions

Study or subgroup	ERAS Events	ERAS Total	Control Events	Control Total	Weight	Risk ratio M-H, random, 95% CI
Mari 2014 (28)	0	25	0	25		Not estimable
Serclova 2009 (20)	0	51	0	52		Not estimable
Anderson 2003 (9)	0	19	0	20		Not estimable
Ionescu 2009 (13)	0	48	0	48		Not estimable
Yang 2012 (24)	0	32	0	30		Not estimable
Gatt 2005 (11)	1	19	4	20	2.1%	0.26 (0.03–2.15)
Feng 2014 (25)	0	57	1	59	0.9%	0.34 (0.01–8.29)
Wang 2011 (23)	4	106	9	104	7.1%	0.44 (0.14–1.37)
Wang 2012 (31)	2	49	3	50	3.1%	0.68 (0.12–3.90)
Vlug 2011 lap (21)	6	100	7	109	8.4%	0.93 (0.32–2.69)
Nanavati 2014 (17)	1	30	1	30	1.3%	1.00 (0.07–15.26)
Vlug 2011 open (21)	7	93	7	98	9.2%	1.05 (0.38–2.89)
Scioscia 2017 (30)	11	62	26	162	22.7%	1.11 (0.58–2.10)
Forsmo 2016 (35)	29	154	21	153	35.2%	1.37 (0.82–2.30)
Muller 2009 (16)	3	76	2	75	3.0%	1.48 (0.25–8.61)
Wang 2012 open (22)	3	41	2	42	3.1%	1.54 (0.27–8.73)
Wang 2012 lap (22)	1	40	0	40	0.9%	3.00 (0.13–71.51)
Khoo 2007 (15)	3	35	1	35	1.9%	3.00 (0.33–27.46)
Ota 2017 (29)	2	159	0	161	1.0%	5.06 (0.24–104.62)
Total (95% CI)		1196		1313	100.0%	1.10 (0.81–1.50)
Total events	73		84			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 8.31$, df = 13 ($p = 0.82$); $I^2 = 0\%$

Test for overall effect: Z = 0.62 ($p = 0.53$)

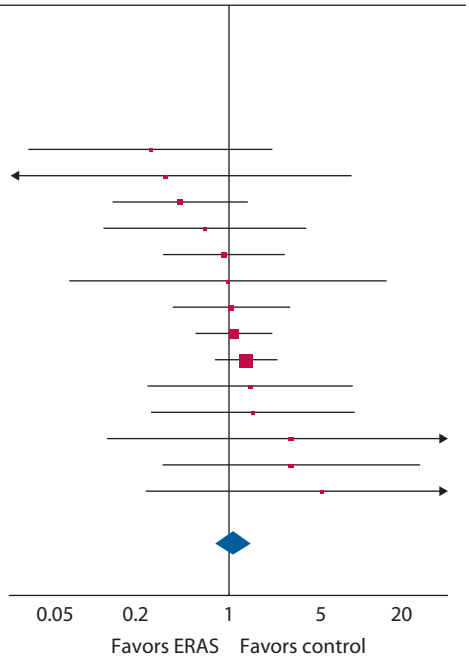


FIGURE 2. (*Continued*)

E

Surgical site infections

Study or subgroup	ERAS Events	ERAS Total	Control Events	Control Total	Weight	Risk ratio M-H, random, 95% CI
Gatt 2005 (11)	0	19	4	20	1.6%	0.12 (0.01–2.03)
Wang 2012 (33)	1	40	3	38	2.6%	0.32 (0.03–2.91)
Feng 2016 (10)	1	116	3	114	2.5%	0.33 (0.03–3.10)
Feng 2014 (25)	0	57	1	59	1.3%	0.34 (0.01–8.29)
Yang 2012 (24)	1	32	2	30	2.3%	0.47 (0.04–4.91)
Wang 2011 (23)	4	106	7	104	9.0%	0.56 (0.17–1 .86)
Muller 2009 (16)	4	76	7	75	9.2%	0.56 (0.17–1.85)
Jia 2014 (14)	6	117	8	116	12.2%	0.74 (0.27–2.08)
Foramo 2016 (35)	10	154	13	153	20.5%	0.76 (0.35–1.69)
Ionescu 2009 (13)	4	48	5	48	8.2%	0.30 (0.23–2.80)
Ota 2017 (29)	5	159	6	161	9.5%	0.84 (0.26–2.71)
Ren 2011 (19)	5	299	5	298	8.5%	1.00 (0.29–3.41)
Wang 2015 (32)	2	57	2	60	3.5%	1.05 (0.15–7.22)
Wang 2012 (31)	3	49	2	50	4.2%	1.53 (0.27–8.77)
Mari 2016 (27)	2	70	1	70	2.3%	2.00 (0.19–21.56)
Anderson 2003 (9)	1	14	0	11	1.3%	2.40 (0.11–53.77)
Nanavati 2014 (17)	1	30	0	30	1.3%	3.00 (0.13–70.83)
Total (95% CI)		1443		1437	100.0%	0.75 (0.52–1.07)
Total events	50		69			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 6.53$, df = 16 ($p = 0.98$); $I^2 = 0\%$

Test for overall effect: Z = 1.60 ($p = 0.11$)

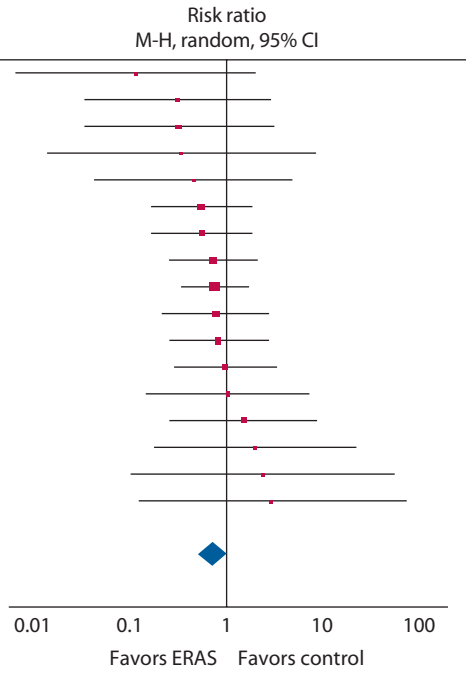


FIGURE 2. (*Continued*)

TABLE 2. Summary of findings for ERAS compared with control for colorectal surgeries

Outcome number (N) of participants (studies)	*Relative effect (95% CI)*	*Anticipated absolute effects (95% CI)* *Without ERAS, %*	*With ERAS, %*	*Difference*	*Quality*	*What happens*
Length of stay, N of participants: 3787 (20 RCTs, 4 CCTs)				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.
Mortality, N of participants: 3255 (18 RCTs, 4 CCTs)	Peto OR 1.79 (0.81–3.95)	0.6	1.0 (0.4–2.1)	4 more per 1000 (1 fewer to 16 more)	⊕⊕○○ Low[a,c]	No statistically significant differences between groups. (Note: most studies reported 30-day all-cause mortality.)
Perioperative morbidity, N of participants: 2919 (16 RCTs, 3 CCTs)	RR 0.66 (0.54–0.80)	29.1	19.2 (15.7–23.3)	99 fewer per 1000 (134 fewer to 58 fewer)	⊕⊕⊕○ Moderate[a]	Fewer complications in both open and laparoscopic ERAS groups vs respective controls.
Readmissions, N of participants: 2515 (18 RCTs, 1 CCT)	RR 1.10 (0.81–1.50)	6.4	7.0 (5.2–9.6)	6 more per 1000 (12 fewer to 32 more)	⊕⊕○○ Low[a,c]	No statistically significant differences between groups.
Surgical site infection, N of participants: 2880 (15 RCTs, 2 CCTs)	RR 0.75 (0.52–1.07)	4.8	3.6 (2.5–5.1)	12 fewer per 1000 (23 fewer to 3 more)	⊕⊕○○ Low[a,c]	No statistically significant differences between groups.

The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
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.
CCT = controlled clinical trial; ERAS = enhanced recovery after surgery; MD = mean difference; OR = odds ratio; RCT = randomized controlled trial; RR = risk ratio.
[a]Mostly high or unclear risk of bias.
[b]I^2 indicated substantial statistical heterogeneity, although all but 2 studies reported lower duration with ERAS.
[c]Wide confidence intervals and/or very few events.

TABLE 3. Summary of findings for ERAS compared with control for surgical approach and clinical indication

	Surgical approach[a]		*Clinical indication*[a]		
Outcome	*Open surgery*	*Laparoscopic surgery*	*Colorectal cancer*	*Rectal cancer*	*Benign conditions*
Length of stay (days)	−2.55 (−3.43 to −1.67)	−2.76 (−3.58 to −1.93)	−2.88 (−4.03 to −1.73)	−2.25 (−3.69 to −0.81)	−3.16 (−3.97 to −2.34)
MD (95% CI)	(14 comparisons)	(9 comparisons)	(10 comparisons)	(3 comparisons)	(3 comparisons)
Mortality	1.17 (0.42 to 3.25)	2.42 (0.55 to 10.75)	1.00 (0.25 to 4.01)	7.52 (0.46 to 122.56)	Not estimable[b]
Peto OR (95% CI)	(12 comparisons)	(9 comparisons)	(9 comparisons)	(4 comparisons)	(2 comparisons)
Morbidity	0.63 (0.49 to 0.83)	0.59 (0.39 to 0.90)	0.61 (0.46 to 0.80)	0.48 (0.27 to 0.88)	0.45 (0.25 to 0.81)
RR (95% CI)	(10 comparisons)	(8 comparisons)	(8 comparisons)	(3 comparisons)	(1 comparison)
Readmissions	0.88 (0.49 to 1.57)	1.06 (0.64 to 1.75)	0.94 (0.45 to 1.98)	0.34 (0.01 to 8.29)	1.10 (0.59 to 2.05)
RR (95% CI)	(11 comparisons)	(7 comparisons)	(8 comparisons)	(1 comparison)	(3 comparisons)
Surgical site infections	0.68 (0.42 to 1.10)	0.90 (0.43 to 1.90)	0.75 (0.48 to 1.18)	0.34 (0.01 to 8.29)	3.00 (0.13 to 70.83)
RR (95% CI)	(10 comparisons)	(6 comparisons)	(10 comparisons)	(1 comparison)	(1 comparison)

ERAS = enhanced recovery after surgery; MD = mean difference; OR = odds ratio RR = risk ratio.
[a]ERAS vs control.
[b]No events.

study attempted to relate compliance to critical outcomes. The number of enhanced recovery protocol elements varied widely across studies, and most of the usual care protocols included some of the enhanced recovery components. 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 for either length of stay or overall morbidity, although we caution that subgroup findings are exploratory and may be insufficiently powered to detect important differences. The studies were conducted in different health care systems and with different care procedures (including discharge protocols), different patient populations (eg, exclusion of patients with ASA grades III or IV), and different outcome definitions. There is no consensus on key components or a "bundle" of components necessary to achieve improved patient outcomes. All but one of the included studies reported outcomes to 30 days or less.

Prior systematic reviews have addressed the topic of enhanced recovery protocols for colorectal surgery. We identified 13 reviews published between 2001 and 2017.[36–48] However, none of the existing reviews reported on subgroups based on surgical approach (open or laparoscopic surgery) or colorectal condition. Although several noted the enhanced recovery protocol components from the included studies, the standard care protocols were not documented. Only 1 systematic review formally rated the overall quality of evidence.[48] Of the existing systematic reviews, Greco et al[39] had the greatest overlap of included studies with our review, although we included 11 studies published after their final search date of June 2012.

Development and implementation of a health care systemwide standardized protocol for ERAS could substantially improve elective colorectal surgical care by decreasing postoperative hospital length of stay and overall 30-day morbidity. For example, Liu et al[49] reported on implementation of an enhanced recovery protocol in an integrated health care delivery system. They showed significant reductions in length of stay and postoperative complication rates based on analysis of data from 3768 patients undergoing elective colorectal resection in a 24-month period (1890 preimplementation, 1878 postimplementation). In addition, 3 single-center studies conducted in the United States that used prepost study design or historical controls reported on the implementation of ERAS as part of quality improvement initiatives.[50–52] These studies reported clinical outcomes and resource utilization benefits associated with ERAS, similar to what we reported from RCT of non-US studies. As the largest integrated health care system in the United States, the VHA collectively performed 3747 colectomy procedures throughout their 137 surgical programs in Fiscal Year 2016. The mean postoperative hospital length of stay was 9.2 days, the 30-day mortality rate was 1.7%, the overall 30-day morbidity rate was 16.4%, the surgical site infection rate was 7.3%, and the 30-day all-cause hospital readmission rate was 12.4% (Source: VHA National Surgery Office, personal communication). Significant reductions in length of stay and morbidity such as those achieved by the US studies would provide a meaningful benefit for Veteran care.

Future RCTs comparing enhanced recovery protocols with usual care might not be feasible or ethical.[29,35] Implementing new enhanced recovery protocols in "total quality improvement" fashion with evaluation and refinement might be the best approach because of the limited applicability of existing RCT data, rapidly evolving standard practice, limited full understanding of implementation, adherence, standardization of enhanced recovery components, and possible barriers. In the process of implementation, detailed information should be gathered describing enhanced recovery components and how they are implemented and compliance is assessed. 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 preoperative and postoperative solids and fluids intake, degree

of mobilization, etc. Surgeon and medical center surgical volume should be considered. Outcomes should include patient and/or caregiver experiences.[53]

CONCLUSIONS

Enhanced recovery protocols for elective colorectal surgery reduced the length of stay and overall perioperative morbidity versus standard care protocols. Mortality, readmissions, and surgical site infections were similar between the groups. However, no studies were conducted in the United States, and 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. Furthermore, there is no reliable evidence on enhanced recovery components, alone or in combination, that are key to improving patient outcomes.

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REFERENCES

1. Ljungqvist O. ERAS–enhanced recovery after surgery: moving evidence-based perioperative care to practice. *JPEN J Parenter Enteral Nutr*. 2014;38:559–566.
2. Ljungqvist O, Scott M, Fearon KC. Enhanced recovery after surgery: a review. *JAMA Surg*. 2017;152:292–298.
3. Sehgal R, Hill A, Deasy J, McNamara DA, Cahill RA. Fast-track for the modern colorectal department. *World J Surg*. 2012;36:2473–2480.
4. Gustafsson UO, Scott MJ, Schwenk W, et al; Enhanced Recovery After Surgery (ERAS) Society, for Perioperative Care; European Society for Clinical Nutrition and Metabolism (ESPEN); International Association for Surgical Metabolism and Nutrition (IASMEN). Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS(®)) Society recommendations. *World J Surg*. 2013;37:259–284.
5. Higgins JP, Greene S. *Cochrane Handbook for Systematic Reviews of Interventions*. 2011; Version 5.1.0. http://handbook-5-1.cochrane.org/. Accessed July 5, 2017.
6. Cochrane Collaboration Review Manager [computer program] Version 5.3. Copenhagen: The Nordic Cochrane Center; 2014.
7. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327:557–560.
8. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. *BMC Med Res Methodol*. 2005;5:13.
9. Anderson AD, McNaught CE, MacFie J, Tring I, Barker P, Mitchell CJ. Randomized clinical trial of multimodal optimization and standard perioperative surgical care. *Br J Surg*. 2003;90:1497–1504.
10. Feng J, Li K, Li L, et al. The effects of fast-track surgery on inflammation and immunity in patients undergoing colorectal surgery. *Int J Colorectal Dis*. 2016;31:1675–1682.
11. Gatt M, Anderson AD, Reddy BS, Hayward-Sampson P, Tring IC, MacFie J. Randomized clinical trial of multimodal optimization of surgical care in patients undergoing major colonic resection. *Br J Surg*. 2005;92:1354–1362.
12. Gouvas N, Gogos-Pappas G, Tsimogiannis K, Tsimoyiannis E, Dervenis C, Xynos E. Implementation of fast-track protocols in open and laparoscopic sphincter-preserving rectal cancer surgery: a multicenter, comparative, prospective, non-randomized study. *Dig Surg*. 2012;29:301–309.
13. Ionescu D, Iancu C, Ion D, et al. Implementing fast-track protocol for colorectal surgery: a prospective randomized clinical trial. *World J Surg*. 2009;33:2433–2438.
14. Jia Y, Jin G, Guo S, et al. Fast-track surgery decreases the incidence of postoperative delirium and other complications in elderly patients with colorectal carcinoma. *Langenbecks Arch Surg*. 2014;399:77–84.
15. Khoo CK, Vickery CJ, Forsyth N, Vinall NS, Eyre-Brook IA. A prospective randomized controlled trial of multimodal perioperative management protocol in patients undergoing elective colorectal resection for cancer. *Ann Surg*. 2007;245:867–872.
16. Muller S, Zalunardo MP, Hubner M, Clavien PA, Demartines N; Zurich Fast Track Study Group. A fast-track program reduces complications and length of hospital stay after open colonic surgery. *Gastroenterology*. 2009;136:842–847.
17. Nanavati AJ, Prabhakar S. A comparative study of 'fast-track' versus traditional peri-operative care protocols in gastrointestinal surgeries. *J Gastrointest Surg*. 2014;18:757–767.
18. Pappalardo G, Coiro S, De Lucia F, Giannella A, Ruffolo F, Frattaroli FM. Open sphincter-preserving surgery of extraperitoneal rectal cancer without primary stoma and Fast Track Protocol. *G Chir*. 2016;37:257–261.
19. Ren L, Zhu D, Wei Y, et al. Enhanced Recovery After Surgery (ERAS) program attenuates stress and accelerates recovery in patients after radical resection for colorectal cancer: a prospective randomized controlled trial. *World J Surg*. 2012;36:407–414.
20. Serclová Z, Dytrych P, Marvan J, et al. Fast-track in open intestinal surgery: prospective randomized study (Clinical Trials Gov Identifier no. NCT00123456). *Clin Nutr*. 2009;28:618–624.
21. Vlug MS, Wind J, Hollmann MW, et al; LAFA study group. Laparoscopy in combination with fast track multimodal management is the best perioperative strategy in patients undergoing colonic surgery: a randomized clinical trial (LAFA-study). *Ann Surg*. 2011;254:868–875.
22. Wang G, Jiang Z, Zhao K, et al. Immunologic response after laparoscopic colon cancer operation within an enhanced recovery program. *J Gastrointest Surg*. 2012;16:1379–1388.
23. Wang G, Jiang ZW, Xu J, et al. Fast-track rehabilitation program vs conventional care after colorectal resection: a randomized clinical trial. *World J Gastroenterol*. 2011;17:671–676.
24. Yang D, He W, Zhang S, Chen H, Zhang C, He Y. Fast-track surgery improves postoperative clinical recovery and immunity after elective surgery for colorectal carcinoma: randomized controlled clinical trial. *World J Surg*. 2012;36:1874–1880.
25. Feng F, Li XH, Shi H, et al. Fast-track surgery combined with laparoscopy could improve postoperative recovery of low-risk

rectal cancer patients: a randomized controlled clinical trial. *J Dig Dis*. 2014;15:306–313.
26. Mari G, Costanzi A, Crippa J, et al. Surgical stress reduction in elderly patients undergoing elective colorectal laparoscopic surgery within an ERAS protocol. *Chirurgia (Bucur)*. 2016;111:476–480.
27. Mari G, Crippa J, Costanzi A, Mazzola M, Rossi M, Maggioni D. ERAS Protocol reduces IL-6 secretion in colorectal laparoscopic surgery: results from a randomized clinical trial. *Surg Laparosc Endosc Percutan Tech*. 2016;26:444–448.
28. Mari GM, Costanzi A, Maggioni D, et al. Fast-track versus standard care in laparoscopic high anterior resection: a prospective randomized-controlled trial. *Surg Laparosc Endosc Percutan Tech*. 2014;24:118–121.
29. Ota H, Ikenaga M, Hasegawa J, et al. Safety and efficacy of an "enhanced recovery after surgery" protocol for patients undergoing colon cancer surgery: a multi-institutional controlled study. *Surg Today*. 2017;47:668–675.
30. Scioscia M, Ceccaroni M, Gentile I, et al. Randomized trial on fast track care in colorectal surgery for deep infiltrating endometriosis. *J Minim Invasive Gynecol*. 2017;24:815–821.
31. Wang G, Jiang ZW, Zhao K, et al. Fast track rehabilitation programme enhances functional recovery after laparoscopic colonic resection. *Hepatogastroenterology*. 2012;59:2158–2163.
32. Wang H, Zhu D, Liang L, et al. Short-term quality of life in patients undergoing colonic surgery using enhanced recovery after surgery program versus conventional perioperative management. *Qual Life Res*. 2015;24:2663–2670.
33. Wang Q, Suo J, Jiang J, Wang C, Zhao YQ, Cao X. Effectiveness of fast-track rehabilitation vs conventional care in laparoscopic colorectal resection for elderly patients: a randomized trial. *Colorectal Dis*. 2012;14:1009–1013.
34. Forsmo HM, Erichsen C, Rasdal A, Körner H, Pfeffer F. Enhanced recovery after colorectal surgery (ERAS) in elderly patients is feasible and achieves similar results as in younger patients. *Gerontol Geriatr Med*. 2017;3:2333721417706299.
35. Forsmo HM, Pfeffer F, Rasdal A, et al. Compliance with enhanced recovery after surgery criteria and preoperative and postoperative counselling reduces length of hospital stay in colorectal surgery: results of a randomized controlled trial. *Colorectal Dis*. 2016;18:603–611.
36. Adamina M, Kehlet H, Tomlinson GA, Senagore AJ, Delaney CP. Enhanced recovery pathways optimize health outcomes and resource utilization: a meta-analysis of randomized controlled trials in colorectal surgery. *Surgery*. 2011;149:830–840.
37. Bagnall NM, Malietzis G, Kennedy RH, Athanasiou T, Faiz O, Darzi A. A systematic review of enhanced recovery care after colorectal surgery in elderly patients. *Colorectal Dis*. 2014;16:947–956.
38. Grant MC, Yang D, Wu CL, Makary MA, Wick EC. Impact of enhanced recovery after surgery and fast track surgery pathways on healthcare-associated infections: results from a systematic review and meta-analysis. *Ann Surg*. 2017;265:68–79.
39. Greco M, Capretti G, Beretta L, Gemma M, Pecorelli N, Braga M. Enhanced recovery program in colorectal surgery: a meta-analysis of randomized controlled trials. *World J Surg*. 2014;38:1531–1541.
40. Lau CS, Chamberlain RS. Enhanced recovery after surgery programs improve patient outcomes and recovery: a meta-analysis. *World J Surg*. 2017;41:899–913.
41. Launay-Savary MV, Mathonnet M, Theissen A, Ostermann S, Raynaud-Simon A, Slim K; GRACE (Groupe francophone de Réhabilitation Améliorée après Chirurgie). Are enhanced recovery programs in colorectal surgery feasible and useful in the elderly? A systematic review of the literature. *J Visc Surg*. 2017;154:29–35.
42. Li P, Fang F, Cai JX, Tang D, Li QG, Wang DR. Fast-track rehabilitation vs conventional care in laparoscopic colorectal resection for colorectal malignancy: a meta-analysis. *World J Gastroenterol*. 2013;19:9119–9126.
43. Lv L, Shao YF, Zhou YB. The enhanced recovery after surgery (ERAS) pathway for patients undergoing colorectal surgery: an update of meta-analysis of randomized controlled trials. *Int J Colorectal Dis*. 2012;27:1549–1554.
44. Rawlinson A, Kang P, Evans J, Khanna A. A systematic review of enhanced recovery protocols in colorectal surgery. *Ann R Coll Surg Engl*. 2011;93:583–588.
45. Spanjersberg WR, Reurings J, Keus F, van Laarhoven CJ. Fast track surgery versus conventional recovery strategies for colorectal surgery. *Cochrane Database Syst Rev*. 2011;(2):CD007635.
46. Tan SJ, Zhou F, Yui WK, et al. Fast track programmes vs. traditional care in laparoscopic colorectal surgery: a meta-analysis of randomized controlled trials. *Hepatogastroenterology*. 2014;61:79–84.
47. Zhao JH, Sun JX, Gao P, et al. Fast-track surgery versus traditional perioperative care in laparoscopic colorectal cancer surgery: a meta-analysis. *BMC Cancer*. 2014;14:607.
48. Zhuang CL, Ye XZ, Zhang XD, Chen BC, Yu Z. Enhanced recovery after surgery programs versus traditional care for colorectal surgery: a meta-analysis of randomized controlled trials. *Dis Colon Rectum*. 2013;56:667–678.
49. Liu VX, Rosas E, Hwang J, et al. Enhanced recovery after surgery program implementation in 2 surgical populations in an integrated health care delivery system. *JAMA Surg*. 2017;152:e171032.
50. Wick EC, Galante DJ, Hobson DB, et al. Organizational culture changes result in improvement in patient-centered outcomes: implementation of an integrated recovery pathway for surgical patients. *J Am Coll Surg*. 2015;221:669–677.
51. Miller TE, Thacker JK, White WD, et al; Enhanced Recovery Study Group. Reduced length of hospital stay in colorectal surgery after implementation of an enhanced recovery protocol. *Anesth Analg*. 2014;118:1052–1061.
52. Shah PM, Johnston L, Sarosiek B, et al. Reducing readmissions while shortening length of stay: the positive impact of an enhanced recovery protocol in colorectal surgery. *Dis Colon Rectum*. 2017;60:219–227.
53. Paton F, Chambers D, Wilson P, et al. Effectiveness and implementation of enhanced recovery after surgery programmes: a rapid evidence synthesis. *BMJ Open*. 2014;4:e005015.