

# Enhanced recovery after surgery for breast reconstruction—a systematic review and meta-analysis

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**Background:** Enhanced recovery after surgery (ERAS) pathways are commonly used in various surgical specialties and are increasingly adopted in the field of reconstructive surgery. This systematic review and meta-analysis aim to review current literature on ERAS protocols for both autologous and implant-based breast reconstruction surgery outcomes and summarize key protocol components.

**Methods:** PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), EMBASE, CINAHL, and Web of Science databases were searched systematically for studies published before 31 March 2023 with data on outcomes after implementation of ERAS protocols in breast reconstruction surgery. Primary outcomes include length of stay (LOS), readmission and reoperation rates, total opioid use, and postoperative complications. Secondary outcomes include postoperative pain scores and cost-savings. Risk of bias assessment and meta-analysis were subsequently performed using a random effects model via the inverse variance and Mantel-Haenszel methods.

**Results:** Initial database search identified 582 studies, out of which 24 original articles were included with a total of 4,377 patients. ERAS protocol implementation significantly reduces LOS [mean difference, -1.06 days; 95% confidence interval (CI): -1.36 to -0.77;  $P < 0.00001$ ;  $I^2 = 94\%$ ] and total opioid use [mean difference, -215.36 mg of oral morphine equivalent (OME); 95% CI: -272.48 to -158.24;  $P < 0.00001$ ;  $I^2 = 95\%$ ] as compared to traditional recovery pathways. No significant difference was observed in readmission and reoperation rates, and postoperative complication rates.

**Conclusions:** The implementation of ERAS protocols in breast reconstruction surgery significantly reduces LOS in patients undergoing autologous reconstructions without an increase in postoperative complication rates. In addition, ERAS pathways also lead to lower opioid consumption and possible healthcare cost-savings, and hence provide better outcomes as compared to traditional recovery pathways for breast reconstruction patients.

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**Keywords:** Enhanced recovery after surgery (ERAS); breast reconstruction; length of stay (LOS); opioid use; postoperative complications

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## Introduction

Breast cancer remains a major health concern and burden for women, being the most common malignancy diagnosed in women (1), with 2.3 million women diagnosed with the disease yearly and 685,000 deaths from breast cancer in 2020 globally (2). It is also estimated that one in eight women will develop breast cancer in their lifetime, therefore advancements in its treatment are likely to benefit many (3). Mastectomy is a common definitive treatment option for non-metastatic breast cancer patients (4) but can have a negative impact on patients' body image and mental well-being (5). Post-mastectomy breast reconstruction provides improved cosmetic and psychological outcomes and an improvement in quality of life (6). Breast reconstruction has evolved over the years and become increasingly popular with women undergoing mastectomy (7). A study in the United States showed an increase in nationwide post-mastectomy autologous breast reconstruction rate from 26.6% in 2009 to 56.5% in 2016 (8). Despite the benefits and increasing popularity, breast reconstruction remains a complicated and major procedure with possible complications such as hematomas, infections, implant failure, and flap loss (9). As such, breast reconstruction surgeries are often costly for patients and involve a long recovery period (10).

One way to improve outcomes and optimize recovery from breast reconstructions is through the implementation of an enhanced recovery after surgery (ERAS) pathway. First described in 1997 by Kehlet *et al.* (11), ERAS is a multimodal, multidisciplinary approach that involves preoperative, perioperative, and postoperative care optimization with the aim to improve surgical outcomes and reduce morbidity and time in hospital after major surgeries (12). Common aspects of ERAS pathways include preadmission counseling, preoperative carbohydrate loading and reduced fasting, antimicrobial and thromboembolism prophylaxis, multimodal analgesia, early mobilization and diet (13). ERAS protocols have been adopted in various different surgical specialties, including orthopedic surgery (14,15), colorectal surgery (13,16,17), liver surgery (18,19),

thoracic surgery (20), and urogynecologic surgery (21,22). The plastic and reconstructive surgery field has also started to incorporate ERAS pathways into recommendation guidelines, in particular for breast (23) and head and neck reconstruction (24).

While there have been previous reviews on the effectiveness of ERAS guidelines in breast reconstruction, it is still a relatively new advancement in the field and there may not be sufficient data in the previous reviews to reach a definitive conclusion on the effectiveness of ERAS pathways in breast reconstruction (25). The latest systematic review and meta-analysis on ERAS pathways in breast reconstruction by Tan *et al.* (26) analyzed data up to May 2019 but did not include studies on implant-based breast reconstruction and analyze data on total opioid consumption. While Tan *et al.* (27) included studies on implant-based reconstructions and analyzed data up to May 2018, repeated studies by the same author in the same institution were included which may have affected the reliability of statistical analysis and results. Offodile *et al.* (28) on the other hand only included six studies for quantitative analysis and included repeat studies under the same institution as well. Previous studies focused mainly on effectiveness of ERAS protocols in improving outcomes for breast reconstruction but there was a lack of focus on the impact and importance of individual components of ERAS pathways, which is an area we will be addressing in our study. While there are previously published guidelines on ERAS protocols for breast reconstruction (23), there are no standardized guidelines across different institutions worldwide. Therefore, our study aims to serve as an update to the existing systematic reviews and meta-analyses, as well as to identify important individual components in ERAS pathways for both autologous and implant-based breast reconstruction to provide more information to allow for better standardization of future institutional guidelines and recommendations. We present this article in accordance with the PRISMA reporting checklist (<https://abs.amegroups.com/article/view/10.21037/abs-23-44/rc>).

## Methods

### *Search strategy*

An electronic literature search was conducted based on the 2020 PRISMA statement (29). The search was conducted across five databases, PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), EMBASE, CINAHL, and Web of Science, from database inception to 31 March 2023. The following keywords were used: “enhanced recovery after surgery”, “critical pathways”, “breast reconstruction”, “mammoplasty”, “breast flap”, and “breast implants”.

### *Inclusion and exclusion criteria*

Inclusion criteria included studies containing original data comparing outcomes of adult female patients undergoing breast reconstruction with ERAS protocols and traditional recovery after surgery (TRAS) protocols. Studies on both autologous and implant-based breast reconstruction were included and outcomes analyzed must involve at least one primary outcome—length of stay (LOS), postoperative opioid use, reoperation rates, readmission rates, or postoperative complications. Non-English articles, animal studies, conference abstracts, oral or poster presentations and studies that did not detail ERAS protocol components were excluded. If an institution published more than one study, the most recent article was selected for analysis.

### *Data extraction*

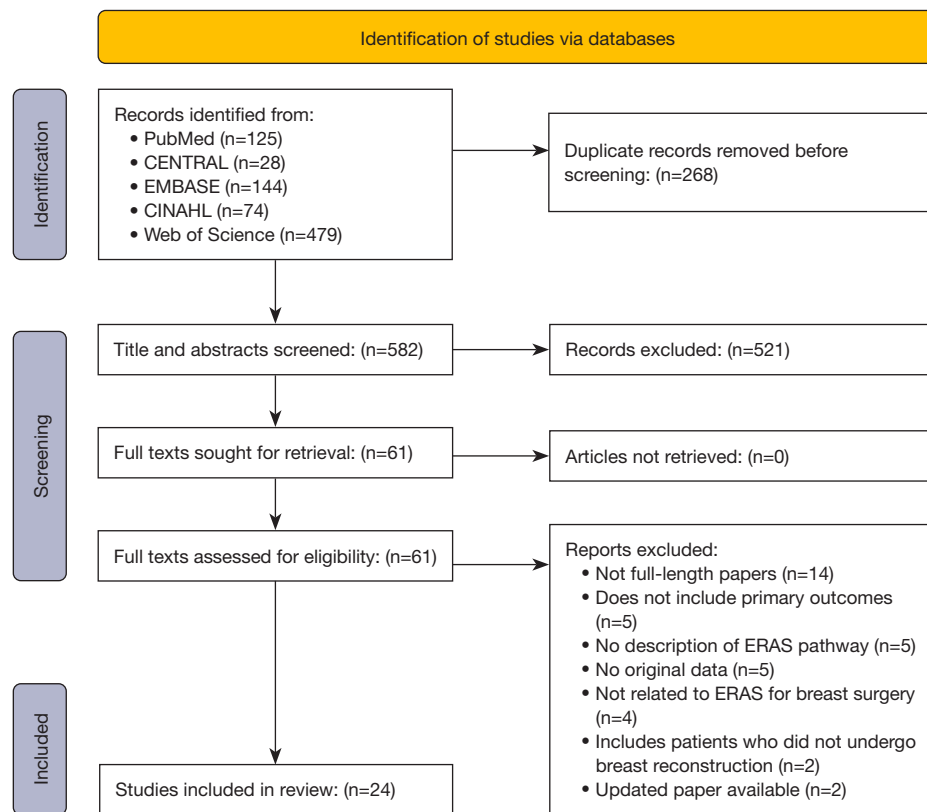
Two separate reviewers screened through the title and abstracts of potentially relevant articles identified in the initial search. Full texts of relevant studies were reviewed by the two authors independently and any differences in opinions were resolved by a third author. Study characteristics collected include study design, year of publication, country, type of reconstruction, timing, laterality, number of patients, and age. Primary outcomes of interest included LOS, readmission and reoperation rates, postoperative opioid use, and postoperative complications. Secondary outcomes included postoperative pain scores and cost savings. Individual components of ERAS protocols from the different studies were also recorded. In addition, data was not extracted from transition groups in which the ERAS protocol was partially implemented to reduce the heterogeneity of the statistical analysis results. Furthermore, opioid use data was converted to units of mg

of oral morphine equivalents (OMEs) from intravenous morphine equivalents (IVMEs) using a ratio of 1:3 based on the Australian and New Zealand College of Anesthetists (ANZCA) guidelines (30).

Postoperative complications were categorized according to the Clavien-Dindo classification into major and minor complications (31). Major complications were defined as complications requiring surgical, endoscopic, or radiological intervention, or life-threatening and require intensive care unit management. Examples include hematomas, total and partial flap loss, mastectomy skin flap necrosis, wound dehiscence, pulmonary embolism, and deep vein thrombosis. On the other hand, minor complications were defined as complications which do not require surgical, endoscopic, or radiological intervention, and may or may not require pharmacological treatment. This includes seromas, cellulitis, urinary tract infections and pneumonia. Flap-related complications such as complete and partial flap loss were also studied in detail. Implant-related complications were however not reported in our review as only one of the three studies on implant-based reconstruction reported implant-related complications (32).

### *Statistical analysis*

All statistical analysis was performed using Review Manager [RevMan (computer program), version 5.4. The Cochrane Collaboration, 2020] Mean differences and odds ratio are reported with 95% confidence intervals (CIs) and results were considered to be statistically significant when  $P < 0.05$ . Interquartile ranges and 95% CIs were used to approximate the standard deviations (SDs) required for meta-analysis based on formulas provided in the Cochrane Handbook if required (33). Data from studies which did not report SD or CI values for continuous outcomes (LOS and total opioid use) were not included in the meta-analysis due to insufficient information to calculate the Forest plots (34–36). The inverse variance method and random effects model were used to calculate the mean differences for LOS and total opioid use due to heterogeneity across studies. On the other hand, the Mantel-Haenszel method and fixed effects model were used to calculate the odds ratios for readmission and reoperation rates and postoperative complications. A random effects model was used for all outcomes because of the heterogeneity across the studies. Statistical heterogeneity was determined based on the  $I^2$  measurement, with  $I^2 < 50\%$  as low, 50–75% as medium, and  $> 75\%$  as high heterogeneity.



**Figure 1** PRISMA flow diagram of study selection process. CENTRAL, Cochrane Central Register of Controlled Trials; ERAS, enhanced recovery after surgery; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

### *Risk of bias and quality assessment*

All the studies were assessed for methodological quality and risk of bias using the Newcastle-Ottawa Scale (NOS), a checklist developed to determine the quality of non-randomized studies in systematic reviews (37). Cohort studies were assessed using the NOS checklist for cohort studies while the case-control studies were assessed using the NOS checklist for case-control studies (38). The studies were scored by two independent reviewers, and a third reviewer resolved any areas of disagreement.

## **Results**

The initial literature review revealed 582 non-duplicate citations, of which 61 were included after title and abstract screening. The full texts of these articles were then reviewed, and 24 articles were found to satisfy the inclusion criteria and were selected for data extraction and analysis (Figure 1). Out of the included articles, 22 were retrospective cohort studies (32,34-36,39-56) while

two were case-control studies (57,58). The methods of breast reconstruction included flap-based reconstruction (deep inferior epigastric perforator flaps, profunda artery perforator flaps; muscle-sparing transverse rectus abdominis myocutaneous flaps, superficial inferior epigastric artery flaps, transverse upper gracilis flaps, and latissimus dorsi flaps) as well as alloplastic reconstruction (implants and tissue expanders). Overall, 4,377 patients were included, with 2,365 patients in the TRAS group and 2,012 patients in the ERAS group. A summary of individual study characteristics is shown in Table 1.

### *Risk of bias and quality score*

The studies were assessed using the NOS checklist for cohort studies and case-control studies and scored from a scale of 0 to 9. Studies with a score of 5 to 7 were deemed to be of moderate quality and studies with a score of 8 or 9 were deemed to be high quality. All articles selected for review were of at least moderate quality (Table 1).

**Table 1** Characteristics of included studies

Author, year	Design	Country	Reconstruction type	Timing	Laterality	No. of patients	Age (years)	NOS score
Atamian <i>et al.</i> (34), 2023	Retrospective cohort	United States	DIEP flap	Immediate and delayed	Unilateral and bilateral	TRAS: 121; ERAS: 148	TRAS: 52; ERAS: 52	7
Cho <i>et al.</i> (42), 2022	Retrospective cohort	United States	PAP flap	Immediate and delayed	Unilateral and bilateral	TRAS: 58; ERAS: 29	TRAS: 51; ERAS: 49	6
Linder <i>et al.</i> (57), 2022	Case-control	Switzerland	DIEP flap	Immediate and delayed	Unilateral and bilateral	TRAS: 37; ERAS: 42	TRAS: 38; ERAS: 53	5
Lombana <i>et al.</i> (41), 2022	Retrospective cohort	United States	DIEP and MS-TRAM flaps	Immediate and delayed	Unilateral and bilateral	TRAS: 36; ERAS: 30	TRAS: 51; ERAS: 49	6
Ochoa <i>et al.</i> (40), 2022	Retrospective cohort	United States	DIEP flap	Immediate and delayed	Unilateral and bilateral	TRAS: 205; ERAS: 204	TRAS: 51; ERAS: 50	7
Rendon <i>et al.</i> (39), 2022	Retrospective cohort	United States	DIEP, MS-TRAM, SIEA, and TRAM flaps	Immediate and delayed	Unilateral and bilateral	TRAS: 46; ERAS: 39	TRAS: 54; ERAS: 55	8
Gort <i>et al.</i> (35), 2021	Retrospective cohort	Netherlands	DIEP flap	Immediate and delayed	Unilateral and bilateral	TRAS: 79; ERAS: 73	TRAS: 50; ERAS: 51	6
Haddock <i>et al.</i> (45), 2021	Retrospective cohort	United States	DIEP flap	Immediate and delayed	Unilateral and bilateral	TRAS: 67; ERAS: 80	TRAS: 53; ERAS: 52	6
Hammond <i>et al.</i> (44), 2021	Retrospective cohort	United States	Implant and tissue expander	Immediate and delayed	Unilateral and bilateral	TRAS: 72; ERAS: 79	TRAS: 49; ERAS: 51	7
Shin <i>et al.</i> (43), 2021	Retrospective cohort	United States	DIEP and MS-TRAM flaps	Immediate and delayed	Unilateral and bilateral	TRAS: 36; ERAS: 87	TRAS: 51; ERAS: 51	6
Anolik <i>et al.</i> (48), 2020	Retrospective cohort	United States	Flap	Immediate and delayed	Unilateral and bilateral	TRAS: 99; ERAS: 138	TRAS: 50; ERAS: 46	5
Guffey <i>et al.</i> (47), 2020	Retrospective cohort	United States	DIEP, MS-TRAM, SIEA, and TRAM flaps	Immediate and delayed	Unilateral and bilateral	TRAS: 39; ERAS: 44	TRAS: 49; ERAS: 49	8
O'Neill <i>et al.</i> (46), 2020	Retrospective cohort	Canada	DIEP flap	Immediate and delayed	Unilateral and bilateral	TRAS: 183; ERAS: 198	TRAS: 52; ERAS: 51	7
Sharif-Askary <i>et al.</i> (51), 2019	Retrospective cohort	United States	DIEP and MS-TRAM flaps	Immediate and delayed	Unilateral and bilateral	TRAS: 138; ERAS: 138	TRAS: 51; ERAS: 46	8
Sindali <i>et al.</i> (50), 2019	Retrospective cohort	United Kingdom	DIEP and TUG flaps	Immediate and delayed	Unilateral and bilateral	TRAS: 72; ERAS: 66	TRAS: 53; ERAS: 54	5
Stein <i>et al.</i> (49), 2019	Retrospective cohort	Canada	LD flap	Immediate and delayed	Unilateral and bilateral	TRAS: 58; ERAS: 20	TRAS: 52; ERAS: 52	7
Astanehe <i>et al.</i> (55), 2018	Retrospective cohort	Canada	DIEP flap	Immediate and delayed	Unilateral and bilateral	TRAS: 169; ERAS: 72	TRAS: 50; ERAS: 53	6
Chiu <i>et al.</i> (54), 2018	Retrospective cohort	United States	Tissue expander	Immediate	Unilateral and bilateral	TRAS: 276; ERAS: 96	TRAS: 49; ERAS: 47	7

**Table 1** (continued)

Table 1 (continued)

Author, year	Design	Country	Reconstruction type	Timing	Laterality	No. of patients	Age (years)	NOS score
Kaoutzanis <i>et al.</i> (53), 2018	Retrospective cohort	United States	DIEP, MS-TRAM, PAP, and SIEA flaps	Immediate and delayed	Unilateral and bilateral	TRAS: 50; ERAS: 50	TRAS: 51; ERAS: 52	6
Oh <i>et al.</i> (52), 2018	Retrospective cohort	United States	Abdominal free flap	Immediate and delayed	Unilateral and bilateral	TRAS: 118; ERAS: 82	TRAS: 49; ERAS: 49	6
Afonso <i>et al.</i> (36), 2017	Retrospective cohort	United States	DIEP, MS-TRAM and TRAM flaps	Immediate and delayed	Unilateral and bilateral	TRAS: 49; ERAS: 42	TRAS: 51; ERAS: 50	6
Dumestre <i>et al.</i> (32), 2017	Retrospective cohort	Canada	Implant and Tissue expander	Immediate and delayed	Unilateral and bilateral	TRAS: 29; ERAS: 29	TRAS: 48; ERAS: 48	6
Batdorf <i>et al.</i> (56), 2015	Retrospective cohort	United States	DIEP, MS-TRAM and TRAM flaps	Immediate and delayed	Unilateral and bilateral	TRAS: 51; ERAS: 49	TRAS: 48; ERAS: 48	7
Bonde <i>et al.</i> (58), 2015	Case-control	Denmark	DIEP and TRAM flaps	–	Unilateral	TRAS: 277; ERAS: 177	TRAS: 51; ERAS: 53	6

NOS, Newcastle-Ottawa Scale; DIEP, deep inferior epigastric perforator; TRAS, traditional recovery after surgery; ERAS, enhanced recovery after surgery; PAP, profunda artery perforator; MS-TRAM, muscle-sparing transverse rectus abdominis myocutaneous; SIEA, superficial inferior epigastric artery; TRAM, transverse rectus abdominis myocutaneous; TUG, transverse upper gracilis; LD, latissimus dorsi.

### Components of reported ERAS protocols for breast reconstruction

Despite variations in the specificities of each individual ERAS protocol, all included studies reported common themes as outlined in the ERAS society guidelines with regards to preoperative, intraoperative, and postoperative care. Preoperatively, ERAS protocols included preadmission counseling, preoperative optimization, minimization of fasting, carbohydrate loading, antimicrobial prophylaxis, and preoperative analgesia. Components of intraoperative protocol elements included intraoperative analgesia, maintenance of normothermia, and appropriate intravenous fluid management. Postoperative analgesia, thromboprophylaxis, early catheter removal, early feeding and ambulation, flap monitoring, and early discharge were commonly reported in postoperative care pathways. A summary of the protocol elements can be found in *Table 2*.

### LOS, readmission and reoperation rates

Twenty-two studies reported LOS and the results of 3,758 patients were pooled into the meta-analysis (*Table 3*). The

majority of studies report a significant decrease in LOS after the implementation of ERAS protocol, except five studies which reported no significant difference in LOS between TRAS and ERAS cohorts (36,41,50,51,54). Overall, implementation of ERAS pathway significantly reduces the LOS (mean difference,  $-1.06$  days; 95% CI:  $-1.36$  to  $-0.77$ ;  $P < 0.00001$ ;  $I^2 = 94\%$ ) (*Figure 2A*). Subgroup analysis of LOS was subsequently performed, revealing a greater decrease in LOS in the autologous breast reconstruction subgroup (mean difference,  $-1.14$  days; 95% CI:  $-1.34$  to  $-0.94$ ;  $P < 0.00001$ ;  $I^2 = 80\%$ ). However, there was no significant decrease in LOS in the implant-based reconstruction subgroup (mean difference,  $-0.03$  days, 95% CI:  $-0.17$  to  $0.11$ ;  $P = 0.66$ ) (*Figure 2B*).

Readmission rates were reported in twelve studies with 80 patients readmitted out of 927 patients in the ERAS pathway as compared to 76 patients readmitted out of 1,060 patients in the TRAS pathway (*Table 3*). There is no statistically significant difference in the readmission rates before and after ERAS protocol implementation (odds ratio, 1.10; 95% CI: 0.79 to 1.54;  $P = 0.57$ ;  $I^2 = 0\%$ ) (*Figure 3*). Since readmission rates were not reported in any of the studies on implant-based reconstruction, subgroup

**Table 2** Components of reported enhanced recovery after surgery protocols for breast reconstruction

Author, year	Preadmission counseling	Preoperative optimization	Minimize fasting	Carbohydrate loading	Preoperative analgesia	Antimicrobial prophylaxis	Nausea and vomiting prophylaxis	Intraoperative analgesia	Normothermia	IV fluids	Postoperative analgesia	Thromboprophylaxis	Early TOC	Early feeding	Early mobilization	Flap monitoring	Discharge POD goal	Discharge criteria
Atamian <i>et al.</i> (34), 2023	Yes	–	Yes	–	–	Yes	–	Bupivacaine	–	–	Ketorolac, oxycodone, paracetamol	Yes	POD 1	POD 0	POD 1	Q1H POD 0; Q2H POD 1; Q4H POD 2	–	–
Cho <i>et al.</i> (42), 2022	Yes	Yes	Yes	Yes	–	Yes	Yes	Bupivacaine, lidocaine, paracetamol	–	Yes	Celecoxib, gabapentin, paracetamol	Yes	POD 1	POD 0	POD 1	Q1H POD 1–2; Q2H POD 2+	POD 2+	–
Linder <i>et al.</i> (57), 2022	Yes	–	–	–	–	–	–	Paracetamol, ropivacaine	–	Yes	Ibuprofen, paracetamol	–	POD 0	–	POD 0	Yes	POD 3–4	–
Lombana <i>et al.</i> (41), 2022	Yes	–	–	–	Gabapentin	–	Yes	Bupivacaine, ketorolac	–	–	Gabapentin, ibuprofen, paracetamol	–	–	–	–	–	–	–
Ochoa <i>et al.</i> (40), 2022	Yes	–	Yes	Yes	Celecoxib	Yes	Yes	Bupivacaine, paracetamol	–	–	Celecoxib, gabapentin, opioids, paracetamol	Yes	–	–	POD 1	Q1H POD 0; Q2H POD 1	POD 3+	–
Rendon <i>et al.</i> (39), 2022	–	–	–	–	Gabapentin, oxycodone, paracetamol	Yes	Yes	Bupivacaine, fentanyl	Yes	Yes	Gabapentin, hydromorphone, ibuprofen, oxycodone, paracetamol	Yes	POD 1	POD 0	POD 1	–	–	–
Gort <i>et al.</i> (35), 2021	Yes	–	–	–	–	–	–	Yes	–	–	Diclofenac, paracetamol	–	POD 2	POD 0	POD 0	Q1H POD 1; Q2H POD 2; Q8H POD 3–4	POD 4	–
Haddock <i>et al.</i> (45), 2021	Yes	Yes	Yes	Yes	Celecoxib, gabapentin, paracetamol	Yes	Yes	Bupivacaine, lidocaine, paracetamol	–	Yes	Gabapentin, hydromorphone, paracetamol	Yes	–	POD 0	Yes	Q1H	–	–
Hammond <i>et al.</i> (44), 2021	Yes	–	–	Yes	Celecoxib, gabapentin, paracetamol	–	Yes	Bupivacaine	–	Yes	Ketorolac, methocarbamol, opioids	–	–	–	–	–	POD 0	–
Shin <i>et al.</i> (43), 2021	Yes	Yes	Yes	–	–	–	–	Yes	–	–	Hydromorphone, morphine, NSAIDs, paracetamol	Yes	POD 0	POD 0	POD 0	Q1H POD 1; Q4H POD 1+	–	Tolerating diet; ambulating without assistance; pain controlled with oral medications; no evidence of flap compromise or donor site complications
Anolik <i>et al.</i> (48), 2020	Yes	Yes	Yes	Yes	Celecoxib, oxycontin, paracetamol, pregabalin	–	Yes	Bupivacaine, fentanyl	Yes	Yes	Celecoxib, oxycodone, paracetamol, pregabalin	–	POD 2	POD 0	POD 1	Yes	POD 3	–
Guffey <i>et al.</i> (47), 2020	Yes	–	Yes	Yes	Celecoxib, gabapentin, oxycontin, paracetamol	Yes	Yes	Bupivacaine	–	–	Celecoxib, gabapentin, hydromorphone, oxycodone, oxycontin, paracetamol	Yes	POD 1	POD 1	POD 1	Q1H POD 0; Q2H POD 1; Q4H POD 2+	POD 3	Reassuring flap exams by physician staff; adequate pain control on oral medications; ability to urinate spontaneously; ambulate independently with waist flexed if needed to minimize tension; tolerance of preoperative diet with return of bowel function
O'Neill <i>et al.</i> (46), 2020	Yes	–	Yes	–	Paracetamol	Yes	Yes	Yes	Yes	Yes	Celecoxib, gabapentin, hydromorphone, paracetamol	Yes	–	POD 1	POD 1	Q1H POD 0–1; Q4H POD 2	POD 3 (unilateral); POD 4 (bilateral)	–

Table 2 (continued)

Table 2 (continued)

Author, year	Preadmission counseling	Preoperative optimization	Minimize fasting	Carbohydrate loading	Preoperative analgesia	Antimicrobial prophylaxis	Nausea and vomiting prophylaxis	Intraoperative analgesia	Normothermia	IV fluids	Postoperative analgesia	Thromboprophylaxis	Early TOC	Early feeding	Early mobilization	Flap monitoring	Discharge POD goal	Discharge criteria
Sharif-Askary <i>et al.</i> (51), 2019	Yes	Yes	Yes	Yes	Celecoxib/naproxen, oxycontin, paracetamol, pregabalin	Yes	Yes	Bupivacaine, fentanyl, ketamine	Yes	Yes	Celecoxib/naproxen, fentanyl, oxycodone, paracetamol, pregabalin	Yes	POD 2	POD 0	POD 1	Yes	POD 3	Medical criteria that the doctor and team will monitor; ambulating and self-care; tolerating liquids enough to stay hydrated and to tolerate po pain regimen
Sindali <i>et al.</i> (50), 2019	Yes	Yes	–	Yes	Gabapentin	Yes	–	Bupivacaine	Yes	Yes	Gabapentin, NSAIDs, opioids, paracetamol	Yes	POD 1	POD 1	POD 1	–	–	Absence of complications; independently mobile; pain controlled with oral analgesia; solid diet resumed; all surgical drains removed
Stein <i>et al.</i> (49), 2019	Yes	Yes	Yes	–	Celecoxib, paracetamol	Yes	Yes	NSAIDs, opioids, ropivacaine	Yes	–	Celecoxib, gabapentin, hydromorphone, paracetamol	Yes	–	POD 0	Yes	–	–	Well-controlled pain; ability to understand instructions; tolerate oral intake; ambulate independently
Astanehe <i>et al.</i> (55), 2018	Yes	–	Yes	Yes	Celecoxib, gabapentin, hydromorphone, paracetamol	Yes	Yes	Bupivacaine, IV analgesics	Yes	Yes	Celecoxib, codeine, gabapentin, hydromorphone, ibuprofen, oxycodone, paracetamol	Yes	POD 1	POD 0	POD 1	Q1H POD 0–1; Q2H POD 2; Q4H POD 3	POD 4	Absence of early complications; return to normal diet; ability to void; independent mobilization and ambulation; adequate pain control with oral analgesics
Chiu <i>et al.</i> (54), 2018	Yes	–	Yes	–	Gabapentin, paracetamol	–	Yes	Bupivacaine, fentanyl, hydromorphone, ropivacaine	Yes	Yes	Hydrocodone/oxycodone, hydromorphone, ibuprofen, paracetamol	–	–	Yes	Yes	–	–	–
Kaoutzanis <i>et al.</i> (53), 2018	Yes	–	Yes	–	Celecoxib, gabapentin, paracetamol	Yes	Yes	Bupivacaine, ketamine, ketorolac, lidocaine, methadone	–	Yes	Celecoxib, gabapentin, ketorolac, hydromorphone, oxycodone, paracetamol	Yes	POD 1	POD 0	POD 0	Yes	–	Sufficient oral intake without nausea and vomiting; adequate ambulation; good urine output; satisfactory pain control with an oral analgesic regimen
Oh <i>et al.</i> (52), 2018	–	–	–	–	Celecoxib, gabapentin, paracetamol	–	Yes	Bupivacaine	–	Yes	Celecoxib, opioids, paracetamol	–	POD 1	POD 0	POD 0	Yes	POD 3–4	–
Afonso <i>et al.</i> (36), 2017	Yes	–	Yes	–	–	–	Yes	Bupivacaine, ketorolac, paracetamol	–	Yes	Ketorolac, opioids	Yes	POD 1	POD 1	POD 1	Yes	POD 3	–
Dumestre <i>et al.</i> (32), 2017	Yes	–	Yes	–	Celecoxib, gabapentin, oxycodone, paracetamol	Yes	Yes	Bupivacaine	–	Yes	Celecoxib, gabapentin, ibuprofen, oxycodone, tramadol-acetaminophen	–	–	–	–	–	POD 0	–
Batdorf <i>et al.</i> (56), 2015	Yes	–	Yes	–	Celecoxib, gabapentin, paracetamol	Yes	Yes	Bupivacaine	Yes	Yes	Celecoxib, opioids, paracetamol	Yes	POD 1	POD 0	POD 0	Yes	POD 3–4	Absence of early complications; tolerance of solid diet; independent mobilization and ambulation; adequate pain control with oral analgesia
Bonde <i>et al.</i> (58), 2015	Yes	–	–	–	–	–	–	Bupivacaine	–	–	Celecoxib, gabapentin, ibuprofen, paracetamol	Yes	POD 1	–	POD 1	Q1H POD 1–2	POD 4	–

IV, intravenous; TOC, trial-off-catheter; POD, postoperative day; Q1H, every 1 hour; Q2H, every 2 hours; Q4H, every 4 hours; Q8H, every 8 hours; NSAID, non-steroidal anti-inflammatory drug.



**Table 3** LOS, readmission and reoperation rates

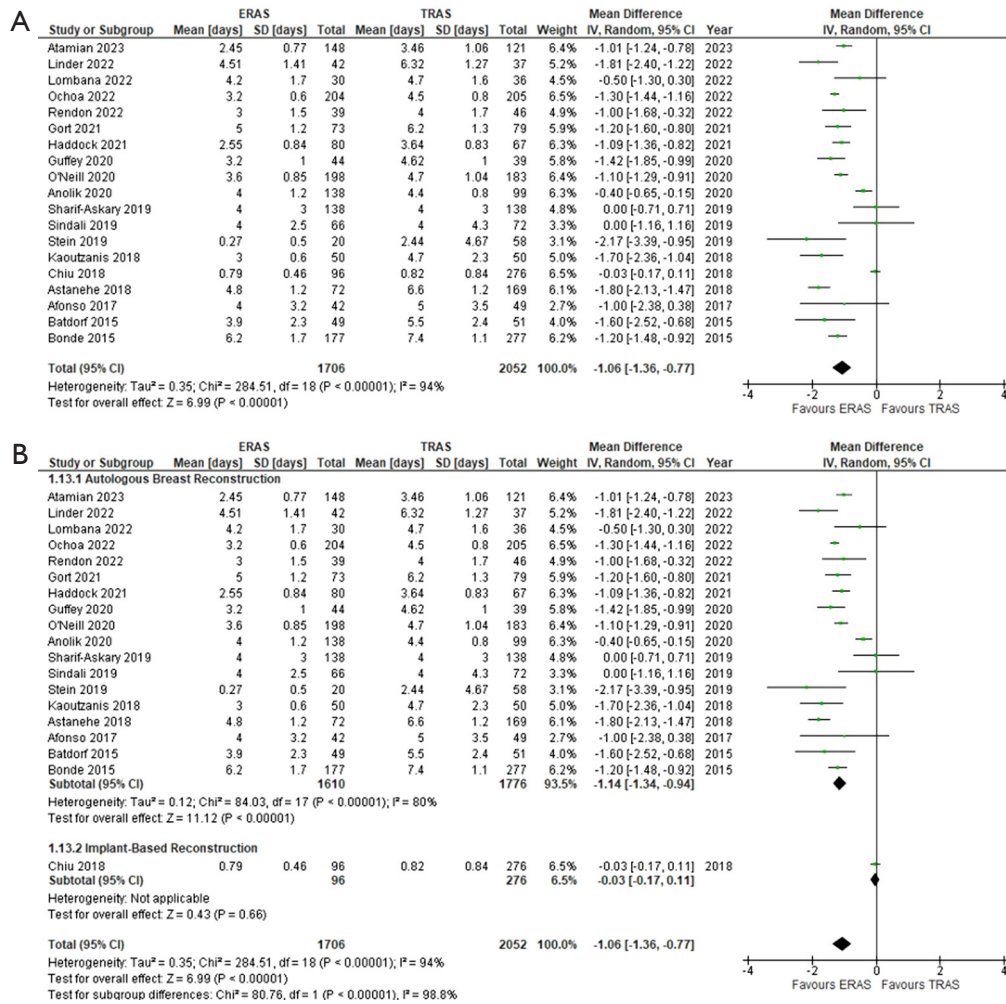
Author, year	LOS		Readmissions		Reoperations	
	TRAS	ERAS	TRAS	ERAS	TRAS	ERAS
Atamian <i>et al.</i> (34), 2023	3.5±1.1 days	2.5±0.8 days	–	–	–	–
Cho <i>et al.</i> (42), 2022	3.8 days	2.6 days	–	–	–	–
Linder <i>et al.</i> (57), 2022	6.3±1.3 days	4.5±1.4 days	0	0	0	0
Lombana <i>et al.</i> (41), 2022	4.7±1.6 days	4.2±1.7 days	5 [14]	6 [20]	5 [14]	5 [14]
Ochoa <i>et al.</i> (40), 2022	4.5±0.8 days	3.2±0.6 days	–	–	10 [4.9]	8 [3.9]
Rendon <i>et al.</i> (39), 2022	4.0 days	3.0 days	–	–	–	–
Gort <i>et al.</i> (35), 2021	6.2±1.3 days	5.0±1.2 days	–	–	–	–
Haddock <i>et al.</i> (45), 2021	3.6±0.8 days	2.6±0.8 days	–	–	–	–
Hammond <i>et al.</i> (44), 2021	–	–	–	–	70 [33]	33 [22]
Shin <i>et al.</i> (43), 2021	4.7 days	2.3 days	–	–	–	–
Anolik <i>et al.</i> (48), 2020	4.4 days	4.0 days	11 [11]	16 [12]	8 [8.1]	16 [12]
Guffey <i>et al.</i> (47), 2020	4.6±1.0 days	3.2±1.0 days	–	–	–	–
O'Neill <i>et al.</i> (46), 2020	4.7±1.0 days	3.6±0.9 days	12 [6.5]	9 [4.5]	–	–
Sharif-Askary <i>et al.</i> (51), 2019	4.0 days	4.0 days	15 [11]	16 [12]	15 [11]	16 [12]
Sindali <i>et al.</i> (50), 2019	4.0 days	4.0 days	8 [11]	4 [6]	15 [21]	7 [11]
Stein <i>et al.</i> (49), 2019	59 h	6.4 h	0	0	–	–
Astanehe <i>et al.</i> (55), 2018	6.6±1.2 days	4.8±1.2 days	2 [1.2]	1 [1.4]	–	–
Chiu <i>et al.</i> (54), 2018	19.8 h	19.1 h	–	–	–	–
Kaoutzanis <i>et al.</i> (53), 2018	4.7±2.3 days	3.0±0.6 days	4 [8]	2 [4]	5 [10]	2 [4]
Oh <i>et al.</i> (52), 2018	–	–	11 [9]	15 [18]	17 [14]	14 [17]
Afonso <i>et al.</i> (36), 2017	5.0 days	4.0 days	1 [2]	1 [2]	5 [10]	2 [5]
Dumestre <i>et al.</i> (32), 2017	1.6 days	0.0 days	–	–	–	–
Batdorf <i>et al.</i> (56), 2015	5.5±2.4 days	3.9±2.3 days	7 [14]	10 [20]	5 [10]	8 [16]
Bonde <i>et al.</i> (58), 2015	7.4±1.1 days	6.2±1.7 days	–	–	–	–

Data are presented as mean ± SD or number [%]. LOS, length of stay; TRAS, traditional recovery after surgery; ERAS, enhanced recovery after surgery; SD, standard deviation.

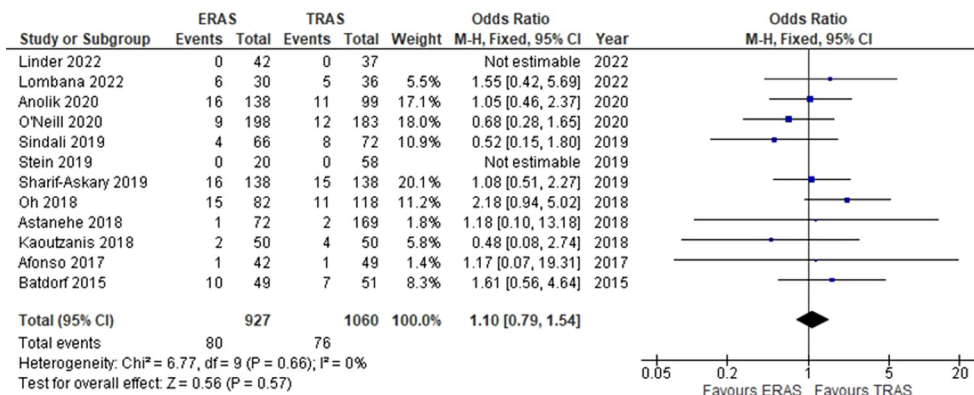
analysis was not performed. Similarly, reoperation rates from 11 studies were pooled (*Table 3*) and no statistically significant difference was found in the reoperation rates before and after ERAS protocol implementation (odds ratio, 0.81; 95% CI: 0.62 to 1.06;  $P=0.13$ ;  $I^2=13\%$ ) (*Figure 4A*). Subgroup analysis of reoperation rates performed also showed no significant differences between ERAS and TRAS cohorts in patients undergoing autologous breast reconstruction and patients undergoing implant-based reconstruction (*Figure 4B*).

### Total opioid use

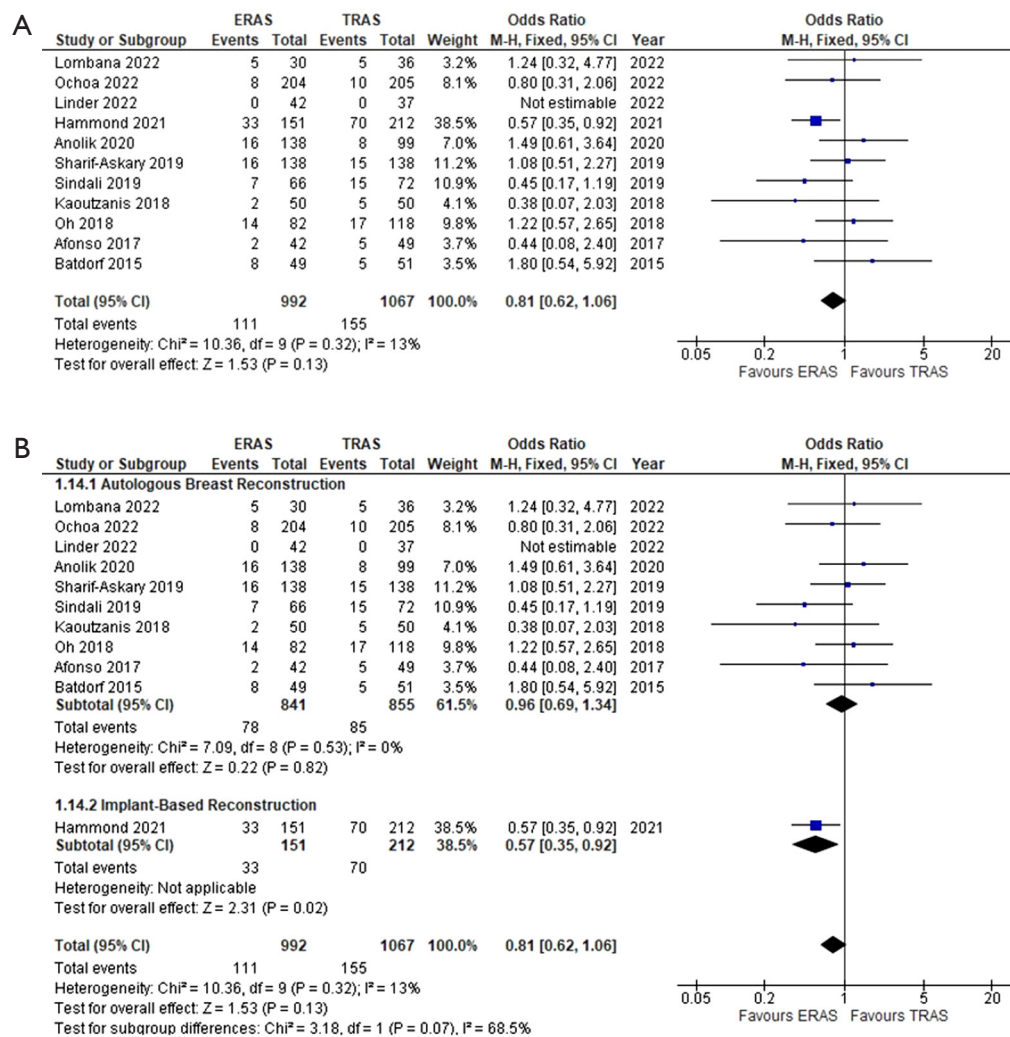
Fourteen studies reported the total opioid use in morphine equivalents and the results from 2,345 patients were pooled (*Table 4*). All studies demonstrated a significant decrease in the total amount of opioid use in ERAS cohorts as compared to TRAS cohorts overall (mean difference,  $-215.36$  mg of OME; 95% CI:  $-272.48$  to  $-158.24$ ;  $P<0.00001$ ,  $I^2=95\%$ ) (*Figure 5A*). To investigate the influence of reconstruction type on the total opioid use, subgroup analysis was performed, showing that a significantly lower amount of



**Figure 2** Forest plot for (A) LOS: overall. LOS was significantly shorter with ERAS than TRAS. (B) LOS: subgroup analysis. LOS was significantly shorter with ERAS than TRAS in autologous breast reconstruction. ERAS, enhanced recovery after surgery; TRAS, traditional recovery after surgery; SD, standard deviation; IV, inverse variance; CI, confidence interval; LOS, length of stay.



**Figure 3** Forest plot for readmissions. There is no significant difference in readmission rate between ERAS and TRAS. ERAS, enhanced recovery after surgery; TRAS, traditional recovery after surgery; M-H, Mantel-Haenszel; CI, confidence interval.



**Figure 4** Forest plot for (A) reoperations: overall. There is no significant difference in reoperation rate between ERAS and TRAS. (B) Reoperations: subgroup analysis. There is no significant difference in reoperation rate between ERAS and TRAS in autologous breast reconstruction. ERAS, enhanced recovery after surgery; TRAS, traditional recovery after surgery; M-H, Mantel-Haenszel; CI, confidence interval.

opioid use is required for both autologous and implant-based reconstruction patients under the ERAS pathway (Figure 5B).

**Overall major and minor complications**

The overall major and minor complication rates are shown in Table 5. No statistically significant difference is evident for overall major complications (197 out of 1,692 on ERAS pathway vs. 262 out of 1,937 on TRAS pathway; odds ratio, 0.86; 95% CI: 0.70 to 1.06; P=0.15; I<sup>2</sup>=42%) (Figure 6). Similarly, there is no difference in the overall

minor complication rates between the ERAS and TRAS cohorts (odds ratio, 0.87; 95% CI: 0.70 to 1.08; P=0.20; I<sup>2</sup>=43%) (Figure 7). Subsequent subgroup analysis performed also revealed no statistical difference between ERAS and TRAS cohorts for patients undergoing autologous and implant-based reconstruction in terms of major and minor complications.

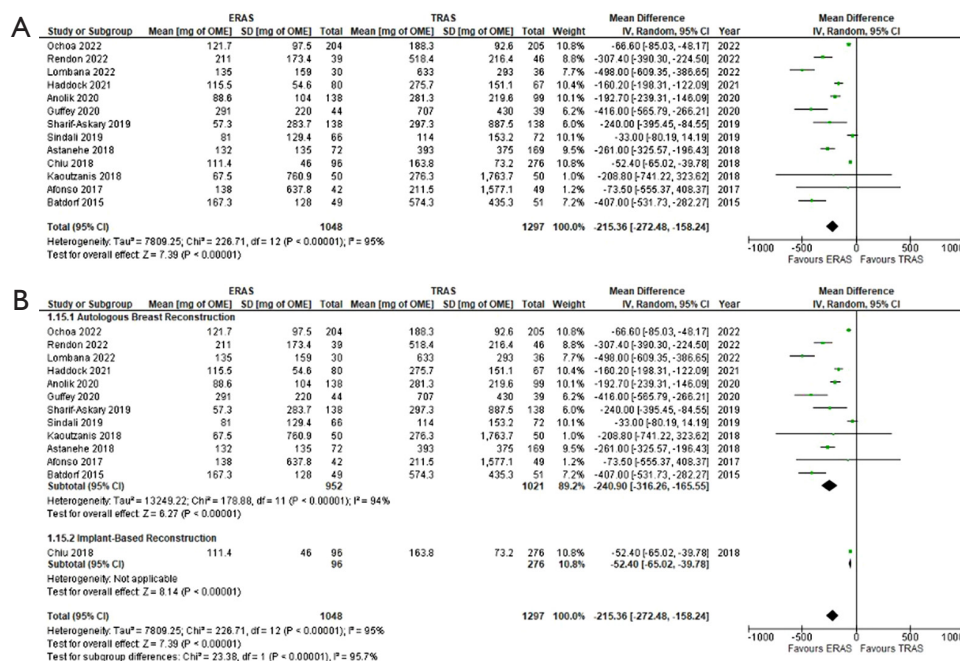
**Flap-related complications**

Flap-related complications including complete flap loss and partial flap loss were reported in 14 studies as shown

**Table 4** Total opioid use and postoperative pain scores

Author, year	Total opioid use		Postoperative pain scores	
	TRAS	ERAS	TRAS	ERAS
Cho <i>et al.</i> (42), 2022	192.1 mg OME	103.7 mg OME	2.7	2.3
Lombana <i>et al.</i> (41), 2022	633±293 mg OME	135±159 mg OME	–	–
Ochoa <i>et al.</i> (40), 2022	188.3±92.6 mg OME	121.7±97.5 mg OME	–	–
Rendon <i>et al.</i> (39), 2022	518.4 [454.2–582.7] mg OME	211.0 [154.8–267.2] mg OME	–	–
Gort <i>et al.</i> (35), 2021	–	–	2.17	1.73
Haddock <i>et al.</i> (45), 2021	275.7±151.1 mg OME	115.5±54.6 mg OME	–	–
Anolik <i>et al.</i> (48), 2020	281.3 [237.5–325.1] mg OME	88.6 [71.1–106.1] mg OME	–	–
Guffey <i>et al.</i> (47), 2020	707±430 mg OME	291±220 mg OME	4	2
Sharif-Askary <i>et al.</i> (51), 2019	297.3 [138.6–437.4] mg OME	57.3 [20.0–115.5] mg OME	5.0	4.0
Sindali <i>et al.</i> (50), 2019	114 [76.5–148.5] mg OME	81 [59.7–123.3] mg OME	–	–
Astanehe <i>et al.</i> (55), 2018	393±375 mg OME	132±135 mg OME	3.0±1.6	2.3±1.3
Chiu <i>et al.</i> (54), 2018	163.8±73.2 mg OME	111.4±46.0 mg OME	–	–
Kaoutzannis <i>et al.</i> (53), 2018	276.3 [12.5–1,015.0] mg OME	67.5 [0–432.5] mg OME	–	–
Afonso <i>et al.</i> (36), 2017	211.5 [30–936] mg OME	138 [0.0–397.5] mg OME	4.0	6.0
Batdorf <i>et al.</i> (56), 2015	574.3±435.3 mg OME	167.3±128.0 mg OME	4.1±1.7	3.3±1.9

Data are presented as mean ± SD or median [range]. TRAS, traditional recovery after surgery; ERAS, enhanced recovery after surgery; OME, oral morphine equivalent; SD, standard deviation.



**Figure 5** Forest plot for (A) total opioid use: overall. Total opioid use was significantly lower with ERAS than TRAS. (B) Total opioid use: subgroup analysis. Total opioid use was significantly lower with ERAS than TRAS in autologous breast reconstruction. ERAS, enhanced recovery after surgery; TRAS, traditional recovery after surgery; OME, oral morphine equivalent; SD, standard deviation; IV, inverse variance; CI, confidence interval.

**Table 5** Overall major and minor complications

Author, year	Overall major complications		Overall minor complications	
	TRAS	ERAS	TRAS	ERAS
Linder <i>et al.</i> (57), 2022	0	0	–	–
Lombana <i>et al.</i> (41), 2022	4	3	12	10
Ochoa <i>et al.</i> (40), 2022	5	8	–	–
Gort <i>et al.</i> (35), 2021	7	6	8	8
Hammond <i>et al.</i> (44), 2021	55	16	19	2
Shin <i>et al.</i> (43), 2021	6	16	9	35
Anolik <i>et al.</i> (48), 2020	3	10	5	9
Guffey <i>et al.</i> (47), 2020	6	3	2	0
O'Neill <i>et al.</i> (46), 2020	31	29	39	34
Sharif-Askary <i>et al.</i> (51), 2019	15	21	19	9
Sindali <i>et al.</i> (50), 2019	17	7	17	10
Stein <i>et al.</i> (49), 2019	6	4	19	6
Astanehe <i>et al.</i> (55), 2018	16	6	–	–
Kaoutzanis <i>et al.</i> (53), 2018	8	3	24	28
Oh <i>et al.</i> (52), 2018	23	14	10	12
Afonso <i>et al.</i> (36), 2017	10	4	3	0
Dumestre <i>et al.</i> (32), 2017	0	2	10	6
Batdorf <i>et al.</i> (56), 2015	11	16	13	21
Bonde <i>et al.</i> (58), 2015	39	29	33	17

Data are presented as number. TRAS, traditional recovery after surgery; ERAS, enhanced recovery after surgery.

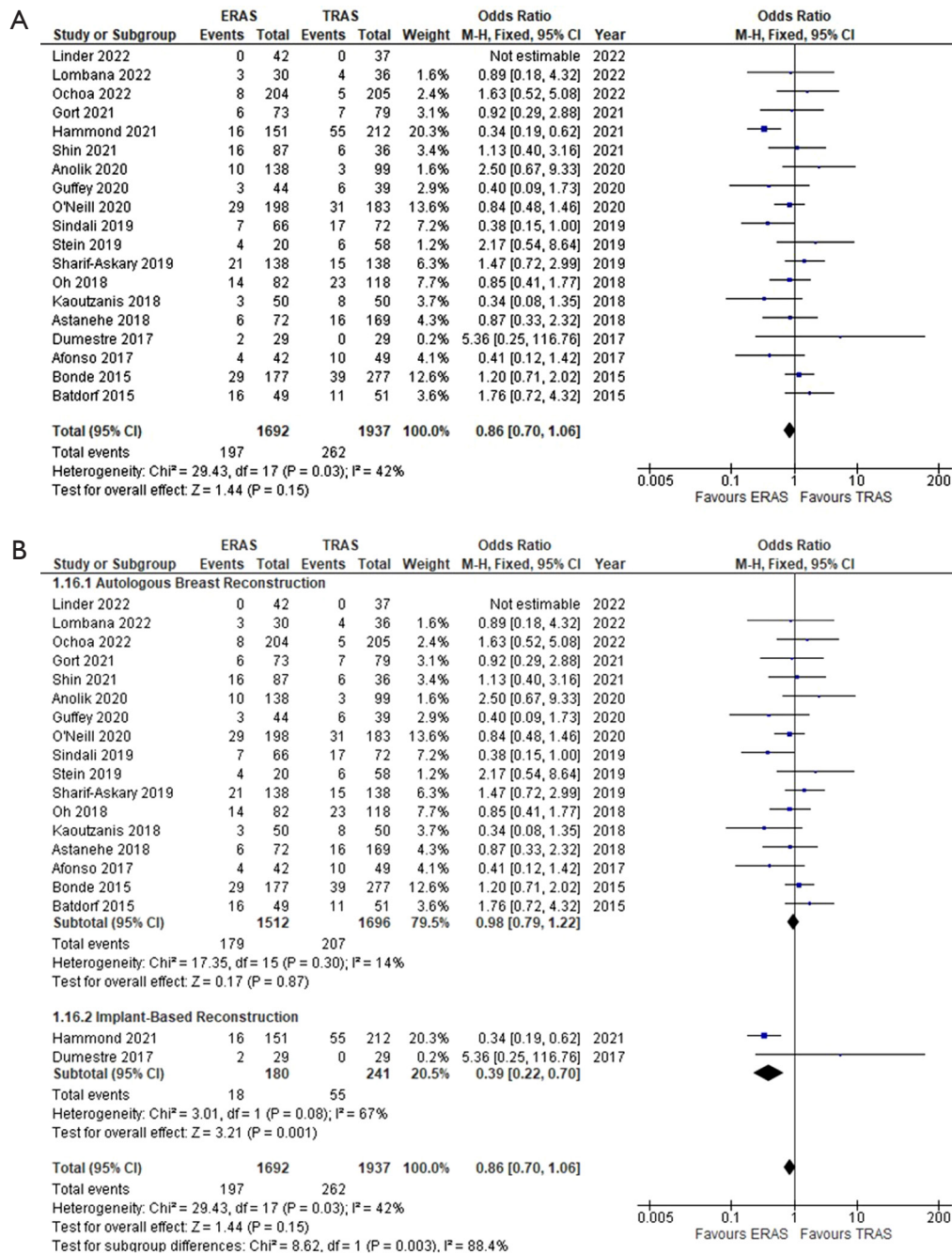
in *Table 6*. Pooled data from the 14 studies were analyzed and shown to have no significant difference between ERAS and TRAS cohorts for complete flap loss (23 out of 1,353 in ERAS cohort *vs.* 21 out of 1,587 in TRAS cohort; odds ratio, 1.24; 95% CI: 0.69 to 2.23;  $P=0.48$ ;  $I^2=0\%$ ) (*Figure 8*) and partial flap loss (18 of 853 in ERAS cohort *vs.* 19 of 1,026 in TRAS cohort; odds ratio, 1.17; 95% CI: 0.63 to 2.18;  $P=0.61$ ;  $I^2=0\%$ ) (*Figure 9*).

### Costs-savings and postoperative pain scores

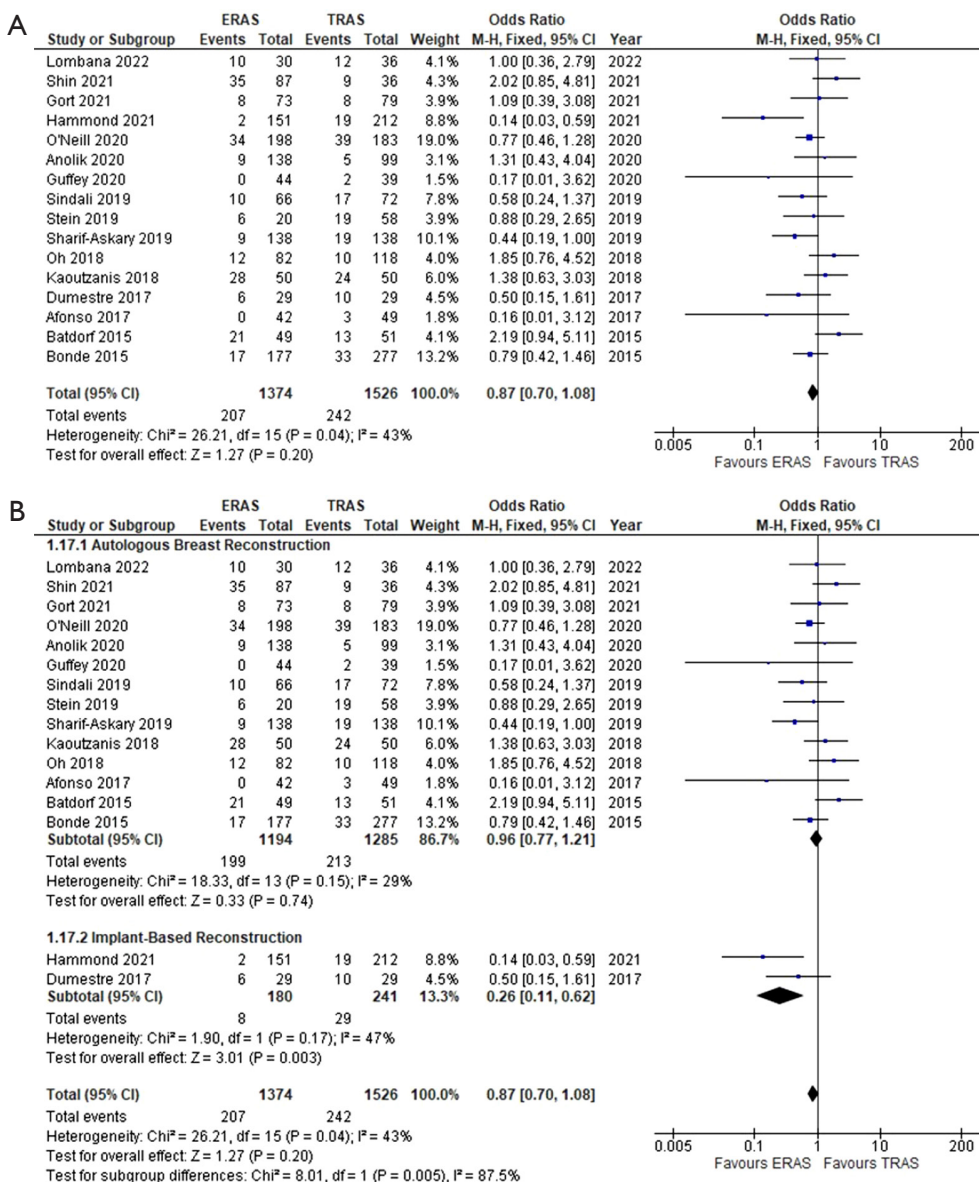
Data for costs was not pooled due to methodological heterogeneity in the determination of costs (*Table 7*). O'Neill *et al.* (46) reported a significant decrease in the inpatient cost after ERAS protocol implementation in both unilateral and bilateral breast reconstruction cases. Similarly, Stein *et al.* (49) showed that using an ERAS protocol instead of TRAS is

associated with a significant cost saving. Oh *et al.* (52) also estimated that the implementation of an ERAS protocol would decrease hospital costs with effect on the costs of physician services.

The postoperative pain scores were not pooled due to the wide variation in the timing of assessing pain scores. In addition, the numerical pain scales used could have been different and pain assessment itself is inherently very subjective. The overall pain score or pain scores taken at 24 hours are shown in *Table 4*. Gort *et al.* (35) reported lower average pain scores in the ERAS cohort as compared to the TRAS cohort. Astanehe *et al.* (55) also reported lower pain scores on postoperative day (POD) 0 and from POD 0–3 in patients managed under ERAS pathway. Afonso *et al.* (36) and Batdorf *et al.* (56) both report lower pain scores at 24 hours, but no significant differences in pain score before 24 hours and after 24 hours postoperatively. On the other



**Figure 6** Forest plot for (A) overall major complications: overall. There is no significant difference in overall major complication rate between ERAS and TRAS. (B) Overall major complications: subgroup analysis. There is no significant difference in overall major complication rate between ERAS and TRAS in autologous breast reconstruction. However, ERAS was associated with a lower overall major complication rate than TRAS in implant-based reconstruction. ERAS, enhanced recovery after surgery; TRAS, traditional recovery after surgery; M-H, Mantel-Haenszel; CI, confidence interval.



**Figure 7** Forest plot for (A) overall minor complications: overall. There is no significant difference in overall minor complication rate between ERAS and TRAS. (B) Overall minor complications: subgroup analysis. There is no significant difference in overall minor complication rate between ERAS and TRAS in autologous breast reconstruction. However, ERAS was associated with a lower overall minor complication rate than TRAS in implant-based reconstruction. ERAS, enhanced recovery after surgery; TRAS, traditional recovery after surgery; M-H, Mantel-Haenszel; CI, confidence interval.

hand, Cho *et al.* (42), Guffey *et al.* (47), and Sharif-Askary *et al.* (51) reported similar pain scores in the ERAS group and TRAS groups at 24 hours.

**Discussion**

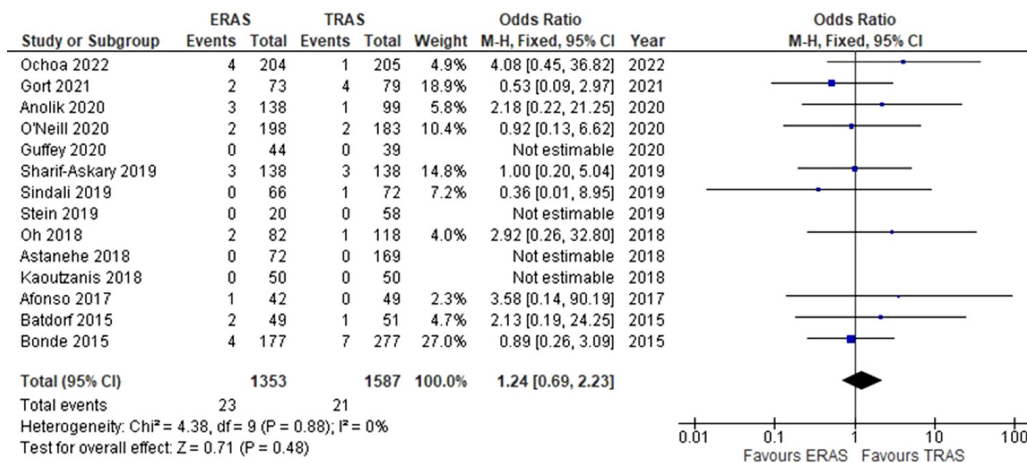
This meta-analysis shows that implementation of ERAS

pathways results in a significant decrease in LOS and opioid use for patients undergoing autologous breast reconstruction surgery without a significant difference in major and minor complication rates, readmission rates, and reoperation rates. On the other hand, for implant-based reconstructions, our study showed a significant decrease in opioid use and complications rates but no significant

**Table 6** Complete and partial flap loss

Author, year	Complete flap loss		Partial flap loss	
	TRAS	ERAS	TRAS	ERAS
Ochoa <i>et al.</i> (40), 2022	1	4	–	–
Gort <i>et al.</i> (35), 2021	4	2	1	0
Anolik <i>et al.</i> (48), 2020	1	3	–	–
Guffey <i>et al.</i> (47), 2020	0	0	–	–
O'Neill <i>et al.</i> (46), 2020	2	2	4	3
Sharif-Askary <i>et al.</i> (51), 2019	3	3	0	1
Sindali <i>et al.</i> (50), 2019	1	0	1	1
Stein <i>et al.</i> (49), 2019	0	0	0	0
Astanehe <i>et al.</i> (55), 2018	0	0	–	–
Kaoutzanis <i>et al.</i> (53), 2018	0	0	3	0
Oh <i>et al.</i> (52), 2018	1	2	1	3
Afonso <i>et al.</i> (36), 2017	0	1	–	–
Batdorf <i>et al.</i> (56), 2015	1	2	0	3
Bonde <i>et al.</i> (58), 2015	7	4	9	7

Data are presented as number. TRAS, traditional recovery after surgery; ERAS, enhanced recovery after surgery.



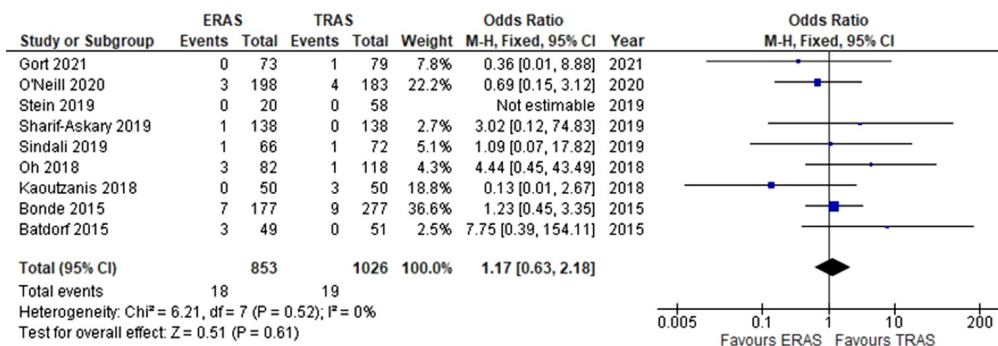
**Figure 8** Forest plot for complete flap loss. There is no significant difference in complete flap loss rate between ERAS and TRAS. ERAS, enhanced recovery after surgery; TRAS, traditional recovery after surgery; M-H, Mantel-Haenszel; CI, confidence interval.

decrease in LOS for patients.

The principle of ERAS protocols is improving patient outcomes and recovery through evidence-based recommendations for perioperative care and simplifying the whole operative and recovery process for both healthcare professionals and patients. In recent years, ERAS

pathways have been increasingly adopted and implemented in the field of reconstructive surgery including breast reconstruction. A few recent reviews compared outcomes in patients undergoing breast reconstruction with ERAS protocols to TRAS care. However, previous reviews have various limitations and there has been many new articles



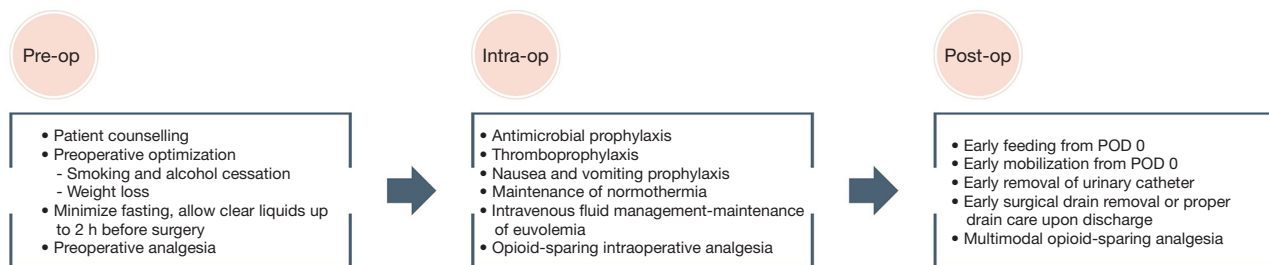


**Figure 9** Forest plot for partial flap loss. There is no significant difference in partial flap loss rate between ERAS and TRAS. ERAS, enhanced recovery after surgery; TRAS, traditional recovery after surgery; M-H, Mantel-Haenszel; CI, confidence interval.

**Table 7** Costs-savings

Author, year	TRAS	ERAS
O'Neill <i>et al.</i> (46), 2020	CAD \$3,932±\$269 in unilateral cases	CAD \$2,821±\$113 in unilateral cases
	CAD \$4,344±\$106 in bilateral cases	CAD \$3,296±\$176 in bilateral cases
Stein <i>et al.</i> (49), 2019	CAD \$8,890.25 (\$5,968.62–\$11,934.45)	CAD \$5,666.80 (\$5,379.35–\$6,381.83)
Oh <i>et al.</i> (52), 2018	USD \$43,264 (\$41,611–\$44,889)	USD \$38,688 (\$37,664–\$39,994)

TRAS, traditional recovery after surgery; ERAS, enhanced recovery after surgery; CAD, Canadian dollars; USD, US dollars.



**Figure 10** Schematic diagram of key elements of ERAS protocol. Pre-op, preoperative; intra-op, intraoperative; post-op, postoperative; POD, postoperative day; ERAS, enhanced recovery after surgery.

published on ERAS protocols for breast reconstruction surgery since the latest review. Our study includes 24 articles for quantitative analysis, and we have highlighted essential and important elements of ERAS protocol for breast reconstruction in a schematic diagram (Figure 10).

The ERAS protocols of the included studies included elements such as preadmission counseling, preoperative carbohydrate loading, maintenance of normothermia intraoperatively, optimization of fluid balance, early feeding, and early mobilization, all of which contributes

to improved recovery rate and consequently a reduced LOS (23). Preadmission counseling and patient education on surgery and anesthesia reduces patients' psychological stress, this in turn improves wound healing and decreases LOS (59,60). Administration of carbohydrate-rich drinks preoperatively reduces insulin resistance after surgery and attenuates depletion of muscle mass postoperatively, which contributes to a decrease in the LOS (61,62). Maintenance of normothermia intraoperatively improves oxidative killing of bacteria, resulting in better wound healing and shorter

hospitalization (63). Goal-directed fluid management results in improved end-operative hemodynamics and reduced complications leading to a shorter LOS (64). Early feeding and mobilization prevent deconditioning and improves patients' functional mobility and is associated with reduced hospital stay (65,66). Defining strict discharge criteria also aids in reducing LOS. However, if inappropriately set, it may lead to an increase in readmission and reoperation rates (67).

LOS was the most frequently evaluated outcome, with 22 studies analyzing this outcome and 17 of these studies reporting a significant decrease in LOS for the ERAS cohort for patients undergoing autologous breast reconstruction. This is consistent with results from existing literature. There are various possible explanations why there was no significant improvement in LOS for the other five studies. In Lombana *et al.*'s institution (41), the protocol in place was to keep patients in the hospital for an average of 4 days, which is similar to the mean LOS in their TRAS cohort. For some other studies, certain factors in their ERAS protocols could impacted LOS. For example, in the ERAS protocol adopted by Sharif-Askary *et al.* (51), urinary catheters were only removed only on POD 2. Meanwhile, Sindali *et al.* (50) did not implement early surgical drain removal in their ERAS pathway and identified that as a possible reason for not seeing a significant shorter LOS. The study by Chiu *et al.* (54) on patients undergoing implant-reconstructions did not show a significant decrease in LOS as well. This is due to the fact that majority of their patients in the TRAS cohort was discharged at POD 1, leaving little to no room for further improvement in LOS. This shows that LOS, which is currently one of the main measures of success of ERAS pathways, may not be the most suitable metric for shorter surgeries such as implant-based breast reconstructions with faster recovery times and other indicators of success should be evaluated as well.

An overall reduction in the LOS also helps to reduce nursing requirements, leading to less costs incurred (52). Furthermore, the ERAS pathway is associated with less use of the intensive care unit environment, which reduces the need for continuous monitoring and utilization of expensive equipment, hence its implementation leads to a reduction in costs incurred (46). However, it is also important to consider that the implementation of additional measures in ERAS protocols could also incur higher costs such as more frequent preoperative clinical visits. Despite the push to discharge patients earlier, there was no significant

difference in readmissions, which shows that patients were not discharged prematurely.

Another common measure of ERAS effectiveness is the total amount of opioid consumption. From our data collected, most studies which incorporated multimodal opioid-sparing analgesia as part of their ERAS protocol resulted in a significant decrease in post-operative opioid use for patients undergoing breast reconstruction surgery. Preoperative and intraoperative administration of non-opioid analgesia such as gabapentin and pregabalin lowers the amount of postoperative analgesia required (68,69). Nonsteroidal anti-inflammatory drugs may also reduce postoperative pain without affecting the risk of bleeding, and hence reduce total opioid consumption (70). The use of bupivacaine through regional anesthesia techniques such as paravertebral blocks can also decrease pain sensation after surgery, reduce the amount of intraoperative fentanyl required and decrease opioid consumption postoperatively (71). A lower opioid use in patient also equates to avoidance of common opioid-related side effects such as sedation, nausea and vomiting, and constipation (72). These side effects can directly delay postoperative mobilization and nutrition which in turn leads to delayed recovery and prolonged hospital stay. Therefore, it is crucial for all disciplines to incorporate opioid-sparing multimodal analgesia in future ERAS protocols.

Our study did not show any significant differences in the overall major or minor complication rates, complete or partial flap loss rates between the TRAS and ERAS cohorts. Although elements of the ERAS protocol such as preadmission optimization, thromboprophylaxis, antimicrobial prophylaxis, maintenance of normothermia, goal-directed fluid management, postoperative flap monitoring, early feeding and mobilization are associated with reduced complication rates, the lack of improvement of complication rates could be attributed to the low incidence of these complications in the TRAS cohort, thereby allowing little room for improvement. In addition, the lack of improvement could also be due to the pre-existing use of certain elements such as antimicrobial prophylaxis and thromboprophylaxis that have been commonly used even before ERAS implementation. On the other hand, this also demonstrates that the implementation of ERAS pathways does not compromise patient safety and increase complication rates.

Healthcare costs are rising at an unsustainable rate worldwide, due to the expansion of ageing populations (73). Despite increasing medical needs, hospitals worldwide are

often faced with reduced bed availability and lack of sufficient healthcare workers (74). Therefore, optimization of healthcare resource utilization is crucial. By implementing ERAS protocols for breast reconstruction surgery, our study shows that the LOS and its associated costs can be reduced, freeing up more beds for other patients in greater need and allowing the utilization of healthcare funding to be redirected to other diseases. This is especially relevant with the ongoing COVID pandemic that have caused a global healthcare manpower and resource shortage over the past few years (75). The reduction in opioid use after ERAS implementation also helps reduce harm related to opioid misuse and abuse which has been plaguing countries worldwide including the United States, the United Kingdom, Australia, and Canada (76-79).

There are some limitations to this study that we have to acknowledge. There is heterogeneity in terms of the specific details of each element in the ERAS protocols implemented across the various studies. Furthermore, compliance with each protocol element in the studies was usually not available and hence not assessed in this review. To address this heterogeneity between studies, the random effects model was used in the meta-analysis. Nevertheless, the differences in components of ERAS protocols across studies are likely to have contributed to the wide CIs observed. In addition, the studies included in this review were retrospective, hence, there is a possibility of chronological bias due to advancement of surgical techniques and treatment during the transition from TRAS to ERAS. LOS and total opioid use data from certain studies were excluded due to the lack of information required to compute the SD required for meta-analysis. There is a very limited number of studies on the implementation of ERAS protocols for patients undergoing alloplastic breast reconstruction, which may result in inconclusive results for such patients. We also recognize that the outcomes of unilateral and bilateral breast reconstructions could differ. However, we were not able to distinguish between the two approaches in our analysis as none of the studies reported data for each one separately.

## Conclusions

The implementation of ERAS pathways in breast reconstruction surgery is associated with reduced LOS which could suggest lower healthcare costs. In addition, ERAS pathways also lead to lower opioid consumption without an increase in readmission or reoperation rates.

Patient safety is not compromised with the transition towards ERAS, without an increase in postoperative or flap-related complications. Despite differences in details of ERAS protocol elements between studies, implementation of ERAS protocol elements under the outlined common themes yields superior outcomes to the traditional recovery pathway. Moving forward, future studies can investigate other indicators of success such as improvement in patient satisfaction and quality of life.

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