Review Article

Enhanced recovery after cardiac surgery: A literature review

ABSTRACT

Enhanced recovery after cardiac surgery (ERACS) represents a constellation of evidence-based peri-operative methods aimed to reduce the physiological and psychological stress patients experience after cardiac surgery, with the primary objective of providing an expedited recovery to pre-operative functional status. The method involves pre-operative, intra-operative, and post-operative interventions as well as direct patient engagement to be successful. Numerous publications in regard to the benefits of enhanced recovery have been presented, including decreased post-operative complications, shortened length of stay, decreased overall healthcare costs, and higher patient satisfaction. Implementing an ERACS program undeniably requires a culture change, a methodical shift in the approach of these patients that ultimately allows the team to achieve the aforementioned goals; therefore, team-building, planning, and anticipation of obstacles should be expected.

Key words: Cardiac surgery, clinical protocols, enhanced recovery after surgery, patient-centered care

Introduction

The philosophy of the implementation of enhanced recovery after surgery (ERAS) continues to expand in different surgical specialties. This model has also extended to the management of cardiac patients as the surgical techniques continue to evolve, minimally invasive methods continue to proliferate, and the overall healthcare expectations for improved outcomes and faster tracking of these patients increase.[1-4]

Enhanced recovery after cardiac surgery (ERACS) represents a constellation of evidence-based peri-operative methods aimed to reduce the physiological and psychological stress patients experience after cardiac surgery, with the ultimate the primary objective of providing an expedited recovery to pre-operative functional status. Overall, the method involves pre-operative, intra-operative, and post-operative interventions; a multi-disciplinary team approach; and direct patient cooperation to be successful. Moreover, implementing an ERACS program undeniably requires a culture change and a methodical shift in the approach of these patients that ultimately allows the team to achieve the above-mentioned goal; therefore, team-building, planning, and anticipation of obstacles are expected.

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Access this article online	
Website: https://journals.lww.com/sjan	Quick Response Code
DOI: 10.4103/sja.sja_62_24	

How to cite this article: Navas-Blanco JR, Kantola A, Whitton M, Johnson A, Shakibai N, Soto R, *et al.* Enhanced recovery after cardiac surgery: A literature review. Saudi J Anaesth 2024;18:257-64.

Jose R. Navas-Blanco, Austin Kantola, Mark Whitton, Austin Johnson, Nasim Shakibai, Roy Soto, Sheryar Muhammad

Department of Anesthesiology, Oakland University William Beaumont School of Medicine, Corewell Health East, Royal Oak, Michigan, USA

Address for correspondence: Dr. Jose R. Navas-Blanco, Department of Anesthesiology, Oakland University William Beaumont School of Medicine, Corewell Health East, Royal Oak, MI, 48073, USA.
E-mail: jrnb2001@icloud.com

Submitted: 04-Feb-2024, **Accepted:** 06-Feb-2024, **Published:** 14-Mar-2024

satisfaction. The majority of data from ERAS comes from colorectal surgery patients, although there has been an increase in data for cardiac surgery patients in recent years. The authors present an updated literature review of the current trends in ERACS.

Enhanced Recovery After Cardiac Surgery

Definition

ERACS is a multi-modal approach used in peri-operative patient care that promotes early recovery, improving patient satisfaction, and reducing post-operative morbidity and mortality as well as the length of hospital stay.[5] ERACS methodology builds off of the 'fast-track' approach to cardiac surgery, which emphasizes the use of shorter-acting anesthetic agents and minimally invasive procedures to achieve earlier extubation and shorter intensive care unit (ICU) stays. In addition to the latter, ERACS methodologies incorporate additional peri-operative measures that allow for more comprehensive management of patients and positive clinical outcomes, which ultimately aims for the goal of quicker return to baseline pre-operative status. The interventions used in ERACS cover the patients' entire surgical experience, including the pre-operative, intra-operative, and post-operative periods.[6]

ERACS versus "fast-track" recovery after cardiac surgery

The concept of "Fast-Track" after cardiac surgery involves intra-op and post-operative methods aimed to early extubation since rapid ventilator weaning has been typically associated with a shorter length of stay (LOS). "Fast-Track" methods in essence involve all the maneuvers that may be applied to bypass the traditional management of cardiac surgery patients in the past, in which extubation was delayed given the "nature of the procedure". The concept of "fast-tracking" dates back to the 1990s, in which the pressure of cost containment became evident in the United States' healthcare system. During this period of time, a fast-tracking peri-operative management aimed to facilitate tracheal extubation within 1–6 hours after cardiac surgery.[7] The problem was to determine which group of patients would fit within these criteria. Multiple risk models were then proposed based on multi-variate analyses to determine which patients and surgical factors would be associated to a higher chance of success in the "fast-tracking" of cardiac surgical patients, but as expected, none of these risk models were flawless as various peri-operative factors play a substantial role in determining the fast-tracking success.[8]

The concept of "fast-track" in cardiac surgery eventually showed shorter extubation times and ICU LOS but did not show promising data in terms of rehabilitation, hospital LOS, decreased costs, and so forth. Nonetheless, it became clear that just performing interventions in the intra- and post-operative periods were not sufficient. The need for post-surgical improvement marks the beginning of ERACS as a continuation of the original ERAS, which showed promising results in patients recovering from colorectal surgery.[8,9] Following the same idea of ERAS, ERACS applies a similar concept, integrating the patient experience before, during, and after surgery, with the purpose of not just achieving earlier extubation times but also allowing earlier recovery, returning to baseline function and rehabilitation.

Level of evidence for ERACS interventions

"ERAS Cardiac" represents a comprehensive multi-disciplinary group, where most recent consensus was published in April 2018. The group selected several interventions included in the phases of the patient's path through recovery, and following the "Classification of Recommendations and Level of Evidence" published by the American College of Cardiology and the American Heart Association as a tool to determine strength of recommendation, the group presented an evidence-based expert consensus statement.[10] A full statement of these recommendations can be found in www.erascardiac.org. A summary of the "Class of Recommendation" and "Level of Evidence" is presented in Table 1.

Pre-operative Interventions

Pre-habilitation (class of recommendation IIa, level of evidence B-NR)

Pre-habilitation programs consisting of cardio-respiratory and muscular training reduce post-operative complications and positively impact patients' length of hospital stay. Patients who train pre-operatively for a period of at least 4 weeks have seen reductions in post-operative pulmonary complications such as severe pneumopathy and atelectasis as well as a decreased length of hospital stay.[11] Exercise represents an intervention that increases functional capacity, improves health status, decreases sympathetic over-reactivity, and improves insulin sensitivity and may be associated to an overall improved psychological readiness for surgery. A comprehensive pre-habilitation program should also be joined with nutrition optimization (N), exercise training (E), and anxiety reduction (W for worry; such intervention is referred as a 'NEW' approach). The main disadvantage of pre-habilitation is time; therefore, it becomes less effective depending on the urgency of the surgery.[12,13]

Carbohydrate loading and avoidance of prolonged fasting (class of recommendation IIb, level of evidence C-LD)

Cardiac surgery can cause metabolic stress which can be exacerbated by pre-operative fasting, resulting in a wide

Table 1: Summary table of expert recommendations for enhanced recovery after cardiac surgery (ERAS Cardiac Society)

Intervention	Class of Recommendation	Level of Evidence
Pre-Operative		
Pre-Habilitation	IIa (Moderate)	B – Non-Randomized
Carbohydrate Loading Avoidance of Prolonged Fasting	IIb (Weak)	C – Limited Data
Correction of Nutritional Deficiency and Support	IIa (Moderate)	C – Limited Data
Pre-operative Smoking and Alcohol Cessation	I (Strong)	C – Limited Data
Patient Engagement and Access to Technology	IIa (Moderate)	C – Limited Data
Intra-Operative		
Anti-Fibrinolytics	I (Strong)	A
Avoidance of Hyperthermia	III: Harm (Strong)	B – Non-Randomized
Infection Reduction Bundle	I (Strong)	B – Non-Randomized
Optimization of Sternal Closure	IIa (Moderate)	B – Non-Randomized
Post-Operative		
Early Extubation	IIa (Moderate)	B – Non-Randomized
Multimodal Analgesia	I (Strong)	B – Non-Randomized
Delirium Screening	I (Strong)	B – Non-Randomized
Goal-Directed Therapy	I (Strong)	B – Randomized
Chemical Thromboprophylaxis	IIa (Moderate)	C – Limited Data
Perioperative Glycemic Control	I (Strong)	B – Randomized
Avoidance of Hypothermia	I (Strong)	B – Non-Randomized
Avoidance of Acute Kidney Injury and Biomarkers for Early Detection	IIa (Moderate)	B – Randomized
Chest Tube Drain Management	I (Strong)	B – Randomized

range of post-operative complications. Administration of a carbohydrate drink has been associated with reducing insulin resistance and tissue glycosylation, enhancing post-operative glucose control, returning of gut function, and reducing LOS. Additionally, prolonged pre-operative fasting may contribute to post-operative insulin resistance. Continuation of a clear liquid diet up to 2 to 4 hours before surgery is a key component of non-cardiac ERAS protocols.[14-16]

Correction of nutritional deficiency and support (class of recommendation IIa, level of evidence C-LD)

It is recommended to assess and treat any underlying nutritional deficiency prior to undergoing cardiac surgery. Albumin is commonly used in pre-operative assessment as an indicator for malnutrition and a predictor of post-operative risk/mortality. Rigorous nutrition supplementation for 5–7 days before the procedure may improve outcomes in patients with a pre-operative serum albumin <3 g/dL.[17] In regard to pre-operative serum glycosylated hemoglobin (HbA1C), a concentration of <6.5% has been associated to decreased post-operative complications including sternal wound infection and myocardial ischemia. In certain cases, depending on the value of HbA1c, it could be necessary to postpone non-urgent surgery to allow for proper glycemic control.[18,19]

Pre-operative smoking and alcohol cessation (class of recommendation I, level of evidence C-LD)

Smoking exposes patients scheduled for surgery to an increased risk of 20% in-hospital mortality and 40% in major post-operative complications. Cessation should be achieved as soon as possible before cardiac surgery for ideal outcomes. In a retrospective analysis involving a total of 3730 male patients undergoing coronary bypass grafting surgery, Ji *et al.* reported that the risk of post-operative pulmonary complications in persistent smokers was 2.41 times greater than that in non-smokers. While the benefits of smoking cessation increase with the length of cessation before surgery, they should be reviewed routinely, independent of the timing of the planned operation. Similarly, excessive alcohol intake can lead to pulmonary complications, impaired wound healing, bleeding, and metabolic and infectious complications.[20-22]

Patient engagement and access to technology (class of recommendation IIa, level of evidence C-LD)

Patient activation and engagement in care is associated with a disposition to obtain preventative care, enroll in physical activities before and after surgery, and more importantly understand the nature of the disease involved and the type of surgery to be performed. Numerous e-health innovations have been developed in the recent years; most of them are self-intuitive and are aimed to assist and increase patient self-engagement and improve surgical care. Such innovations aid in the education of the patients, and from the providers' perspective, it could also allow for patient-reported outcomes to be captured. On the contrary, less engaged patients are roughly three times as likely to have unmet medical needs and twice as likely to delay medical care.[23,24]

Pre-procedure anemia optimization

Optimization of anemia before cardiac surgery is not included in the algorithm proposed in the ERACS protocol developed in 2018. The development of a pre-operative patient blood management (PBM) program aiming to detect and correct iron-deficiency anemia is recommended to reduce adverse outcomes after cardiac surgery. The three pillars of PBM programs are anemia management, minimizing patient blood loss, and analysis of the appropriateness of blood transfusion. Optimizing pre-operative anemia before surgery is an intervention that can be used to reduce the need for intra- and post-operative blood transfusions and reduce the risk of negative post-operative events.[11,25]

In a review conducted by Williams *et al.*, including data from 182,599 patients who underwent primary isolated on-pump coronary artery bypass grafting (CABG), pre-operative anemia was associated with complications such as mortality, renal failure, deep sternal wound infection, and prolonged hospital stay. Results showed the lowest frequencies of death or complications observed with pre-operative HCT levels of at least 42%. Iron supplementation and erythropoiesis-stimulating agents have been indicated as treatment options for anemic patients with the recommendation to tailor treatment to patients' specific diagnoses.[25,26]

Intra-operative Interventions

Anti-fibrinolytics (class of recommendation I, level of evidence A)

Anti-fibrinolytic agents in the form of either tranexamic acid (TXA) or epsilon aminocaproic acid have been shown in large randomized controlled trials to provide a significant reduction in the need for blood transfusions in patients undergoing cardiac surgery. These agents work by inhibiting the lysis of polymerized fibrin, blocking the lysine binding site of plasminogen, causing clot stability. TXA is 6–10 times more potent than its similar aminocaproic acid, and higher doses (>100 mg/kg) may lead to seizures, especially in patients with lower seizure threshold and in patients >50 years of age. It is important to emphasize that concurrent administration of systemic heparin does not affect the activity of either drug.[27,28]

Avoidance of hyperthermia (class of recommendation III, level of evidence B-R)

Hyperthermia (>37.9°C) while rewarming on cardiopulmonary bypass is potentially harmful and should be avoided as cerebral hyperthermia after cardiac surgery is associated with neurologic injury and dysfunction. Additionally, hyperthermia has also been linked to increased rates of mediastinitis and post-operative acute renal failure.[29-31]

Infection reduction bundle (class of recommendation I, level of evidence B-R)

Surgical site infections can be reduced through implementing a "bundle" of evidence-based best practices. Care bundles have demonstrated decreased sternal wound infections and donor site infections by 4.7% and 1.5%, respectively. The ERACS program emphasizes that in order to obtain the best results, such care bundles should not be implemented individually as synergistic application of these measures leads to better results.[32]

Care bundles include pre-operative chlorhexidine showers, standardization of surgical field preparation, wound protectors, daily washing of the incision with chlorhexidine, administration of cefazolin or cefuroxime 30–60 minutes prior to skin incision, and to continue antibiotic regime for no longer than 48 hours.[33,34]

Optimization of sternal closure (class of recommendation IIa, level of evidence B-R)

Concerns for inadequate bone healing after surgery due to lack of appropriate sternal stabilization promote that cardiac surgery patients recover under "sternal precautions", which impairs their overall recovery and mobilization. The ERACS consensus recommends rigid plate fixation of the sternum after cardiac surgery as a measure to improve bone healing and reduce mediastinal wound complications. A randomized controlled trial comparing rigid plate fixation and wire cerclage demonstrated better wound healing in the former group as well as fewer sternal complications, improved reported patient outcomes, and no additional costs at 6 months after surgery. Rigid fixation should be specially considered in high-risk patients including morbidly obese, prior chest wall radiation, severe chronic obstructive pulmonary disease, and chronic steroid use.[35,36]

Post-operative Interventions

Early extubation (class of recommendation IIa, level of evidence B-NR)

Prolonged mechanical ventilation after cardiac surgery leads to an increased length of ICU and hospital stays, higher costs, and increased morbidity and mortality rates. Early extubation is safe, effective, and practical as part of a cardiac surgery-enhanced recovery protocol and is the gateway to early mobilization and nutrition and a decreased ICU length of stay. It is important to emphasize that the concept of "fast-track" originates for the mere need of early extubation after cardiac surgery, and as clinical concepts have evolved during the last years, ERACS methods have been added to assure that patients get not only extubated faster but also

re-inserted back into their pre-surgery lives as smoothly as possible. The ERACS Cardiac Society and the Society of Thoracic Surgeons recommend strategies to ensure extubation within 6 hours of surgery.[37,38]

The benefits of early extubation include earlier patient mobilization, improved hemodynamics without ventilator risks, return to normal feeding, reduced pneumonia risk, reduced need for ICU stay, and reduced duration and dose of sedatives, thereby decreasing delirium incidence and improving cognitive and cardio-vascular recovery. Several factors play a significant role in predicting the "success" of an early extubation protocol, details of which extend beyond the scope of this article, although some of these include a younger age (mean of 61 years old), a lower body mass index (mean of 26.9 kg/m^2), absence of chronic lung disease and diabetes, a minimally invasive surgical approach, pre-operative albumin >4 g/dL, isolated CABG, and elective operational status. Brovman *et al.* demonstrated in a large multi-center analysis that early extubation after surgery (within 6 hours) was not associated with a higher risk of re-intubation after isolated CABG or isolated aortic valve replacement.[37,39]

Multi-modal analgesia (class of recommendation I, level of evidence B-NR)

Opioids are associated with respiratory depression, nausea, vomiting, undesirable sedation, and post-operative ileus. Multi-modal analgesia consists of an essential component of all ERAS pathways based on the "synergistic" effect of non-opioid analgesics. The line between allowing a non-opioid approach and adequate pain control could be very fine, and optimizing pain control after cardiac surgery hastens return to a "normalization" of quality of life and functionality in these patients.[40]

Opioid doses should be reduced to a goal of <20 mcg/kg of fentanyl (or equivalent). ERACS protocols emphasize the importance of minimizing the use of benzodiazepines and supplementing pain control with other opioid sparing approaches including but not limited to non-steroidal anti-inflammatory drugs when feasible and indicated (i.e., ketorolac, ibuprofen), acetaminophen (either orally pre-operatively or intravenously after surgery), peri-operative gabapentin, dexamethasone, and local anesthetics (either locally as lidocaine transdermal patch, or locally infiltrated after the skin is closed). Regional anesthesia in the formal of truncal blocks (i.e., serratus anterior plane blocks, para-sternal intercostal blocks, para-vertebral blocks) is also an important tool that can be entertained in certain cases, depending on the incision and the type of procedure performed.[41]

Delirium screening (class of recommendation I, level of evidence B-NR)

Delirium has long been recognized as a complication following cardiac surgery. Delirium is noted for its role in delayed extubation times as well as poor surgical outcomes, increased costs, increased morbidity and mortality rates, and its association with reduced cognitive and functional recovery. Overall, post-operative delirium after cardiac surgery is multi-factorial. Certain risks increase the vulnerability of patients to delirium, including frailty, pre-operative depression, and sub-clinical Alzheimer's dementia. In addition, women tend to be more prone to develop delirium after cardiac surgery. Current reports estimate that about 20% of patients in cardiac surgery experience delirium post-operatively, nearly twice that of elective non-cardiac procedures. An optimal balance of sedation, analgesia, anxiety, and delirium management may result in reduced post-operative pain, decreased anxiety and delirium, enhanced sleep quality, and improved recovery. An optimal balance of sedation, analgesia, anxiety, and delirium management may result in reduced post-operative pain, decreased anxiety and delirium, enhanced sleep quality, and improved recovery.[42,43]

Goal-directed therapy (class of recommendation I, level of evidence B-R)

Goal-directed therapy (GDT) is a system of hemodynamic treatment goals used to aid in the decisions surrounding the administration of fluids, inotropes, and vasopressors to improve the delivery of oxygen to tissues. The "macro" goals of GDT revolve around the maintenance of patient hemodynamics including cardiac index, systemic blood pressure, and systemic venous oxygen saturation. GDT "micro" goals are generally laboratory parameters that represent biochemical processes such as lactate clearance, inflammation, oxygen consumption, and acute kidney injury biomarkers. Implementation of GDT has shown reduced LOS, reduced infection rates, and a lower incidence of low-cardiac-output syndrome.[6,11,39]

Chemical thromboprophylaxis (class of recommendation IIa, level of evidence C-LD)

Vascular thrombotic events (VTEs), including deep vein thrombosis (DVT) and pulmonary embolism (PE), are a potentially preventable form of morbidity and mortality for patients recovering from cardiac surgery. A meta-analysis performed by Ho *et al.* found that chemical thromboprophylaxis could significantly reduce VTE risk without increasing the risk of bleeding or cardiac tamponade. According to the ERACS society, the strength of this recommendation is limited due to the incorporation of low-quality studies. Despite the sparse data, they suggest thromboprophylaxis as soon as

hemostasis is achieved, in addition to mechanical measures via intermittent pneumatic compression devices.[44,45]

Peri-operative glycemic control (class of recommendation I, level of evidence B-R)

Peri-operative hyperglycemia is widely recognized as an indicator of poor post-operative surgical outcomes, associated to direct glycemic toxicity, enhanced oxidative stress and inflammation, and promoting a pro-thrombotic state and increased risk for infections. Improving glycemic control reduces wound-healing complications and reduces post-operative morbidity and mortality. A glycated hemoglobin of less than 7% should be achieved, ideally less than 6.5%. A multi-disciplinary discussion should be contemplated in patients undergoing elective cardiac surgery with a glycated hemoglobin >7% in order to out-weigh risks versus benefits. Educating patients about exercise, diet, cessation of smoking, and minimizing alcohol intake is necessary as these impact HbA1c levels.

Consider using intravenous insulin infusions in hyperglycemic patients undergoing urgent or emergency cardiac surgery, especially if glucose remains above 180 mg/dL, as this is the most effective way to tightly maintain glycemic control (class of recommendation IIa, level of evidence B-NR).[46,47]

Avoidance of hypothermia (class of recommendation I, level of evidence B-NR)

Hypothermia in cardiac surgery is rather common as the majority of the procedures imply the use of cardio-pulmonary bypass, which is usually associated with different degrees of hypothermia. Nevertheless, even mild hypothermia may lead to multiple physiologic derangements including but not limited to increased myocardial demand and further risk of ischemia, delayed wound healing, coagulopathy, prolonged emergence and delayed awakening from anesthesia, and prolonged ventilator use and hospital stay. Active measures should be implemented throughout the peri-operative period to preserve the core body temperature around 36°C–37°C, especially in the intra-operative period and soon after ICU arrival. The use of forced-air warming blankets, warmed intravenous fluids, and warming irrigation are some of the measures that can be implemented to preserve the core body temperature in these patients.[48,49]

Avoidance of acute kidney injury and biomarkers for early detection (class of recommendation IIa, level of evidence B-R)

Cardiac surgery-associated acute kidney injury is a major and common complication and is independently associated with worse short- and long-term outcomes. Varying degrees of acute kidney injury after cardiac surgery can be seen in up to 42% of patients, with 1–5% of these patients requiring renal replacement therapy. Early recognition and implementation of preventive maneuvers are the pinnacle of the management of these patients. Urine output is a functional marker with low sensitivity. Serum creatinine does not become significant before 50% of the renal glomerular filtration capacity is limited and therefore is a "late" indicator of renal injury.[50,51]

Serum biomarkers may allow us to accurately identify patients who had a normal glomerular filtration rate at risk for post-operative acute kidney injury before its onset. Two novel serum biomarkers, insulin-like growth factor-binding protein 7 (IGFBP7) and tissue inhibitor of metalloprotease-2 (TIMP-2), have been proposed and currently are under study to determine patients at risk for cardiac surgery-associated acute kidney injury. The goal ultimately is to identify patients "earlier" and implement measures to avoid kidney injury and decrease costs. Interventions to prevent kidney injury include avoidance of peri-operative hypotension, avoidance of nephrotoxic agents, discontinuation of angiotensin-converting enzyme inhibitors, and angiotensin II receptor blockers.[51,52]

Chest tube drain management (class of recommendation I, level of evidence B-R)

Maintenance of chest tube patency is recommended to prevent retaining blood in the mediastinal or pleural spaces. Active tube clearance has been shown to prevent chest tube occlusion, and several studies have demonstrated a direct relationship between tube clearance and reduction of rates of re-operation for bleeding and post-operative atrial fibrillation. However, high chest tube output of retained mediastinal blood may lead to mechanical compression of heart and lungs, resulting in the requirement of further re-interventions. Small volumes of retained mediastinal blood promote an inflammatory process that may lead to peri-cardial effusions and increase the risk of atrial fibrillation. Stripping or "milking" chest tubes have been widely recognized to be time-consuming and ineffective, and breaking the sterile field to remove a clot is not recommended by the ERACS society (class of recommendation III, level of evidence A).[53-55]

Implementing an ERACS Program

Starting an ERACS program requires an institutional commitment to cultural change, which includes a multi-disciplinary team building with representation of all key stakeholders including but not limited to nursing, anesthesiology, surgery, mid-level providers, and other related associated clinical teams. A center-specific ERACS protocol following the pre-operative, intra-operative, and post-operative considerations explained above is achievable,

ensuring all interested parties have an opportunity to provide input, initiate educational activities to disseminate the program within the institution, and finally perform continuous process monitoring, identification of mishaps, evaluation, and improvement. Standardization is a key driver of success of an ERACS protocol to assure that a protocol that has been widely agreed upon gets executed and to minimize out-of-protocol interventions unless the ERACS coordinators agree.[56,57]

Conclusion

The ERACS program represents a comprehensive pathway to manage cardiac patients throughout all the peri-operative phases of care, with the primary goal of returning to baseline functioning, early recovery, minimizing opioid use, and reduction in health care cost. The application of ERACS protocol standardization requires a multi-disciplinary team commitment, culture change, and sustainability in order to assure the success of the program. Site-specific protocols may be implemented in addition to those suggested by the ERACS program in order to tailor the needs of the institution to the population they serve.

Financial support and sponsorship

Support was provided solely from institutional and/or departmental sources.

Conflicts of interest

There are no conflicts of interest.

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