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REVIEW

# Enhanced recovery after surgery (ERAS) pathways in breast reconstruction: systematic review and meta-analysis of the literature

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## Abstract

**Purpose** Enhanced recovery after surgery (ERAS) pathways are increasingly promoted in post-mastectomy reconstruction, with several articles reporting their benefits and safety. This meta-analysis appraises the evidence for ERAS pathways in breast reconstruction.

**Methods** A systematic search of Medline, EMBASE, and Cochrane databases was performed to identify reports of ERAS protocols in post-mastectomy breast reconstruction. Two reviewers screened studies using predetermined inclusion criteria. Studies evaluated at least one of the following end-points of interest: length of stay (LOS), opioid use, or major complications. Risk of bias was assessed for each study. Meta-analysis was performed via a mixed-effects model to compare outcomes for ERAS versus traditional standard of care. Surgical techniques were assessed through subgroup analysis.

**Results** A total of 260 articles were identified; 9 (3.46%) met inclusion criteria with a total of 1191 patients. Most studies had "fair" methodological quality and incomplete implementation of ERAS society recommendations was noted. Autologous flaps comprised the majority of cases. In autologous breast reconstruction, ERAS significantly reduces opioid use [Mean difference (MD) = − 183.96, 95% CI − 340.27 to 27.64, $p = 0.02$) and LOS (MD) = − 1.58, 95% CI − 1.99 to 1.18, $p < 0.00001$] versus traditional care. There is no significant difference in the incidence of complications (major complications, readmission, hematoma, and infection).

**Conclusion** ERAS pathways significantly reduce opioid use and length of hospital stay following autologous breast reconstruction without increasing complication rates. This is salient given the current US healthcare climate of rising expenditures and an opioid crisis.

**Keywords** Breast reconstruction · Enhanced recovery after surgery (ERAS) · Fast-track surgery · Length of stay · Postoperative opioid consumption

## Introduction

Enhanced recovery after surgery (ERAS), often-labeled *fast-track surgery*, is a multidisciplinary, multimodal, and evidence-based approach to perioperative management [1]. It represents a paradigm shift from traditional surgical care delivery; one that relies heavily on continuous audits and the dissemination of clinical pathways [1]. Initially reported in 1997 by Kehlet et al [2], ERAS guidelines have since been successfully applied to many major surgical procedures with promising results [3–10]. In particular, reduced post-operative morbidity and shortened hospital length of stay (LOS) have been consistently reported [11, 12].

In 2017, there were approximately 106,000 breast reconstructions performed in the United States; this represents

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a 35% increase from 2000 [13]. In a health care climate increasingly focused on optimizing care quality, patient experience, and containing costs, it comes as no surprise that health systems leverage ERAS pathways as a quality improvement initiative in breast reconstruction. Several studies have examined the safety and benefits of ERAS pathways in patients undergoing breast reconstruction, particularly free flaps [14–16]. The ERAS society recently performed an audit of care processes associated with high-quality outcomes in breast reconstruction and put forward recommendations for optimal perioperative management [17].

The aim of this review and meta-analysis is to appraise the existing literature for ERAS in breast reconstruction, specifically (a) the current state of ERAS implementation (i.e., to what extent are the core elements of published guidelines adopted in clinical practice), and (b) safety and efficacy of ERAS on reducing length of stay (LOS) and opioid use.

## Methods

### Data sources and search strategy

This study was submitted to the PROSPERO registry a priori (CRD42018085433), and performed in accordance with the Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) guidelines. A comprehensive electronic literature search of EMBASE, Cochrane library, and PubMed databases was performed on January 22, 2018 (see Supplemental data file 1 for search terms). All articles from 1975 to present were included without language or further study design restrictions.

### Inclusion and exclusion criteria

Criteria included full-length reports of studies involving ERAS implementation among females at least 18 years old, undergoing breast reconstruction. Reported outcomes included at least one of length of stay (LOS), opioid use, or major complications. Studies involving aesthetic or mastectomy alone procedures, or male patients were excluded. Editorials, opinion letters, review articles, purely technical descriptions, and meeting abstracts were excluded. To reduce heterogeneity in statistical analysis, results abstracted from "transition groups" wherein there was partial or incomplete implementation of ERAS pathway elements were excluded [15, 18].

### Study selection and data extraction

Two independent reviewers (CG and SB) performed the initial search and abstract screen in duplicated. Discrepancies were settled by reviewing the full article. All included abstracts were then subject to a full article review in duplicate. Discrepancies at this stage were settled by a third reviewer (ACO).

Data collection for the articles was performed using a standardized data extraction form tested by four independent reviewers (ACO, CG, SB, and CJC). Variables included lead author, publication year, study design, patient characteristics, breast reconstruction modality, ERAS protocol details, and post-operative complications. Variables collected for each ERAS protocol included preoperative consult, preoperative diet, preoperative medications, preoperative opioids, intraoperative antibiotics, intraoperative medications, postoperative medications, and goals of care.

### Outcome measures

In line with prior studies, our primary outcomes are length of stay (standardized to days) and opioid use reported as milligrams (mg) of oral morphine equivalents (OME) while in hospital. OME values, an objective measure of post-operative pain, are calculated using a web-based conversion calculator (available at: http://clincalc.com/opioids/default.aspx). Secondary outcomes of interest include patient-reported pain scores using a numerical rating scale (0–10) and complication rates. Complications include overall short-term (i.e., 30 day) major complications, and specifically readmission, hematoma, and infection. Missing or inconsistent outcomes data were addressed by contacting the respective study authors (first and senior/corresponding) via email for clarification, which occurred once [15]. The authors were successfully contacted and data outcomes were confirmed directly [15].

### Data synthesis

The Downs and Black Checklist was used to scrutinize study quality and risk of bias [19]. Quality reporting of included studies is derived from the total Downs and Black score: excellent (≥26), good (20–25), fair (15–19), and poor (≤14) [20, 21].

Statistical analyses were performed using Review Manager 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark 2011). Where applicable, prosthetic and autologous breast reconstruction cases are reported separately. Mean differences are reported with 95% confidence intervals. When necessary, interquartile ranges are used to estimate standard deviations according to methods published in the Cochrane Handbook [22]. The minimal clinically important difference (MCID) for length of stay is considered one day. The MCID for total opioid use is considered a 20% reduction. Results are also interpreted with Cohen's effect size, where a small effect size is $>0.2$, medium $>0.5$, and large $>0.8$ [23]. Inter-study heterogeneity

is quantified using the $I^2$ measurement as follows: $I^2 < 50\%$ low, 50–75% medium, and > 75% high [24]. For both primary outcomes, a random effects model (REM) is used to address the heterogeneity (methodological and clinical) across and within the included studies.

## Results

### Search results

Our initial search strategy resulted in 260 citations. Following title and abstract screening, 13 articles underwent full-text review and nine articles (3.46%) satisfied inclusion criteria [14–16, 18, 25–29] (Fig. 1). Among these are reports of five retrospective cohort studies, three case series, and one prospective cohort study. All studies were performed in a single-institution, tertiary-care setting. Four were conducted in Canada, three in the United States, and two in Denmark. Methods of breast reconstruction are implants in one study [18], pedicled flaps (latissimus dorsi and pedicled transverse abdominis muscle) in two studies [27, 28] and free flaps (deep inferior epigastric perforator and muscle sparing transverse rectus abdominis muscle) in five studies [14–16, 25, 26] (Table 1). Two studies include patients who received either pedicled or free flap reconstruction [14, 29]. A total of 1191 patients are included in our potential analytic sample, 566 in the ERAS group, and 625 in the control group.

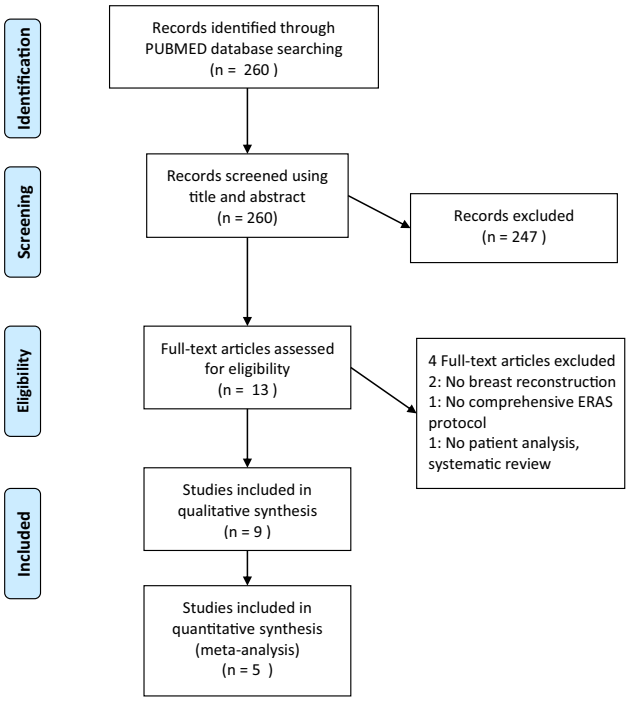


**Fig. 1** Flow diagram of search and study selection

Study characteristics are outlined in Table 1. The predominant reconstruction timing is delayed rather than immediate, and most cases are bilateral.

### Risk of bias and quality score

There are no randomized controlled trials included in our analysis. Most studies are characterized as having "fair" methodological quality according to our instrument. This is reflected in a median score of 16 points (range 14–18). Weaknesses in study design included insufficient blinding of subjects (9/9 studies), non-contemporaneous recruiting of subjects (7/9 studies), retrospective bias (8/9 studies), and lack of pre-hoc power analysis (9/9 studies).

### Current state of ERAS in clinical practice

Although a number of interventions have been formally proposed by the ERAS Society, variable implementation is observed [17]. Using categories consistent with society guidelines [17], the common themes are preoperative consultation, multimodal analgesia, nausea and vomiting prophylaxis, venous thrombosis prophylaxis, intraoperative analgesia, and targeted discharge planning (Table 2). The latter varies according to the type of reconstruction. Less commonly used ERAS elements include early feedings, perforator mapping in free flaps, minimization of hypothermia, and a priori wound management strategy. Detailed descriptions of the ERAS pathway elements implemented across studies are provided in supplemental data file 2.

### Impact on opioid consumption

Opioid use while in hospital is reported in five studies, and outcomes for the respective 623 patients are pooled [14, 15, 26, 28, 29] (Table 3). ERAS pathways significantly reduce total opioid use, mean difference (MD) − 183.96, 95% CI − 340.27 to − 27.64, $p = 0.02$ (Fig. 2). This is a medium effect size, given standardized mean difference (SMD) − 0.68, 95% CI − 1.11 to − 0.25. However, there is considerable heterogeneity between studies ($I^2 = 95\%$), mitigated via subgroup analysis according to the dominant reconstructive procedure (pedicled versus free flaps). This sub-grouping is justified because pain outcomes for these procedures are likely to be different. Repeat analysis including predominantly free flap reconstruction demonstrates a greater opioid reduction with ERAS, MD -248.13, 95% CI − 387.95 to − 108.32, $p < 0.001$, $I^2 = 69\%$ (Fig. 2b). This subgroup still represents a medium effect size, and it is clinically significant at the lower limit of the confidence interval, a reduction of over 100 morphine equivalent doses. The Davidge et al. study included only pedicled reconstructions, demonstrating a significant reduction in opioid use among ERAS patient

**Table 1** Characteristics of included studies

| Author, year, design | Setting, country | Type of surgery (C/ERAS) | Timing | Laterality | Age (mean, SD) | Control/ERAS (N) | MD&B score, quality |
|---|---|---|---|---|---|---|---|
| Afonso (2017) [29], retrospective cohort | Tertiary center, United States | DIEP: 28/28<br>MS-TRAM: 16/14<br>TRAM: 5/0 | Control: IBR 29 (59%) DBR 20 (41%)<br>ERAS: IBR 30 (71%) DBR 12 (29%) | Control: Uni 29 (59%) Bi 20 (41%)<br>ERAS: Uni 21 (50%) Bi 21 (50%) | Control: 51<br>ERAS: 50 | 49/42 | 18, fair |
| Astanehe (2018) [15], retrospective cohort | Tertiary center, Canada | FF | Control: IBR 23 (14%) DBR 144 (85%) IBR/DBR 2 (1%)<br>ERAS: IBR 18 (25%) DBR 40 (56%) IBR/DBR 14 (19%) | Control: Uni 64 (38%) Bi 105 (62%)<br>ERAS: Uni 27 (38%) Bi 45 (63%) | Control: 50.2 (8.2)<br>ERAS: 52.7 (7.7) | 169/72 | 16, fair |
| Armstrong (2016) [27], Case Series | Tertiary center, Canada | Pedicled TRAM: NA/27<br>Pedicled LD: NA/13 | ERAS: IBR 37 (92.5%)<br>DBR 3 (7.5%) | ERAS: Uni 38 (95%)<br>Bi 2 (5%) | ERAS: 50.5 (8.2) | NA/40 | 14, poor |
| Batdorf (2015) [14], retrospective cohort | Tertiary center, United States | DIEP: 39/60<br>MS-TRAM: 44/25<br>TRAM: 9/4 | Control: IBR 28 (30%) DBR 64 (70%)<br>ERAS: IBR 32 (36%) DBR 57 (64%) | Control: Uni 10 (20%) Bi 41 (80%)<br>ERAS: Uni 9 (18%) Bi 40 (82%) | Control: 47.5 (9.8)<br>ERAS: 48.3 (9) | 51/49 | 18, fair |
| Bonde (2015) [16], retrospective cohort | Tertiary center, Denmark | DIEP: 44/124<br>MS-TRAM: 233/53 | | | Control: 51 (median)<br>ERAS: 52/55 (median for DIEP/TRAM) | 277/177 | 14, poor |
| Bonde (2016) [25], Case Series | Tertiary center, Denmark | DIEP | | | ERAS: 52 (median) | NA/16 | 16, fair |
| Davidge (2013) [28], case series | Tertiary center, Canada | Pedicled TRAM | ERAS: IBR 17 (19%) DBR 74 (81%) | ERAS: Uni 69 (76%) Bi 22 (24%) | ERAS: 50 (8.5) | NA/91 | 15, fair |
| Dumestre (2017) [18], prospective cohort | Tertiary center, Canada | Implant | Control: IBR 90%<br>ERAS: IBR 90% | Control: Unilateral 38% Bilateral 62%<br>ERAS: Unilateral 17% Bilateral 83% | Control: 48<br>ERAS: 48 | 29/29 | 15, fair |
| Kaoutzanis (2018) [26], retrospective cohort | Tertiary center, United States | DIEP: 42/44<br>MS-TRAM: 2/0<br>SIEA: 1/0<br>PAP: 1/0<br>DIEP + MS-TRAM: 3/5<br>DIEP + SIEA: 1/0 | Control: IBR 6 (12%) DBR 44 (88%)<br>ERAS: IBR 1 (2%) DBR 49 (98%) | Control: Uni 27 (54%) Bi 23 (45%)<br>ERAS: Uni 28 (56%) Bi 22 (44%) | Control: 51 (10)<br>ERAS: 51.9 (8.9) | 50/50 | 17, fair |

*ERAS* enhanced recovery after surgery, *C* control group or standard treatment arm, *MD & B* modified downs and black, *FF* free flap; *DIEP* deep inferior epigastric perforator flap, *IBR* immediate breast reconstruction, *MS-TRAM* muscle sparing transverse rectus abdominis muscle flap, *DBR* delayed breast reconstruction, *TRAM* transverse rectus abdominis muscle flap, *IBR/DBR* combined immediate and delayed breast reconstruction, *LD* latissimus dorsi flap, *Uni* unilateral breast reconstruction, *Bi* bilateral breast reconstruction

**Table 2** Components of implemented ERAS protocols

| Paper | Preadmission counseling | Perioperative fasting | VTE prophylaxis | Antimicrobial prophylaxis | Nausea and vomiting prophylaxis | Intraoperative analgesia | IVF | Multimodal analgesia (excluding opioids) | Preop opioids use | Postop opioid use[a] |
|---|---|---|---|---|---|---|---|---|---|---|
| Afonso [29] | + | + | − | − | + | + | + | − | − | − |
| Astanehe [15] | − | + | + | + | + | + | + | + | + | − |
| Armstrong [27] | + | − | + | − | + | + | − | + | + | ± oxycodone |
| Batdorf [14] | + | + | + | + | + | + | + | + | − | − |
| Bonde 2015 [16] | − | + | + | − | − | + | + | − | − | − |
| Bonde 2016 [25] | + | − | + | + | − | + | − | + | − | − |
| Davidge [28] | + | − | + | − | + | + | − | + | ± oxycodone | − |
| Dumestre [18] | + | + | − | + | + | + | − | + | + | − |
| Kaoutzanis et al. [26] | + | + | + | + | + | + | + | + | − | − |

| Paper | Lines, Tubes, Drains | Early feeding | Early Mobilization | Flap Monitoring | Discharge POD Goal | Discharge Criteria |
|---|---|---|---|---|---|---|
| Afonso [29] | + | + | + | − | POD3 | − |
| Astanehe [15] | + | + | + | + | POD4 | − |
| Armstrong [27] | − | − | + | − | POD1 | PADS discharge criteria assessment score based on vital signs, surgical bleeding, pain, activity, nausea, and vomiting |
| Batdorf [14] | + | + | + | + | POD3/POD4 | Discharge criteria: absence of early comp, tolerance of solid diet, ind mobilization + ambulation, adequate pain control w/oral analgesia |
| Bonde 2015 [16] | + | − | + | + | POD4 | − |
| Bonde 2016 [25] | + | + | + | + | POD2/3 | Mobilized > 4 h/day, regular diet, drains removed, pain < 4, able to shower and use toilet, GI function, flap monitoring discontinued |
| Davidge [28] | − | − | − | − | POD1 | − |
| Dumestre [18] | − | − | − | − | POD1/2 | − |
| Kaoutzanis et al. [26] | + | + | + | − | POD1/2 | Sufficient oral intake w/o N/V, adequate ambulation, good urine output, satisfactory pain control w/oral analgesics |

*VTE* venous thromboembolism, *IVF* intravenous fluid, *POD* Post-operative day, *N/V* Nausea and vomiting

[a]Did not include opioids for breakthrough pain. Only scheduled opioids included

**Table 3** Post-operative pain

| Paper | Outcome definition | Unit of measurement | Control (mean, SD) | ERAS (mean, SD) |
|---|---|---|---|---|
| Afonso et al. [29] | Opioid consumption | Mg of IV morphine | 70.5 | 46 |
| | Use of PCA | OME (conversion) | 141 (815.4) | 92 (357.8) |
| | | Percentage | 98% | 21% |
| | Pain scores | Likert Pain Scale | | |
| | OR end − 4 h | | 4 | 4.75 |
| | 4–8 h | | 3 | 3 |
| | 8–12 h | | 3 | 3.5 |
| | 12–18 h | | 4 | 4.5 |
| | 18–24 h | | 4 | 6 |
| | 24–48 h | | 5 | 6 |
| | 48–72 h | | 5 | 6 |
| Astanehe et al. [15] | Quantity of parenteral narcotics used during first 3 postop days (POD0-3) | Mg of IV morphine | 131 (125) | 44 (45) |
| | | OME (conversion) | 330 (310) | 110 (110) |
| | Pain scores | Visual Analogue Scale | | |
| | POD0 Pain | | 2.8 (2) | 1.7 (1.4) |
| | POD0-3 Pain Avg | | 3 (1.6) | 2.3 (1.3) |
| Armstrong et al. [27] | Pain Scores | Visual Analogue Scale | | |
| | POD1 | | N/A | 3.8 (2.2) |
| | POD2 | | | 4.1 (2.4) |
| | POD4 | | | 3.4 (1.6) |
| | POD7 | | | 2.5 (1.2) |
| Batdorf et al. [14] | Opioid use in the first 3 postop days | Mg of OME | 574.3 (435.8) | 167.3 (128) |
| | Use of PCA | Percentage | 96.1% | 20.5% |
| | Pain Scores | Visual Analogue Scale | | |
| | Hospital Admission | | 4.7 (3.1) | 3.3 (2.2) |
| | 4 h | | 4.4 (2.6) | 3.5 (2.1) |
| | 8 h | | 4.5 (2.4) | 3.8 (2.2) |
| | 12 h | | 4.2 (2.2) | 3.8 (1.9) |
| | 18 h | | 4.2 (2) | 3.8 (2.1) |
| | 24 h | | 4.1 (1.7) | 3.3 (1.9) |
| | 48 h | | 3.4 (1.8) | 3.2 (1.9) |
| | 72 h | | 3.1 (1.5) | 3.4 (1.4) |
| Davidge et al. [28] | Total in hospital opioid use | Mg of morphine equivalents | 75.4 (31.3) | 47 (23) |
| Kaoutzanis et al. [26] | Opiate use within 45 days from index operation Use of PCA | Mg of OME | 276.3 (median) | 67.5 (median) |
| | | Percentage | 100% | 6% |

*ERAS* enhanced recovery after surgery, *PCA* patient-controlled analgesia, *OME* oral morphine equivalents

[28]. The lower limit of the confidence interval is 15.94; this is likely not clinically significant. There is a significant difference between subgroups, $p = 0.002$.

## Impact on length of stay

Length of stay is reported in eight studies, and outcomes for 1151 patients are pooled [14–16, 18, 25, 26, 28, 29] (Table 4). Results are consistent between studies. ERAS protocol significantly reduces length of stay, MD -1.58, 95% CI − 1.99 to − 1.18, $p < 0.00001$, $I^2 = 65\%$ (Fig. 3). This is a large effect, SMD − 0.95, 95% CI − 1.29 to − 0.62. It is also clinically significant, because the lower limit of the confidence interval represents a length of stay one day shorter versus standard protocol. Moderate heterogeneity is again present and explored with subgroup analysis of patient comorbidities influencing length of stay. The 2016 Bonde study [25] was removed from this analysis for the following reasons: (a) absence of a control group and (b) patients were already included in a preceding 2015 article [16] ("double counting"). Repeat analysis demonstrated a greater reduction in LOS, MD − 1.78, 95% CI − 2.07 to − 1.48, $p < 0.001$, $I^2 = 6\%$ (Fig. 3b). This represents approximately a day and half at the upper end of

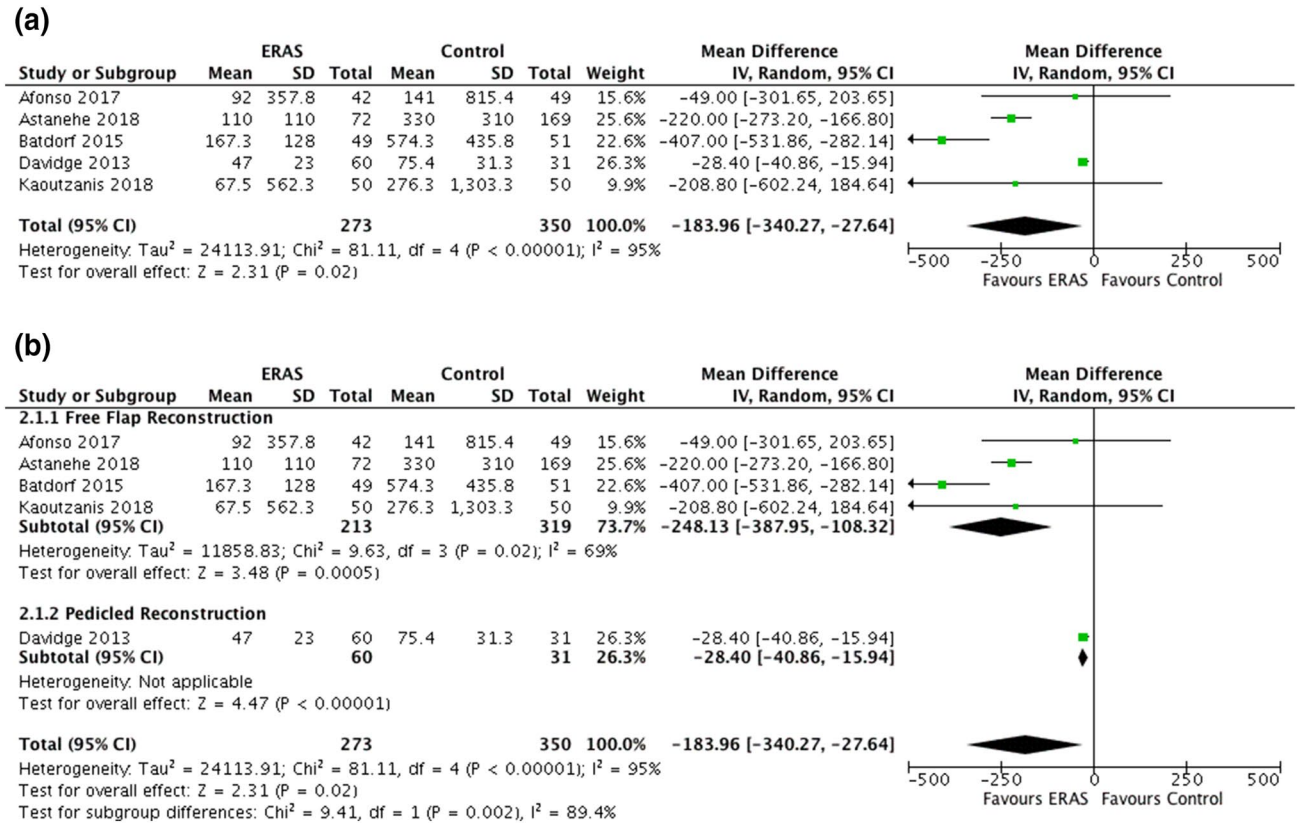


**Fig. 2** **a** Total opioid use for ERAS versus traditional recovery pathway. **b** Subgroup analysis of total opioid use for ERAS versus traditional recovery pathway

**Table 4** Length of stay

| Paper | Outcome definition | Unit of measurement | Control (mean, SD) | ERAS |
|---|---|---|---|---|
| Afonso et al. [29] | LOS | Days | 5 (2.7) | 4 (2.7) |
| Astanehe et al. [15] | LOS | Hr | 158 (29) | 116 (29) |
| | | Days | 6.6 (1.2) | 4.8 (1.2) |
| Batdorf et al. [14] | LOS | Days | 5.5 (2.4) | 3.9 (2.3) |
| Bonde 2015 [16] | LOS | Days | 6.2 (1.7) | 3.1 (0.3) |
| Bonde 2016 [25] | LOS | Days | 7.4 (1.1) | 6.2 (1.7) |
| Davidge et al. [28] | LOS | Hr | N/A | 38.7 (27.6) |
| | | Days | | 1.6 (1.15) |
| Dumestre et al. [18] | LOS | Nights in hospital | 1.6 | 0 |
| Kaoutzanis et al. [26] | LOS | Mean nights in hospital | 4.7 (2.3) | 3 (0.6) |

*ERAS* enhanced recovery after surgery, *LOS* length of stay

the confidence interval. There is a significant difference between subgroups, $p = 0.006$.

## Post-operative pain scores

Studies cannot be pooled given methodological heterogeneity in the timing of pain assessment, and high subjectivity inherent with numerical rating scales (Table 3). Afonso et al. report lower maximum pain scores on POD1-2 in the traditional recovery cohort compared to ERAS recipients [29]. Maximum pain scores after POD2 are not significantly different between the two groups. On the other hand, Batdorf et al. report lower pain scores in the ERAS group at 24 h post-operatively compared to the traditional recovery group [14]. Astanehe et al. [15] also demonstrate consistently reduced mean pain scores with ERAS in patients who

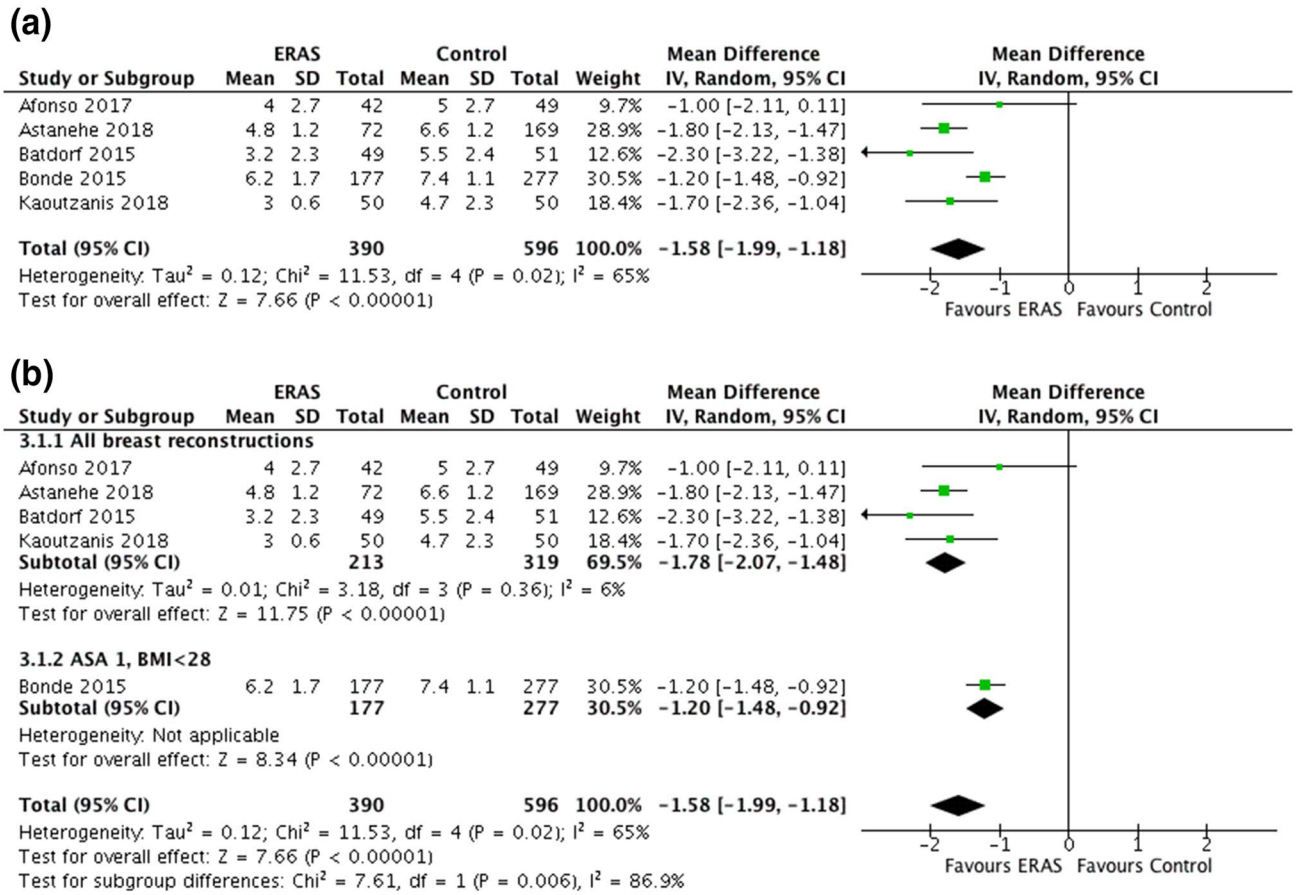


**Fig. 3** **a** Length of stay for ERAS versus traditional recovery pathway. **b** Subgroup analysis of length of stay for ERAS versus traditional recovery pathway

underwent autologous microvascular reconstruction compared to the traditional recovery groups (Table 3). Armstrong et al. show low mean pain scores, over time, after implementing ERAS pathway; however, control group scores are not available for comparison [27]. Multiple regression analysis identifies preoperative pain, type of surgery, and current use of anxiolytic and/or antidepressant medications as independent predictors of post-operative pain.

## Patient safety—complications

Most studies evaluated post-operative complications in order to assess the safety of enhanced recovery pathways in patient undergoing breast reconstruction (Table 5). No important differences are identified between ERAS and traditional recovery groups. Analysis includes overall major complications, readmission, hematoma, and infection. Major complications are reported at 30–45 days post-operatively for 1086 patients from six studies [15, 16, 18, 26, 29]. There is no difference in overall major complications between patients managed with ERAS versus traditional pathways, OR 0.86, 95% CI 0.55–1.34, $p=0.51$, $I^2=31\%$ (Fig. 4). Unplanned readmissions are reported in four studies [14, 15, 26, 29] entailing 532 patients; there is no difference between ERAS and traditional pathways, OR 1.17, 95% CI 0.52–2.62, $p=0.71$, $I^2=0\%$ (Fig. 5). Post-operative hematomas are reported in six studies [14–16, 18, 26, 29], entailing 1086 patients; there is no difference between ERAS and traditional pathways, OR 1.12, 95% CI 0.67–1.86, $p=0.68$, $I^2=0\%$ (Fig. 6). Post-operative infections are reported by six studies [14–16, 18, 26, 29], with 1086 respective patients and no difference between ERAS and traditional pathways, OR 1.27, 95% CI 0.67–2.42, $p=0.46$, $I^2=14\%$ (Fig. 7).

In the Batdorf et al. study, 30 days post-operative complication rates are similar for the ERAS and traditional recovery groups, except for a higher rate of skin flap cellulitis in the ERAS group (20% vs 6%; $p=0.03$) [14]. Additionally, there are three partial and two complete flap losses reported in the ERAS group compared to 0 and 1 in the traditional pathways group, respectively; this is not significantly different. Finally, Kaoutzanis et al. demonstrate no difference in major and minor complications among enhanced and traditional recovery groups, with the exception of delayed wound healing in the ERAS group (36% vs. 16%, $p=0.02$) [26].

**Table 5** Post-operative complications

| Paper | Total outcomes | Control (%) | ERAS (%) | Specific complications reported | Control (%) | ERAS (%) | Definitions/Comments |
|---|---|---|---|---|---|---|---|
| Afonso et al. [29] | 30 Day complication rates | 22 | 9.5 | (1) Seroma/hematoma | (1) 8 | (1) 5 | |
| | | | | (2) Cellulitis/wound infection | (2) 2 | (2) 0 | |
| | Unplanned reoperations | 10 | 5 | (3) Mastectomy flap necrosis | (3) 4 | (3) 2 | |
| | | | | (4) Flap loss | (4) 0 | (4) 2 | |
| | Hospital readmissions | 2 | 2 | (5) Medical complications (DVT, PE, PNA) | (5) 12 | (5) 0 | |
| Astanehe et al. [15] | 30-Day complication rates | 9.5 | 8.3 | (1) Hematoma requiring evacuation | (1) 2.4 | (1) 4.2 | |
| | Hospital readmissions | 1.2 | 1.4 | (2) Infection requiring admission and IV abx | (2) 0.6 | (2) 1.4 | |
| | | | | (3) Vascular compromise requiring repair | (3) 5.9 | (3) 2.8 | |
| | | | | (4) Flap loss | (4) 0 | (4) 0 | |
| | | | | (5) Medical complications (DVT/PE) | (5) 0.6 | (5) 0 | |
| Batdorf et al. [14] | 30-Day major complication rates | 22 | 33 | (1) Seroma/Hematoma (breast/donor) | (1) 8/6 | (1) 6/2 | Major Complication: hospital readmission, partial or complete flap loss, unplanned reoperation, DVT, PE) |
| | Unplanned reoperations (in 30 days) | 10 | 16 | (2) Cellulitis/Infection/Abscess (b/d) | (2) 6/12 | (2) 24/18 | |
| | | | | (3) Wound dehiscence | (3) 6 | (3) 6 | |
| | | | | (4) Flap loss | (4) 2 | (4) 10 | |
| | | | | (5) Medical complications (PNA, UTI, DVT, PE) | (5) 8 | (5) 2 | |
| Bonde 2015 [16] | Total complications | 21.8 | 22.7 | (1) Hematoma | (1) 6.5 | (1) 7.9 | Increased hematoma in ERAS thought to be due to use of COX-II inhibitor. Incidence decreased after change to NSAID |
| | | | | (2) Infection | (2) 3.4 | (2) 1.7 | |
| | | | | (3) Flap loss | (3) 5.4 | (3) 5.8 | |
| | | | | (4) Medical complications (UTI, PNA) | (4) 2.4 | (4) 2.3 | |
| Bonde 2016 [25] | Total complications | N/A | 12.5 | (1) Seroma | N/A | (1) 6.25 | |
| | Unplanned reoperations | | 0 | (2) Partial flap necrosis | | (2) 6.25 | |
| | | | | (3) Medical Complications | | (3) 0 | |
| Dumestre et al. [18] | Total complications | 21 | 17 | (1) Seroma/Hematoma | (1) 6 | (1) 4 | Major: hematoma, cellulitis w/abx, cellulitis w/explantation<br>Minor: partial wound necrosis, seroma, minor cellulitis |
| | | | | (2) Cellulitis/Wound Infection | (2) 6 | (2) 6 | |
| | Major complications | 0 | 6% | (3) partial wound necrosis/flap necrosis | (3) 19 | (3) 9 | |
| | Minor complications | 21 | 11 | (4) ER Visit within 30 days | (4) 13.8 | (4) 10.3 | |

**Table 5** (continued)

| Paper | Total outcomes | Control (%) | ERAS (%) | Specific complications reported | Control (%) | ERAS (%) | Definitions/Comments |
|---|---|---|---|---|---|---|---|
| Kaoutzanis et al. [26] | Rate of pts with complications | 54 | 60 | (1) Seroma/Hematoma | (1) 10 | (1) 0 | Major: related directly to index admission and required hospital readmission or reoperation within 45 days from index operation, partial, or complete flap loss |
| | | | | (2) Cellulitis/Wound Infection | (2) 6 | (2) 4 | |
| | Unplanned reoperations | 10 | 4 | (3) Wound dehiscence/delayed wound healing | (3) 10 | (3) 0 | |
| | Hospital Readmissions | 8 | 4 | (4) Flap compromise/loss | (4) 6 | (4) 2 | |
| | Major complications | 16 | 6 | (5) Medical complication | (5) 0 | (5) 2 | |
| | Minor complications | 48 | 56 | (6) ER Visits | (6) 8 | (6) 10 | |

*ERAS* enhanced recovery after surgery, *DVT* deep vein thrombosis, *PE* pulmonary embolus, *PNA* pneumonia, *UTI* urinary tract infection, *ER* emergency room, *Abx* ANTIBIOTIC

## Discussion

In this meta-analysis, we demonstrate statistically significant reductions in post-operative LOS and opioid consumption following ERAS implementation in recipients of breast reconstruction. Of equal importance, patient safety is not shown to be compromised, as there are no meaningful differences in complications. This added *value* of the ERAS program is consistent with published meta-analysis findings in other surgical specialties such as liver surgery [30], colorectal surgery [11], pancreatic surgery [31], orthopedic surgery [32], and bariatric surgery [33]. Our results fill a gap in the extant literature because of the dearth of published systematic reviews analyzing the utility of ERAS in breast reconstruction [34].

ERAS is a systematic, protocol-driven approach to the management of surgical patients. Core tenets of the ERAS pathway have been outlined previously and are positioned along the entire surgical care continuum: pre-, intra-, and post-operative phases [1]. Examples include but are not limited to the following: preoperative counseling, goal-directed fluid resuscitation, opioid-sparing regimens for pain control and early ambulation [1, 17]. The bulk of the available literature investigating the safety and efficacy of ERAS pathways in breast reconstruction is centered on free flap recipients. The resource-intensive nature, longer inpatient time horizon, and higher cost structure, relative to implant-based reconstruction, make this population uniquely suited for the continuous audit and protocol-driven care processes inherent to ERAS.

We believe that our study findings will be of great interest to the many stakeholders involved with the delivery of surgical care: patient groups, payers, hospital management, and policy makers. Length of stay reduction, a reliable proxy for hospital resource utilization and costs [35, 36], is a performance metric that is germane to health care delivery today. An isolated single-center analysis involving 50 ERAS cases and 50 traditional pathway cases projected the savings from ERAS directed-care to be $279,258 per annum for free flap breast reconstruction [26]. An estimated $4400 savings per ERAS patient was determined due to a reduction in LOS by 1.7 days resulting in a total reduction of 108 inpatient days. With health-related expenditures rising uncontrollably in the US (17.8% of the 2016 gross domestic product) [37], the main themes of current discourse are how to reimburse for the quality and efficiency of services delivered ("value-based care") in lieu of volume and intensity of services ("fee-for-service").

Our reduced LOS among ERAS recipients is commensurate with the lower OME consumption observed in this group. Intuitively, this makes sense because inadequate post-operative pain management is an established driver

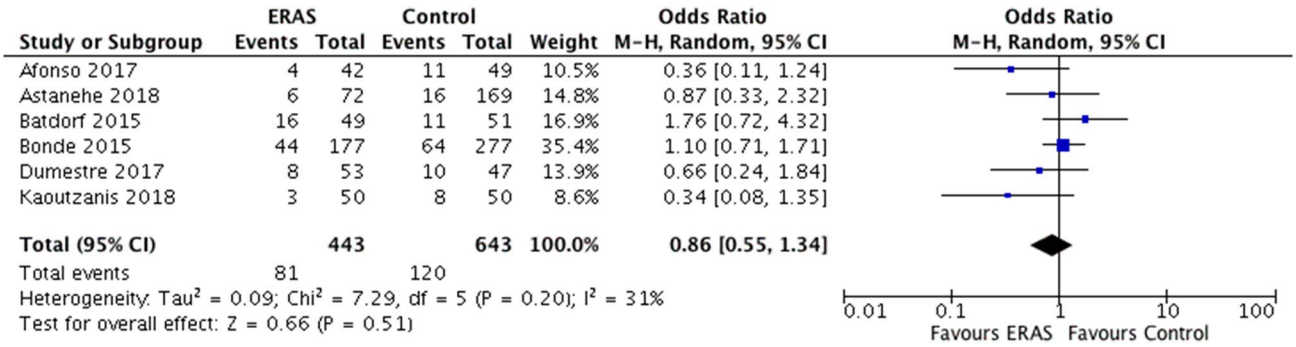


**Fig. 4** Overall major complications for ERAS versus traditional recovery pathway

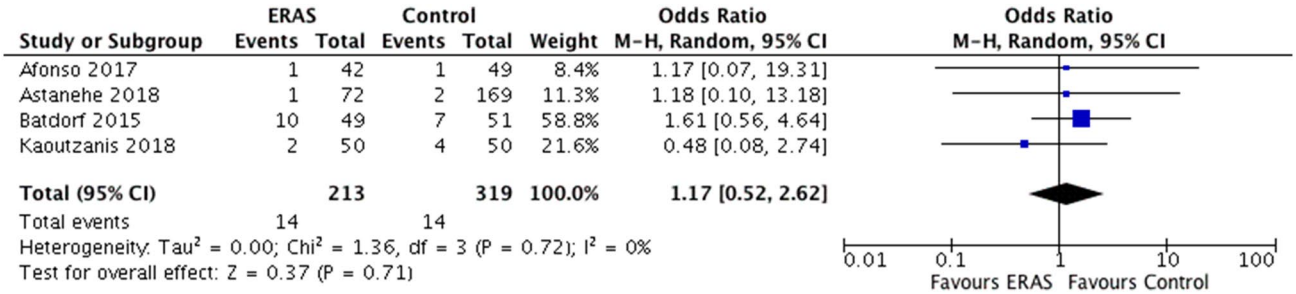


**Fig. 5** Readmissions for ERAS versus traditional recovery pathway

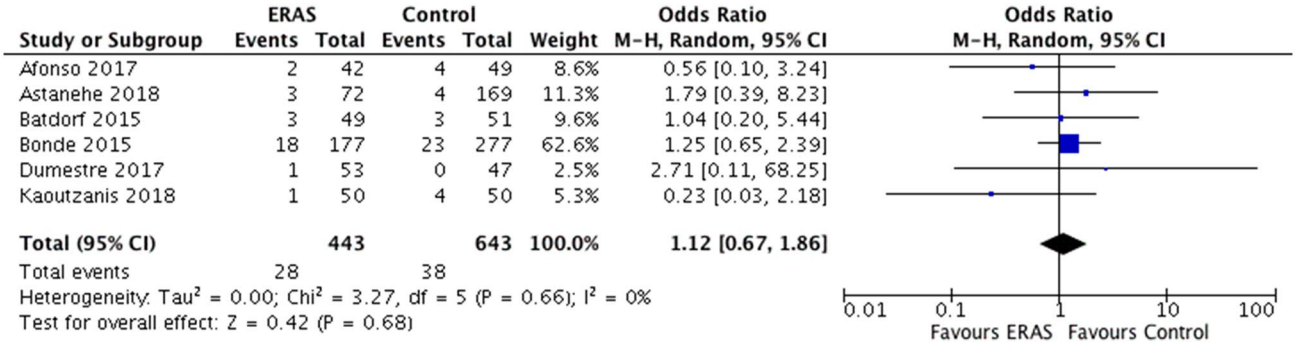


**Fig. 6** Hematomas for ERAS versus traditional recovery pathway

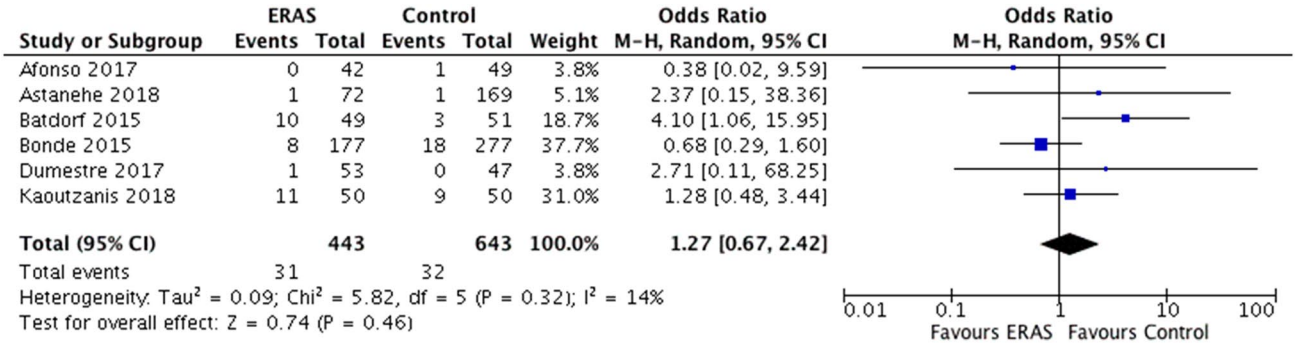


**Fig. 7** Infections for ERAS versus traditional recovery pathway

of prolonged hospital stay following breast reconstruction [38]. Furthermore, the ongoing US prescription opioid crisis adds a powerful public health dimension to the potential *value* of ERAS implementation. In 2015, there were over 33,000 deaths attributable to an opioid overdose [39]. Accompanying these alarming data is robust evidence showing a positive correlation between average daily OME and both opioid-related mortality and dependence [40]. The use of multimodal perioperative analgesia, characteristic of ERAS, might be a viable strategy for lowering systemic opioid use post-operatively and better physician stewardship of opioid prescriptions [39].

This potential for ERAS to optimize perioperative resource allocation while generating savings and maintaining quality, makes a compelling case for it to become the standard of care in free flap reconstruction. However, despite mounting evidence of the benefits of ERAS, it is clear that gaps in education and execution still persist [1]. Inconsistent and incomplete implementation of *all* elements of an archetypal breast reconstruction ERAS program [17] was observed across the nine included studies (Table 2). Study-specific pathways were instead observed [34]. This might reflect a need for greater institutional support for these programs in order to ensure their sustainability and optimal performance.

Regardless of the level of hospital administration or local leadership "buy-in," updating perioperative practice is a notoriously arduous process [41]. However, there is evidence to show that adopting a structured ERAS implementation plan in step with provider education might generate improved and sustained front-line compliance with all components of the ERAS pathway [1]. Additionally, level 1 evidence by way of randomized controlled clinical trials is also lacking and might present a barrier to widespread, complete dissemination. This is because their absence may call to question the veracity of the evidence base with which we are updating current clinical practice. A systematic examination of the economic benefits of ERAS pathways, i.e., healthcare-related cost savings, would also be a worthwhile area of future study. Lastly, the medium- and long-term outcomes of ERAS-facilitated surgical recovery are still largely unknown: cancer-specific 5 year mortality, patient satisfaction, aesthetic outcomes, and long-term complications.

Our review has several limitations that should be acknowledged. Across the included studies, we encountered considerable variations in surgical technique, unbalanced patient comorbidities between analytic groups, varied reconstruction techniques, retrospective study designs, and small sample sizes. Furthermore, despite our attempts to identify as many qualified studies as possible, only nine studies fulfilled inclusion criteria. There are numerous sources of clinical heterogeneity identified between studies: ERAS protocol elements, type of reconstruction (pedicled versus free tissue), and patient comorbidities. While heterogeneity was incorporated into random effects model throughout analyses, these factors likely explain the wide confidence intervals observed.

## Conclusion

The implementation of ERAS programs is associated with improvements in the outcomes of post-mastectomy reconstruction. Subsequent implications for clinical practice are manifold. The shortened recovery times, with no increased risk of readmissions, will positively impact cost efficiency and institutional productivity given the fact that breast reconstruction, especially that involving autologous tissue, is a resource-intensive enterprise [42]. Reduced LOS will also improve patient access to breast reconstruction [42]. Finally, the demonstrated superiority of ERAS protocols in reducing post-operative opioid consumption points to a sustainable path for improved surgeon stewardship of prescription narcotics.

Our results can also inform future research efforts, as there are little data outlining the operational challenges associated with ERAS implementation. Future studies are still needed to elucidate the long-term clinical outcomes and economic benefits associated with ERAS implementation in this patient population.

### Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Research involving human participants and/or animals** This article does not contain any studies with human participants or animals performed by any of the authors.

**Informed consent** Not applicable.

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