Center for Innovative Drug Development and Therapeutic Trials for Africa

Enhanced Recovery After Surgery Protocol as Innovative Solution for Improving Surgical Patients' Outcome in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis.

THESIS SUBMITTED TO ADDIS ABABA UNIVERSITY, COLLEGE OF HEALTH SCIENCES, CDT AFRICA IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE MASTER OF SCIENCE DEGREE IN CLINICAL TRIAL

BY:

PENIEL KENNA

ADVISORS:

Dr. GIRMAY MEDHIN (BSc, MSc, PhD, Associate Professor of Epidemiology and Biostatistics, Head of Data Management Unit of CDT-Africa, Addis Ababa University)

Prof. ABEBAW FEKADU (MD, PhD, MRC-Psych, Centre Leader of CDT-Africa, Addis Ababa University)

Dr. TIHITENA NEGUSSIE (MD, Associate Professor of Pediatrics Surgery, Pediatric Surgery Division, Consultant General & Pediatrics Surgeon, School of Medicine Addis Ababa University)

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INFORMATION

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Candidate: Peniel Kenna

Advisors: Dr. Girmay Medhin,

Prof. Abebaw Fekadu,

Dr. Tihitena Negussie

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Acronyms/ Abbreviation

Sustainable Development Goals	SDG
Low- and Middle-Income Countries	LMICs
Enhanced Recovery After Surgery	ERAS
World Health Organization	WHO
Length of Stay	LOS
Health Related Quality of Life	HQoL
International Prospective Register of Systematic Reviews	PROSPERO
Preferred Reporting Items for Systematic Reviews and Meta-Analyses	PRISMA
Population, Intervention, Comparator and Outcome	PICO
Randomized Controlled Trials	RCT
RR	Relative Risk
MD	Mean Difference
SMD	Standardized Mean Difference
Newcastle-Ottawa Scale	NOS
Upper-Middle Income	UMI,
Lower-middle Income	LMI
Low Income	LI

Abstract

Introduction: Close to a third of the global disease burden is accounted for by surgical conditions. The 76th World Health Assembly Agenda item 13.1 highlighted urgent actions needed to enhance surgical care. With 18-25% postoperative complication rate, application of the Enhanced Recovery After Surgery (ERAS) protocol is advised. The aim of this study was to assess the effectiveness of the ERAS protocol in improving short-term and intermediate surgical patient outcomes in Low- and Middle- Income Countries (LMICs). **Methodology:** We conducted systematic review and meta-analysis and the protocol was registered in the PROSPERO database (CRD42024524807). A systematic search for observational studies and clinical trials was conducted in PubMed, Scopus, Cochrane, and Web of Sciences along with online trial registries and Google Scholar. Search strategy includes keywords related to "Enhanced Recovery After Surgery", "ERAS", "Fast-Track Surgery", "LMICs", and names of LMICs. Reference sections of the included studies were manually searched. Risk of bias of included studies were assessed using Cochrane risk of bias and Newcastle-Ottawa scale. **Results:** A total of 1332 studies were initially identified and after removing duplicates, 1243 studies remained, with 56 papers eligible for full-text review. Eight studies were identified from reference section and were added to evidence synthesis. Thirty-five studies, 23 clinical trials and 12 observational studies were included for review and 33 studies were included for meta-analysis. Eighty-four percent of the publications were from south and southeast Asia. Comparable number of participants were distributed in the intervention (3,163) and control (3,243) groups. The studies comprised mostly abdominal surgeries (n=17). Each study compared ERAS protocols with routine perioperative care. Meta-analysis indicated significant reduction of postoperative morbidity following the implementation of the ERAS protocol [(RR=0.73; 95%CI, 0.55 to 0.76) with (I^2) of 1.1% (P-value of 0.44)]. Also, significant reduction in postoperative length of hospital stay was observed when ERAS protocol was implemented [(SMD= -0.67 [95%CI -0.54 to -0.82]) with I^2 = 76.8]. There was no significant difference in postoperative mortality and readmission rate. **Conclusion:** Improved patient outcomes related to reduced postoperative complication rate and length of hospital stay were observed with ERAS application. The ERAS protocol appears promising in LMICs for enhancing surgical patient outcomes; Hence, we recommend its application. Although there could be ERAS implementation cost, its role in expediting patient recovery could reduce costs related to hospitalization.

Keywords: ERAS, LMIC, Postoperative Mortality, Postoperative Morbidity, Length of Stay

Introduction

In response to the universal Sustainable Development Goals (SDG) to which Ethiopia is one of the signatories, countries are working to improve the wellbeing and health of their people (1,2). The 76th World Health Assembly agenda item 13.1 calls for timely additional efforts globally to strengthen the planning and provision of emergency, critical and operative care services as part of Universal Health Coverage (UHC), so as to meet population health needs, improve health system resilience and ensure public health security (3). Strengthening the provision of operative care is crucial especially in the perioperative area, where 28 – 32% of the global burden of disease is amenable to surgical care (4). However, the reported crude mortality rate after major surgery is 0.5-5% (5–7) and 18-25% of patients that undergo through surgery develop complications after inpatient operations in which half of the harms could have been prevented (5,7). This is disappointingly high rate and antithetical to the intention of surgical procedures that are implemented to enhance wellbeing and quality of life. Evidence-based practices, such as the Enhanced Recovery After Surgery (ERAS) protocol were developed to help reduce perioperative and anesthetic-related adverse events (8).

Evidence based practice in the medical sector, uses scientific findings when managing the health of patients. It serves as a catalyst for health innovation by grounding practice in evidence, promoting continuous improvement, and ultimately benefiting patients and healthcare systems alike (9). On the other hand, health innovation pulls together evidence to develop novel solutions, technologies, or approaches to address healthcare challenges. Thus, the World Health Organization (WHO) defines health innovation as a fresh or refined solution that has the potential to be transformative and lead to positive wellness impacts (10). It includes new or improved ideas, and a care pathway that has clear benefits when compared to what is currently done (11).

The ERAS protocol is a new approach that is evidence-based patient centered guideline in the perioperative settings (12). The ERAS protocol has the potential to alter the traditional way of practice resulting in a paradigm shift in the pre, intra- and post-operative period. The Denmark professor, Henrik Kehlet, the first person to implement ERAS and to win the first surgical Nobel prize, has played a big part in revolutionizing clinical practices in several surgical fields and improving outcomes for surgical patients (13). In the late 1990, when the protocol was

implemented for the first time, it resulted in a major shift on the postoperative recovery of patients that underwent sigmoid resection. There was significant reduction in hospital length of stay (LOS) with median stay of 2 days where with traditional practices took 5-10 days, and required prolonged rehabilitation (14). Then in 2001, the ERAS study team was established to develop guidelines based on best available evidences (15,16). The first ERAS consensus protocol, consisting of various interventions, was published in 2005 using evidence from colorectal surgery (17). These initial sets of intervention, along with other components as illustrated in table 1, is now known as the accelerated or fast track surgery (22). Currently the pathway includes perioperative interventions (elements or components), divided into three distinct phases – the preoperative, intraoperative, and postoperative periods and not all components are equally weighted with respect to their influence on postoperative recovery (18). ERAS society is currently developing amendments of the protocol for different surgical specialties and auditing the implementation of the protocol for new hospitals (19).

The physiological mechanism of how ERAS works is through modulating stress hormone release to maintain postoperative physiological function, thereby improving outcome (20). Efficient implementation of ERAS requires synchronized surgical teamwork across the multi- disciplines. Furthermore, the collaborative work is not only limited within the health professionals but looks for active engagement of the patients and their family. Growing recognition of the generality of interventions and applicable breakthroughs in postoperative outcomes has made them the standard of care for a number of surgical operations in the developed world. This innovative, evidence-based protocol, that helps with the endorsement of high quality of care, will assure patients to have fast recovery from anesthesia and surgery with improved post - operative outcome (21,22). The ability to spread and scale ERAS international guidelines is promising, and health systems should consider how to spread and scale this innovation to ensure ERAS for all (20).

***Table 1**:Enhance Recovery After Surgery Guideline components derived from Reporting on ERAS Compliance, Outcomes, and Elements Research (RECOvER) Checklist (23)*

Preoperative Period	Intraoperative Period	Postoperative Period
Preadmission patient education regarding the protocol	Standard Anesthetic Management	Management of postoperative fluids
Preadmission screening and optimization		Postoperative analgesia and anti-emetic plans
		Plan for opioid minimization
Fasting and carbohydrate loading guidelines	Prevention of Intraoperative Hypothermia	Drain and line management
		Early mobilization strategy
Pre-emptive analgesia		Postoperative diet and bowel regimen management
Anti-emetic prophylaxis	Intraoperative fluid management strategy	Criteria for discharge
		Tracking of post-discharge outcomes

Literature Review

ERAS protocol is currently becoming the standard of care for many developed nations (24). It is believed to improve short term outcomes, particularly post operative pain, nausea and vomiting, gastrointestinal motility, and hospital LOS. Intermediate outcomes such as morbidity, mortality, and readmission, and long-term outcomes namely Health Quality of Life (HQoL), functional and cognitive return(25) are also improved. Many studies from higher income countries have investigated the impact of ERAS protocol in regard to the recovery process by measuring hospital LOS, morbidity, readmission and mortality.

The post-operative LOS, when the ERAS protocol is implemented, decreased significantly without increasing the complications and readmission rates, in a surgical specialty dependent manner. Systematic review and meta-analysis done by Sauro et al., (26) indicated a statistically significant reduction of patient hospital LOS and postoperative LOS stay in ERAS group Vs. routine care pathways, Mean Difference (MD), 1.88 days; 95% Confidence interval (CI), 0.95-2.81 days; I^2 =86.5%; P < .001 of 44 studies and MD, 2.83 days; 95% CI, 2.10-3.55days; I^2 = 0%;P < .001 of 22 studies, respectively. All types of surgical procedures from across the world were included in their qualitative synthesis, but only Randomized Clinical Trials (RCT) were involved for the meta-analysis. Similarly, a meta-analysis of five studies by Riad et al., (27) indicated reduced patients postoperative LOS. This review by Raid et a., included countries from LMIC, specifically lower-middle income and low income, and the surgical specialty revolved around abdominal and neurology procedures. Additionally, a meta-analysis done by Kanani et al, (28) indicated a shorter patient hospital LOS in ERAS group compared to the routine care pathways (MD: -4.04, 95% CI: -4.94 to -3.14). This study in contrast to aforementioned meta-analysis, reviewed articles originated from Africa and focused on colorectal procedures.

Regarding postoperative morbidity, Sauro et al. in their meta-analysis of 14 studies identified that patients under ERAS care pathways have 27% decreased risk of post-operative complication when compared with patients under routine care pathways with Relative Risk (RR)=0.73; 95% CI, 0.56-0.94; I^2 =86.3%. Surgical specialty-based analysis indicated a similar decrement in postoperative morbidity rate in patients under ERAS protocol compared with traditional care pathways. A meta-analysis of 39 abdominal surgery studies other than colorectal procedures by Visioni et al. (29) indicated 30% decreased risk of postoperative complication in ERAS group patients when compared to traditional group (RR=0.70; 95%CI: 0.56-0.86, P = 0.001 emergency abdominal

surgery, meta-analysis of six studies conducted by Hajibandeh et al.(30) has revealed a 50% decreased risk of overall postoperative complication in patients under ERAS pathways when compared with routine care pathways with Odd Ratio (OR) =50%; p-value <0.01. For gynecologic oncology procedures, a meta-analysis of 27 studies by Bisch et al. (31) have indicated a reduced postoperative complication by 32% in patients under ERAS protocol and a meta-analysis of 10 studies by Meng et al. (32)indicated a 50% decreased risk of postoperative morbidity in ERAS group when compared to traditional pathways (RR: 0.50, 95% CI: 0.37 to 0.68, $p < 0.00001$). All the afore mentioned studies involved observational studies and RCT for the quantitative synthesis and were not country income specific.

However, the impact of ERAS on 30-day postoperative readmission and mortality rate is unclear. While some studies found no statistically significant difference, (26,28,30,32) other studies had found the contrary. Sauro et al. (26) and Kanani et al. (28) did not found a statistically significant postoperative readmission rate between the ERAS and routine care pathway groups (RR 1.04; 95%CI,0.81-1.35 of 19 studies) and (RR: 1.10, 95% CI: 0.49 to 2.48, P = 0.82, of eight studies), respectively. Additionally, Hajibandeh et al. (30) and Meng et al. (32) did not find difference in readmission rate. Whereas, Bisch et al. (31) indicated a 20% reduction in readmission (OR 0.80, 95% CI 0.64-0.99) for ERAS patients when compared with routine care pathways. Related to 30-day postoperative mortality, Sauro et al (26) found non-significant result when the ERAS group and non-ERAS groups are compared (OR 0.61, 95% CI 0.23-1.6).

Again, the quality improvement inpatient outcome granted by ERAS needs to have an idea of process evaluation (20). Though it's known that multiple measurement is needed to capture the enhanced recovery, some might try to use specific components of ERAS and try to follow patient outcomes. Of course, this could be attributed to its broadness, which makes it difficult to manage and monitor its compliance (33) as well as individual components could have different influences on postoperative patient outcome. In a retrospective review of 840 patients (Oslo et al. in 2021) two independent machine-learning statistical algorithms were used to determine which subset of ERAS elements was most impactful on LOS <3 days and hospital readmission. The finding showed that specific elements of ERAS protocol such as multimodal pain control, limited opioid use, and early mobilization- are highly related with decreased LOS and readmission (34). Moreover, Bisch et al. (31) meta-analysis has identified a non-significant association between the number of ERAS component

applied or ERAS compliance to patient's postoperative outcome. Yet, to have the best outcome in the quality measurement there is a need to have increased compliance with ERAS guidelines (33,34). This demands a new strategy for its effective implementation in order to increase adherence (33). For instance, there is protocol for LMIC and could play a role in proficient implementation of the protocol to proactively create responsible anesthesia, perioperative, and surgical systems that are cost and technology appropriate, and limit complications and hospital stays (34).

Statement of the Problem

The health goals set out in UHC and the SDG for 2015 and beyond will be difficult to ensure by disregarding the availability and safety of surgical and anesthesia care (35). The focus needs to be not only on the physical and geographical availability of health services but also need to consider the required changes in the health system to incorporate evidence-based strategies to maximize health outcomes (3). In the context of the epidemiological transition in LMICs where non-communicable diseases that require surgical care are increasing, broader system changes are necessary (20). This is leading to shift in attitude about surgery and anesthesia from a luxury to essential care (36).

Poor quality and limited perioperative care have resulted in an increase of mortality and morbidity rate. ERAS application as a protocol is believed to decrease time spent in hospital for patients. It reduces LOS by an average of 2.35 days across multiple surgical subspecialties (37). Prolonged hospital stay can lead to increase in hospital complications for patients like acquiring infection, and increased costs for patients and the healthcare system (38). With ERAS protocol implementation, healthcare costs per patient is reduced by $639.06 ($639.064; 95%CI: -933.850 to -344.278) (37). Inadequate control of acute postoperative pain leads to increased complication, decreased function and quality of life, prolonged recovery time, increased continuance of opioid use associated with healthcare costs escalating, finally turning itself for chronic pain (39). Additionally, ERAS protocol and its impact on long-term patient outcome in certain domains of HQoL, such as pain and fatigue, may improve with the protocol (40).

Significance of the study

To achieve a high level of quality-of-care access and good outcomes, the scaling up of surgical care should focus on standardized, evidence-based care that was cost-effective and supported by quality data. One request to the director general on the 74 WAH is to work on strengthening the evidence base for operative care interventions by encouraging research and supporting Member States to execute research on operative care delivery (3). The findings from this study could provide invaluable input in directing the practice in surgical care in LMICs.

Furthermore, the protocol needs modification in order to be feasible in LMICs, where there is common limitation in infrastructure, resources and access for surgical care. The evidence output from this study will help to generate proof in regard to patient outcome and the implementation of the protocol. This data may provide timely generated practical proof to assist modification of the protocol.

In countries where the perioperative care still follows traditional approach, and where there is scarcity of researches about ERAS and the economic status of the state, the findings of this study will serve as a baseline affirmation to work for quality improvement guideline that is considerate to the country' economical and resource status.

Objective

General Objective

To evaluate the effectiveness of the ERAS protocol in improving short-term and intermediate surgical patient outcomes in LMICs.

Specific Objective

- To evaluate the impact of ERAS protocol implementation on post operative morbidity surgical patients in LMICs
- To evaluate the impact of ERAS protocol implementation on LOS on surgical patients in LMICs
- To evaluate the impact of ERAS protocol implementation on post operative readmission among surgical patients in LMICs
- To evaluate the impact of ERAS protocol implementation on post operative mortality among surgical patients in LMICs

Research questions:

1. What are the components of ERAS protocol implemented in the perioperative period in LMICs?
2. What is the reported improved outcome in LOS, post operative morbidity and readmission associated with the adoption of ERAS protocols compared with routine practice in various surgical specialties in LMICs?

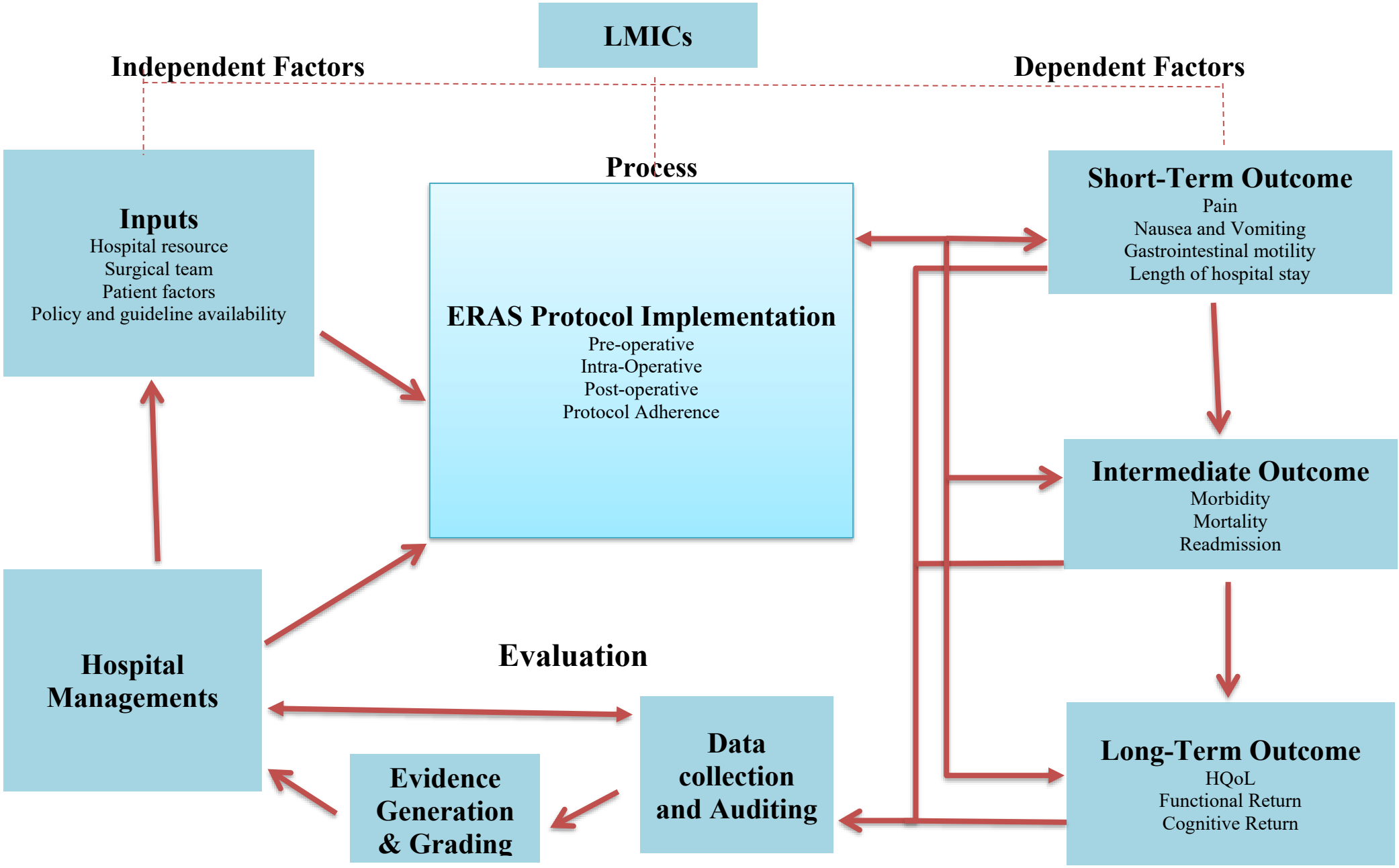

Figure 1 *Conceptual Framework of ERAS protocol in LMICs based on the contextual factors, implementation process and patient outcome measures using the Donabedian Model (41)*

Methodology

This is a systematic review and meta-analysis of studies available in various electronic databases. The protocol was registered at the International Prospective Register of Systematic Reviews (PROSPERO; CRD42024524807). The preferred reporting items for systematic reviews and meta-analyses (PRISMA) guideline (42) were followed to describe the process of literature search and reporting of finding.

Eligibility Criteria

Inclusion criteria

Both randomized and non-randomized clinical studies evaluating ERAS protocol across LMICs on all types of surgical specialties were included.

The Population, Intervention, Comparator, and Outcome (PICO) format was used to identify suitable studies.

Participants involved in the studies

Adult surgical patients aged 18 years and older who underwent surgical operation.

Interventions used in the studies

Application of the ERAS protocol in the pre, intra and post operative period according to the surgical specialty.

Comparator

Adult surgical patients that underwent surgery with routine approach in the perioperative period.

Outcome

Post operative patient outcome to assess the effect of the intervention. This included

1. Length of hospital stay
2. Post-operative Morbidity
3. Readmission Rate
4. Post-operative mortality

Exclusion criteria

Non-comparative studies, studies with less than 50% ERAS protocol components report, and reports that do not explain the ERAS components explicitly and do not include the outcomes of interest.

Search Strategy

Electronic Database Search

A systematic search of electronic databases, including PubMed, Scopus, Embase, Cochrane and Web of Sciences were conducted as part of the research process. The search strategy was developed to include keywords related to LMICs, names of LMICs, Enhanced Recovery After Surgery (ERAS), and Fast-Track Surgery (***see annex I***).

Searching other resources

The reference sections of the included studies and other relevant reviews were checked for the possibility of any additional papers. In addition, online trial registries: such as ClinicalTrials.gov (clinicaltrials.gov), and for ongoing or unpublished trials were searched.

For additional grey literature, such as unpublished reports, dissertation and theses, other online sources, for example, Google scholar were searched.

Data collection and analysis

The Cochrane Handbook for Systematic Reviews of Interventions was followed. Furthermore, the software package provided by Cochrane (RevMan 5.4.1) and additionally, R-Studio software was used.

Selection of studies

Mendeley software was used to import and manage searched articles from electronic databases. Studies that met the eligibility criteria were included in this review. The searched literature and full-text of potentially related trials and observational studies were reviewed by two independent professionals. Controversies in the screening process were resolved through discussion. The

screening and selection processes of the papers are reported using the PRISMA flow chart.

Data extraction and management

Titles and abstracts of RCTs and observational studies generated from electronic searches were reviewed by two independent professionals. Full text review information to be extracted from the papers include methods, number of participants, type of surgical specialty, type of interventions, patient outcomes, and applied components of the ERAS protocol. Moreover, relevant information such as title, journal, year of publication, study design, study setting, baseline characteristics of study participants, follow-up period, sample size, outcomes, and country for each study and for each care pathway were collected using a well-prepared data extraction format. The data extraction format is a tabular format adopted from Cochrane and modified to fit the purpose of the current study (***see annex II***). At last, the number of subjects with an event and the total number of subjects in each care pathway was recorded for dichotomous outcomes and the arithmetic means and standard deviations and/or the median and interquartile range for each group were extracted for continuous outcomes.

Assessment of risk of bias in the included studies

The risk of bias for each trial was evaluated by two professionals independently. The Cochrane Collaboration's tool for assessing the "Risk of bias" (43) was used for the assessment (***see annex II***). The findings from the risk of bias assessment were reported in six domains: sequence generation; allocation concealment; blinding (of participants, personnel, and outcome assessors); incomplete outcome data; selective outcome reporting; and other sources of bias. The risk of bias was rated as high risk, unclear risk, and low risk, and interpretations of the presented data were guided by this information. For non-randomized studies the risk of bias was assessed using the Newcastle-Ottawa Scale (NOS) (44), risk of bias was evaluated for three domains: Selection; Outcome; and Exposure (***see annex***). The two risk of bias assessment tools and the results are attached in the annex part and result section of this document.

Measures of treatment effect

The main outcomes in this review are surgical patient postoperative outcome in regard to hospital LOS, morbidity, readmission rate and mortality rate. RR was used to report pooled results of

dichotomous outcomes. For continuous outcomes we reported the standardized mean differences.

Unit of analysis issues

Participants were included according to the care pathway allocation in each of the studies.

Dealing with missing data

Whenever data from the study reports are not sufficient, ambiguous, or lacking required information, it was planned to communicate authors for clarification. When there is no response for the request, it was planned to exclude the study or the specific outcome.

Assessment of heterogeneity

Heterogeneity between the included studies was evaluated by looking at the forest plots (to detect overlapping CI). The I^2 statistic which is based on Cochrane Q was used to quantify heterogeneity in each analysis, and the Chi2 test with a $p < 0.10$ was used to suggest statistical significance in heterogeneity. The I^2 greater than 40% was used as indicator for existence of heterogeneity that directs the need for subgroup analysis.

Outlier and influence case analysis

When there was between-study heterogeneity that is correlated with one or more studies that have extreme effect sizes, there was an assessment of distortion in the pooled effect estimate. This is important as it can give evidence that the result is robust which is not heavily dependent on effect of a single study. Thus, in studies with low quality or very small studies, the pooled effect was repeatedly evaluated by withholding outliers from the analysis.

Baujat Plot was used to further investigate the contribution of each study to the overall heterogeneity that might be observed in meta-analysis. Studies on the right side (especially in the lower part) of the plot were considered as causes for the observed heterogeneity (45).

Assessment of reporting biases

Possibility of publication bias was examined by looking for asymmetry on the funnel plots. The quantitative assessment for the asymmetry noticed on funnel plot was further analyzed using Egger's test. If the intercept on the test is greater than 0 and p-value is significant it was interpreted

that there is possibility of publication bias.

Data synthesis

To assist with easy clarification, individual codes were given to included studies together with the first author, and year of publication. Included studies were listed in forest plots in chronological order of the year which the studies were published. Since the studies were conducted in different countries, surgical setup and various surgical specialties were included as the random effect model for effect estimation.

Subgroup analysis and investigation of heterogeneity

Meta-analysis was not only used to compute effect size but when there is possibility of heterogeneity it was also served as an instrument to navigate variation of the evidence. The following moderator analyses can be considered in this study:

- The type of surgical case specialty
- Study type (observational versus clinical trial)
- Economic class of countries where the study was conducted (Upper-Middle Income (UMI), Lower-middle Income (LMI), and Low Income (LI)

Sensitivity analysis

To assess sensitivity of primary analysis, there were adding and excluding studies which were classified as high risk for bias back into the analysis in a stepwise fashion. To navigate the effect of small-study on the results of the meta-analysis, fixed-effect and random-effects estimates of the intervention effect were compared. Moreover, the robustness of the meta-analysis results was supported through the leave-one-out method.

Operational Definition

1. **Hospital LOS**: In hospital duration of stay, from admission to discharge, including ICU, Ward, PACU stay.
2. **Postoperative LOS:** In hospital duration of stay, from end of procedure to discharge, including ICU, Ward, PACU stay.

3. **Post-operative Morbidity:** Reported postoperative complication of the surgical procedure
4. **Post-operative Mortality:** Reported postoperative futility within 30 postoperative days.
5. **Readmission Rate:** Revisiting the health care center after discharge, including ICU, operation room, PACU, Ward readmission.
6. **Surgical Patient:** Patients that received anesthesia and have major surgery.
7. **Major surgery**: is a procedure that involves the removal of an organ or body part, or the repair of a large body part
8. **LMICs:** are those countries with a gross national income (GNI) per capita between $1,146 and $14,005, which is categorized as Upper-middle income, low-middle income, and lower income (46).
9. **Upper-middle income**: are those countries with a GNI per capita between $4,516 and $14,005
10. **Low-middle income**: are those countries with a GNI per capita between $1,146 and $4,515
11. **Lower income**: those countries with a GNI per capita below $1,146**.**
12. **ERAS:** an innovative evidence-based approach in the perioperative care pathway.
13. **Routine Care:** is the traditional approach to perioperative care.

Ethical Consideration

The study protocol was submitted to the CDT Africa scientific and ethics review committee. Since this study is systematic review and meta-analysis, we requested for waiver of informed consent. After accessing approval from the committee, the review was commenced.

Result

The search identified a total of 1332 articles. After removing 89 duplicates, 1243 titles and abstracts were reviewed in detail, and 54 papers were eligible for full text review. Eight studies were identified through reference searching and were also assessed for eligibility. Following full text review 31 articles were excluded: studies with participants under 18 years of age (n=4), inadequate ERAS protocol adherence (n=17), lack of ERAS component description (n=6) and study design (n=4). Thus, 33 articles (47–79), with two of the articles(52,59) containing two additional independent experiments, were included. Of these, the 31 articles (47–60,63–79), which include the articles with the two independent experiments (52,59), were eligible for meta-analysis.

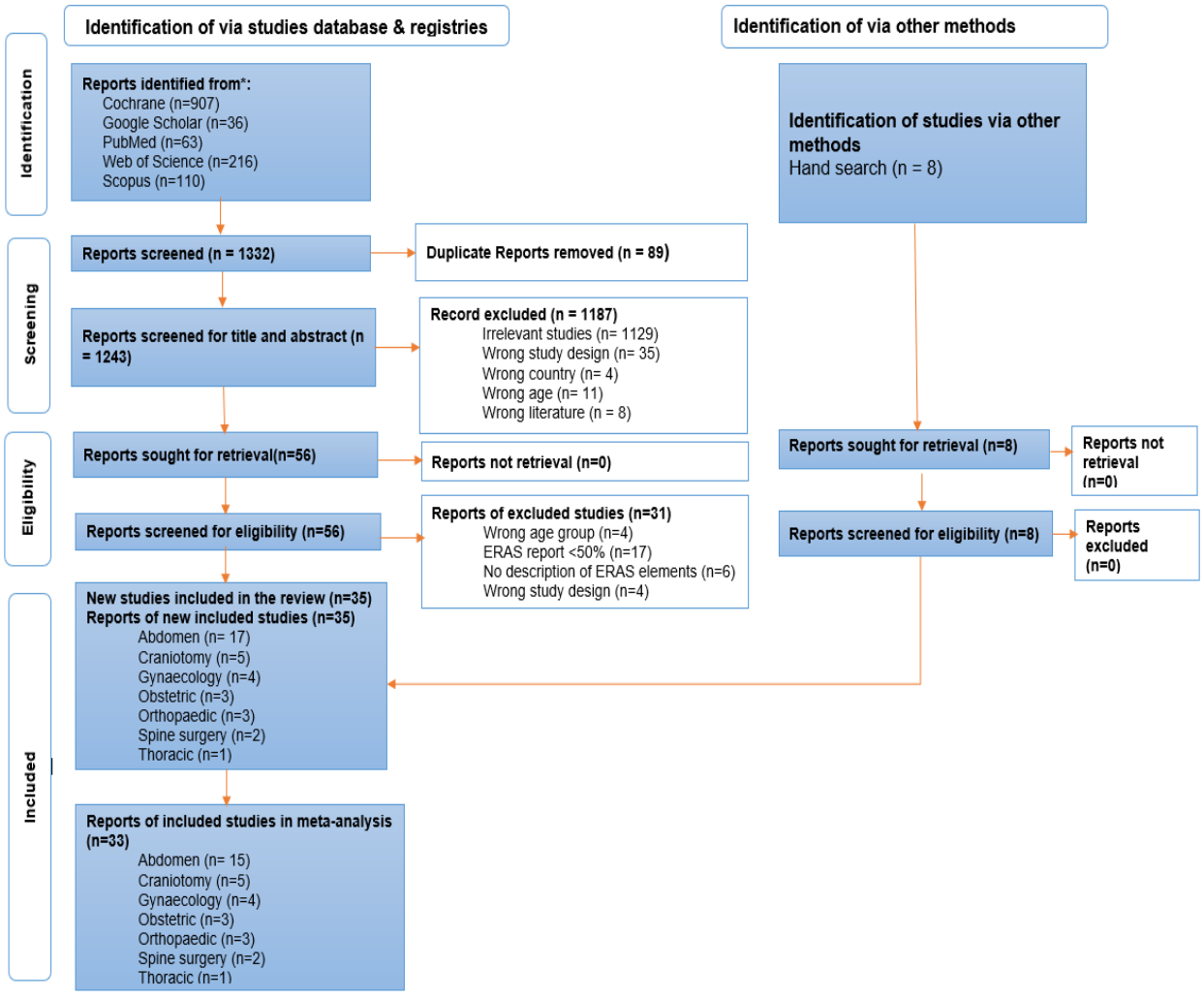

Figure 2 PRISMA flow diagram for study selection in systematic review and meta-analysis

Characteristic of Included Studies

The studies included 23 clinical trials(47–49,51–53,55,57–61,63,64,66–68,70–72,74,75) and 12 observational studies (50,54,56,62,65,69,73,76–79) covering a range of surgical procedures. Most were abdominal surgeries: 6-gastric(48,51,52,61,71,74), 3-colorectal(47,49,50), 3-emergency laparotomy(62,68,75), 1-bariatric(56), 1-liver(64), 1- pancreaticoduodenectomy(54) and 1-esophageal(70) procedures. Other procedure comprised 4-craniotomy(55,60,63,72), 3-gynecologic(57,59,69), 3-obstetric(58,65,76), 3-orthopedic(53,67,73), 2-spine(78,79), 1-Ear, Nose and Throat (ENT) procedure(66), and 1-thoracic(77) operations. A total of 6177 participants, 2776 males and 3410 females, were involved in these studies. Comparable number of participants were allocated in the intervention and control group, 3163 and 3243 participants, respectively. Related to the economic status of the countries on which these studies took place, 21 studies (47–55,60,64,66,67,70–73,76–79), 11(56,57,59,61–63,65,68,69,74,75) and 1 study was from lower income country (58). Approximately, 84% of the publications were from south and southeast Asia (47–52,54–56,60–68,70–72,74–79), while the rest were from Africa(57–59,69,73) and Latin America(53,76). A further description on geospatial allocation and characteristics of the included studies are summarized on *Figure 3 and Table 2*.

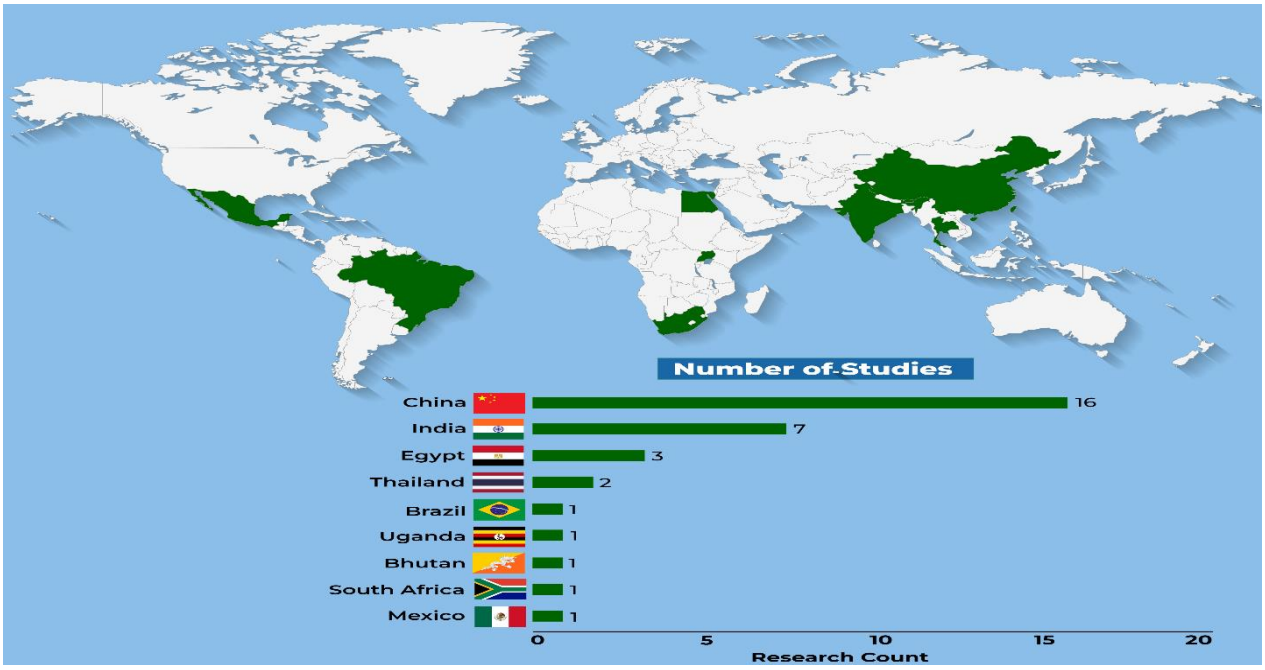

Figure 3 Geospatial overview of studies comparing ERAS protocol with routine care pathway for surgical patients in LMICs

Table 2: Characteristics of the thirty-three included studies

Author	Year of publication	Journal	Country	Economic Level	Surgical Specialty	Type of Research	Sample Size (ERAS/Routine)	Outcome Assessment
Ren et al.(47)	2012	World J. Surg.	China	Upper-middle	Abdominal/colorectal	RCT	299/298	LOS, Morbidity, Mortality
Feng F et al.(48)	2013	World J. Gastroenterol.	China	Upper-middle	Abdominal/ Gastrotomy	RCT	59/60	LOS, Morbidity, Mortality, Readmission
Li et al.(49)	2014	Asia Pac. J. Clin. Nutr.	China	Lower-middle	Abdominal/colorectal	RCT	208/237	LOS, Morbidity, Mortality
Lohsiriwat et al,(50)	2014	World J. Gastroenterol.	Thailand	Upper-middle	Abdominal/colorectal	Cohort	20/40	LOS, Morbidity, Mortality, Readmission
Abdikarim et al.,(51)	2015	World J. Gastroenterol.	China	Upper-middle	Abdominal/gastric ca	RCT	30/31	LOS, Morbidity, Mortality, Readmission
Bu et al, (52) **Experiments 1**	2015	Journal Of Gastrointestinal Surgery	China	Upper-middle	Abdominal/gastric ca	RCT	64/64	LOS, Readmission
Bu et al, (52) **Experiment 2**	2015	Journal Of Gastrointestinal Surgery	China	Upper-middle	Abdominal/gastric ca	RCT	64/64	LOS, Readmission
Alito et al,(53)	2016	Nutrition journal	Brazil	Upper-middle	Ortho	RCT	15/17	LOS
Su et al, (54)	2017	MEDICINE	China	Upper-middle	Abdominal/pancreaticoduodenectomy	Cohort	31/31	LOS, Morbidity, Readmission
Wang et al., (55)	2018	J.of Neurosurgery	China	Upper-middle	Neurology	RCT	70/70	LOS, Mortality, Readmission
Aktimur et al,(56)	2018	Surgery For Obesity and Related Ds.	India	Lower-middle	Abdominal/Bariatric	Cohort	216/92	LOS, Morbidity, Mortality, Readmission
Ferghali et al,(57)	2020	Assiut Scientific Nursing Journal	Egypt	Lower-middle	Gynecology	RCT	70/70	LOS, Morbidity, Mortality, Readmission
Baluku et al.,(58)	2020	Anesthesia and Analgesia	Uganda	Low	Obstetric	RCT	76/77	Readmission
Abdelrazik et al,(59) **Experiment 1**	2020	Ain-Shams Journal of Anesthesiology	Egypt	Lower-middle	Gynecology	RCT	54/55	LOS, Morbidity, Readmission
Abdelrazik et al,(59) **Experiment 2**	2020	Ain-Shams Journal of Anesthesiology	Egypt	Lower-middle	Gynecology	RCT	52/55	LOS, Morbidity, Readmission
Qu et al.,(60)	2020	International Journal of Medical Sciences	China	Upper-middle	Neurology	RCT	64/64	LOS, Readmission
Kate et al.,(61)	2020	International Journal of Surgery	India	Lower-middle	Abdominal/gastric ca	RCT	29/29	-
Gopakumar et al,(62)	2020	Journal of Evolution of Medical and Dental Sciences	India	Lower-middle	Abdominal	Cohort	78/78	-
Elayat et al.,(63)	2021	BMC Neurology	India	Lower-middle	Neurology	NRCT	35/35	LOS, Morbidity

Kang et al.,(64)	2021	Frontiers in Surgery	China	Upper-middle	Liver surgery	RCT	55/125	LOS, Morbidity, Mortality, Readmission
Tamang et al,(65)	2021	BMC Pregnancy and Childbirth	Bhutan	Lower-middle	Obstetric	Cohort	84/87	LOS, Readmission
Huang et al.,(66)	2021	BMC Anesthesiology	China	Upper-middle	ENT	RCT	59/36	LOS, Morbidity, Mortality
Zhao et al.,(67)	2021	World journal of clinical cases	China	Upper-middle	Ortho	RCT	53/54	LOS, Mortality, Readmission
Purushothaman et al.,(68)	2021	Trauma surgery & acute care open	India	Lower-middle	Abdominal emergency	RCT	30/30	LOS, Morbidity, Mortality, Readmission
Magid et al.,(69)	2021	Egyptian Journal of Hospital Medicine	Egypt	Lower-middle	Gynecology	Cohort	27/27	LOS, Morbidity, Mortality, Readmission
Zhang et al.,(70)	2022	Annals of Translational Medicine	China	Upper-middle	Abdominal/Esophagectomy	Cohort	374/594	LOS, Morbidity, Readmission
Tian et al,(71)	2022	Annals of Surgery	China	Upper-middle	Abdominal/gastric ca	RCT	184/186	LOS, Morbidity, Mortality, Readmission
Wang et al., (72)	2022	J. of Neurosurgery	China	Upper-middle	Neurology	RCT	76/75	LOS, Mortality, Readmission
Beukes et al,(73)	2022	South African Orthopaedic J.	SA	Upper-middle	Ortho	Cohort	60/59	LOS, Morbidity, Mortality, Readmission
Pathrika et al.,(74)	2023	Cureus J. of Medical SCIENCE	India	Lower-middle	Abdominal/gastric	RCT	19/22	LOS
Aggarwal et al.,(75)	2023	World Journal of Surgery	India	Lower-middle	Abdominal/emergency	RCT	30/30	LOS, Morbidity, Mortality, Readmission
Sordia-Pineyro et al.,(76)	2023	Ginekologia Polska	Mexico	Upper-middle	Obstetric	Cohort	139/156	LOS, Morbidity, Readmission
Laohathai et al.,(77)	2023	Indian J. of Thoracic and C.V Surgery	Thailand	Upper-middle	Thoracic	Cohort	247/74	LOS, Mortality
Yuan et al.,(78)	2023	BMC Musculoskeletal Disorders	China	Upper-middle	Spine	Cohort	54/54	LOS, Morbidity, Readmission
Yi et al.,(79)	2024	Spine Journal	China	Upper-middle	Spine	Cohort	138/166	LOS, Morbidity

ERAS- Enhanced Recovery After surgery, RCT, Randomized control Trial, NRCT-Non randomized control trial, LOS- Length of Stay

Risk of Bias Assessment

The Cochrane risk of bias assessment was employed to evaluate the quality of the 20 RCTs (47–49,51–53,55,57–61,64,66,68,71,72,74,75,78). The analysis indicated a low risk of bias in categories such as, selection bias (≈15%), and attrition bias and reporting bias (≈10%). However, a high level of bias risk was observed in the performance bias category (≈80%), Increased levels of unclear risk of bias were identified on allocation concealment or selection bias (≈65%), detection bias assessment (≈60%) and other bias (60%). (Figure 4 & 5).

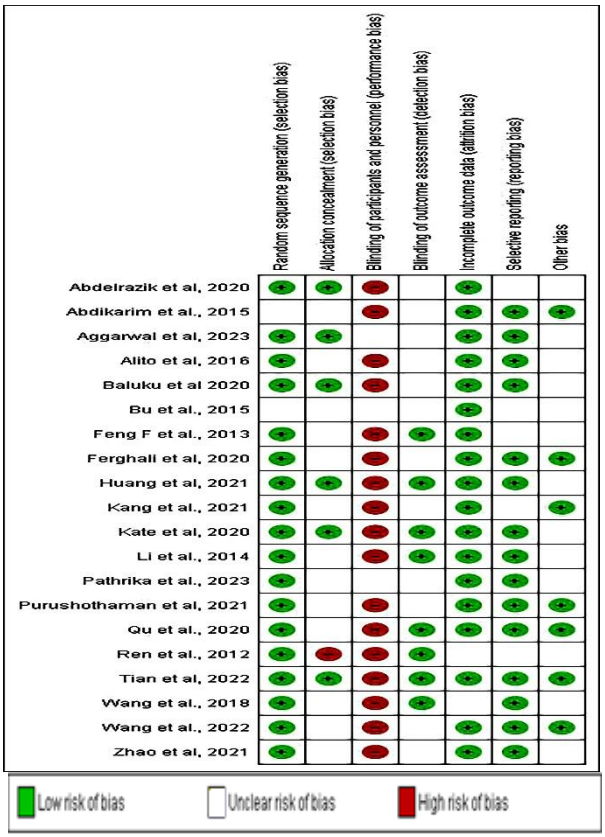

Figure 6 Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies

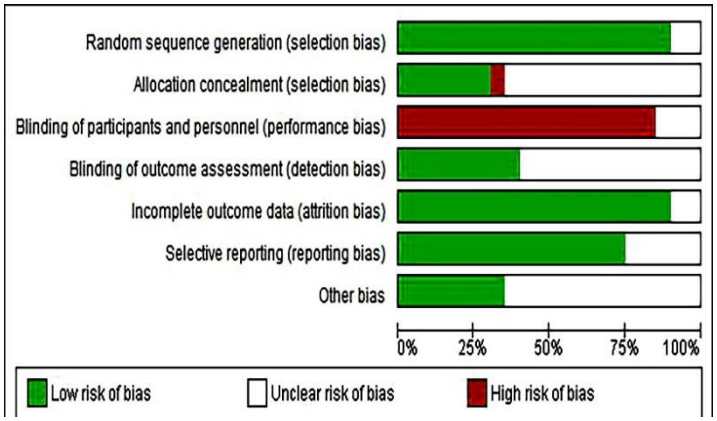

Figure 7 Risk of bias summary: review authors' judgements about each risk of bias item for each included study

On the other hand, to evaluate bias in 12 observational cohort studies(50,54,56,62,65,69,70,73,76–79) and one non-randomized clinical trial(63) the NOS was used (*Table 3*). Approximately 77% of the publication achieved a NOS score of 7 or greater, suggesting reduced risk of bias. The remaining studies obtained NOS scores between 5 and 6, indicating a moderate level of risk for bias.

Table 3: NOS grading for quality assessment of cohort (n=11) and non-randomized studies (n=1)

Authors and Year of Publication	Selection (out of 4)	Comparability (out of 2)	Outcome (out of 3)	Total (out of 9)
Lohsiriwat, 2014(50)	3	2	1	6
Su et al, 2017(54)	4	2	2	8
Aktimur et al, 2018 (54)	3	0	3	6
Gopakumar et al, 2020(62)	3	1	1	5
Elayat et al., 2021(63)	4	1	2	8
Tamang et al, 2021(65)	4	2	3	9
Magdi et al, 2021(69)	4	2	3	9
Zhang et al, 2022(70)	4	1	3	8
Beukes et al, 2022(73)	4	2	3	9
Sordia-Pineyro et al, 2023(76)	4	2	3	9
Laohathai et al, 2023(77)	4	2	3	9
Yuan et al, 2023(78)	4	2	2	8
Yi et al, 2024(79)	4	2	2	8

NOS: Newcastle Ottawa Scale

Intervention

All included studies compared the ERAS protocol with routine care practice across multiple surgical specialties. The implemented ERAS protocol components fluctuate according to the surgical specialty and resource availability, but all studies have at least 50% adherence to the protocol. The adoption of perioperative components varied, with postoperative components achieving a higher report of 82%, while intraoperative components were reported approximately 70%. The lowest report (≈60%) was observed for the preoperative components. Among the postoperative components, postoperative analgesia and anti-emetic plans, plans for opioid minimization, drain and line management, early mobilization strategy, and postoperative diet and bowel regimen management were the most frequently implemented. All intraoperative component applications showed high application. In the preoperative phase, pre-admission patient education regarding the

protocol, as well as fasting and carbohydrate loading guidelines, were routinely practiced ERAS components, 77.8% and 87.1%, respectively as illustrated in figure 6. Further description of individual studies report of each ERAS component is illustrated in *Appendix I, Table 6*.

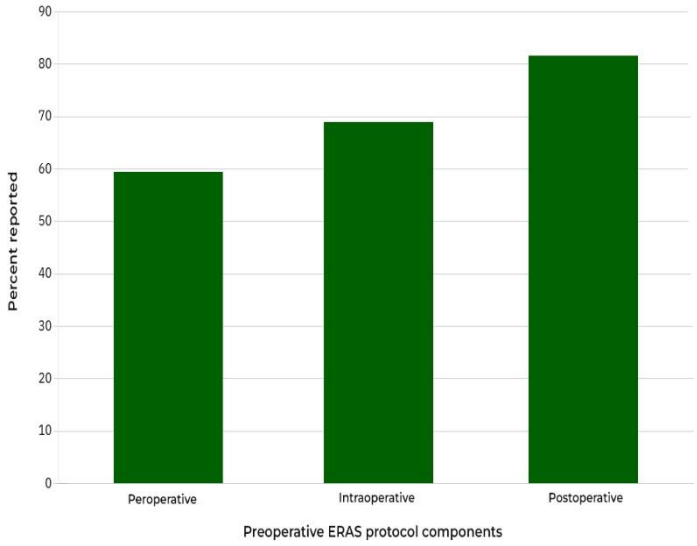

Figure 9 Perioperative ERAS protocol adherence across studies

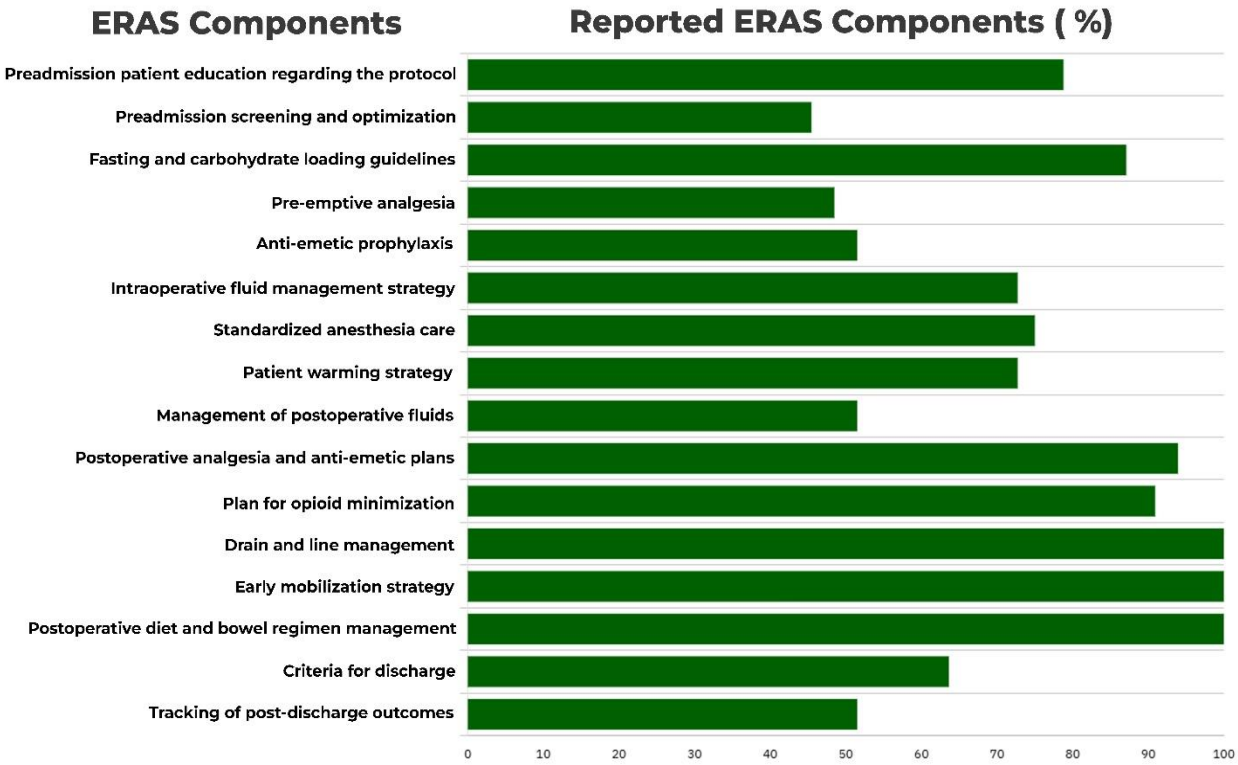

Figure 8 ERAS protocol components adherence across studies

An analysis of ERAS protocol report in relation to a country's economic status showed varying implementation levels across different components. Lower-middle income nations demonstrated higher application to preadmission patient education (95%), early postoperative mobilization (100%), diet and bowel management (100%), criteria for discharge (77%), and post-discharge outcome tracking (54%) compared to their upper-middle income counterparts. Conversely, studies from upper-middle income countries exhibited greater implementation of preadmission screening and optimization (55%), fasting and carbohydrate loading guidelines (90%), intraoperative fluid management strategies (84%), and standardized anaesthesia care protocols (75%). The remaining ERAS components showed comparable application levels across all countries included in this review.

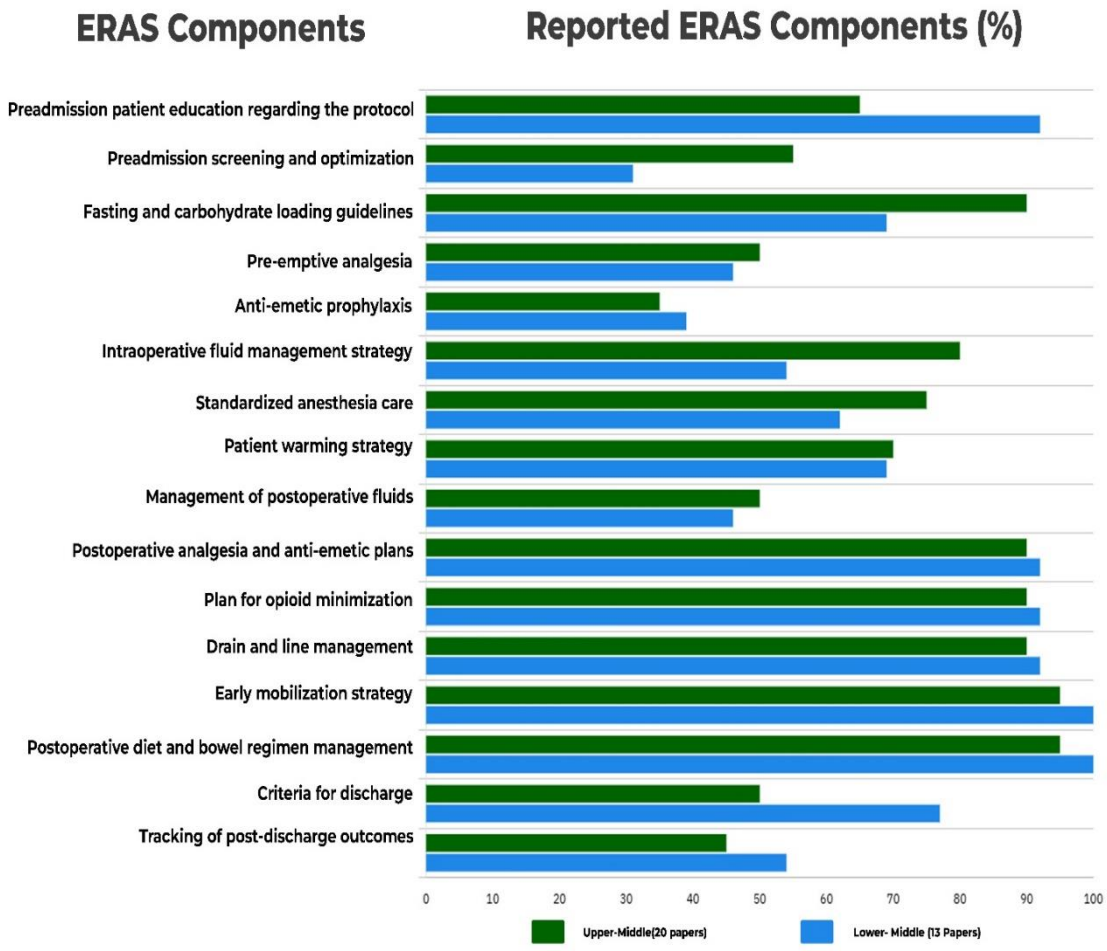

Figure 10 ERAS protocol components adherence in terms of countries economic level

Postoperative Morbidity

Sixteen studies(47–51,54,57,59,63,64,69–71,73,78,79) showed decreased occurrence of the overall postoperative morbidity rate as the result of implementing ERAS protocol, although four studies(56,66,68,76) reported a greater occurrence of postoperative morbidity in the ERAS group. The pooled RR of postoperative complication occurrence was reduced by 27% in the ERAS protocol implementation group (RR=0.63;95%CI 0.66 to 0.55), with acceptable between studies heterogeneity (I^2) of 1.1% (P-value of 0.44).

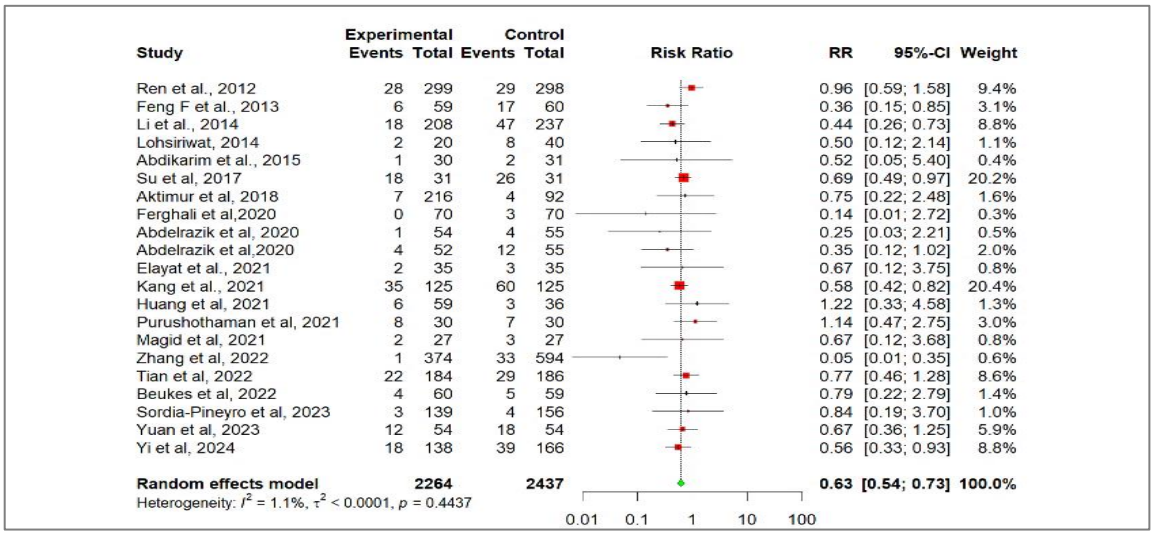

Figure 12 A forest plot of 21 studies reporting postoperative morbidity

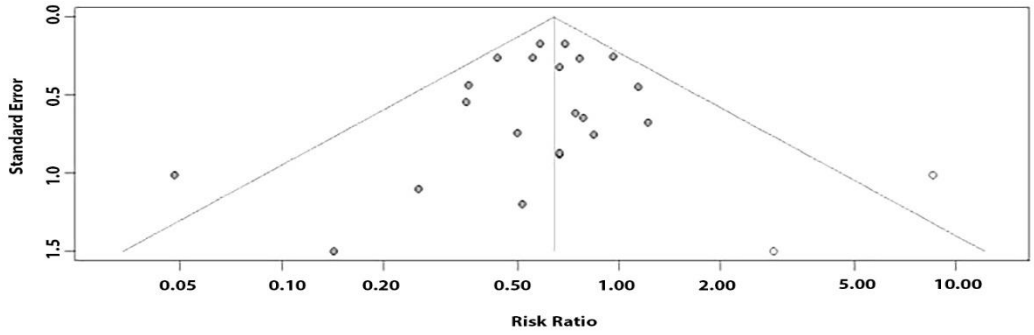

Figure 11 A funnel plot of publication bias in 21 studies reporting postoperative morbidity

The funnel plot shows mild asymmetry, however, the quantitative analysis resulted bias estimate of -0.47, with P-value=0.25 (*Figure 10*).

The subgroup analysis using surgical specialty as the main category (as further show in Appendix II figure 18) indicated that gynecological procedures had a lower occurrence of postoperative complications (RR=0.36; 95% CI 0.16 - 0.81), followed by spine surgery (RR=0.60; 95%CI 0.40-0.79), and abdominal procedures (RR=0.64; 95% CI 0.49%-0.84). The subgroup analysis excluded other surgical categories, as they failed to meet the necessary criteria to be included in the analysis.

Related to study design, the subgroup analysis showed approximately similar effect sizes for studies with clinical trials and observational design (as further shown in Appendix II figure 19). Moreover, subgroup analysis based on the economic level of the countries revealed that the ERAS protocol was very effective in reducing the incidence of postoperative complications in lower-middle-income countries compared to upper-middle-income countries (RR= 45% Vs. RR=35%), as illustrated further in *Appendix II, Figure 19.*

Length of Hospital Stay

The reported clinical outcome regarding LOS among patients under the ERAS protocol care pathway was reported by all studies. Among these studies seven publications (57,59,68,73–75,77) report was not clear whether they are indicating postoperative LOS or total hospital LOS while five studies (50,51,56,61,62) reported LOS starting from hospital admission to discharge. Whereas 20 studies (47–49,51–55,60,63,64,66,67,70–72,76,78,79) reported LOS in terms of postoperative stay in hospital starting from end of surgery till discharge and one study (65) from start of surgery to discharge. Four studies (55,60,66,70) have reported both hospital and postoperative LOS. From the 20 studies, four studies (49,52,63,66) showed a comparable difference in postoperative LOS between the ERAS and routine care pathways while the remaining studies (47,48,51–55,60,64,65,67,70–72,76,78,79) revealed a statistically significant decrement in postoperative LOS in ERAS group. The pooled analysis of these 20 studies on postoperative stay showed a statistically significant reduction, SMD= -0.68 [95%CI -0.47 to -0.90] and p-value < 0.0001, in the ERAS group. Between-study heterogeneity was (the I^2) = 86.7%.

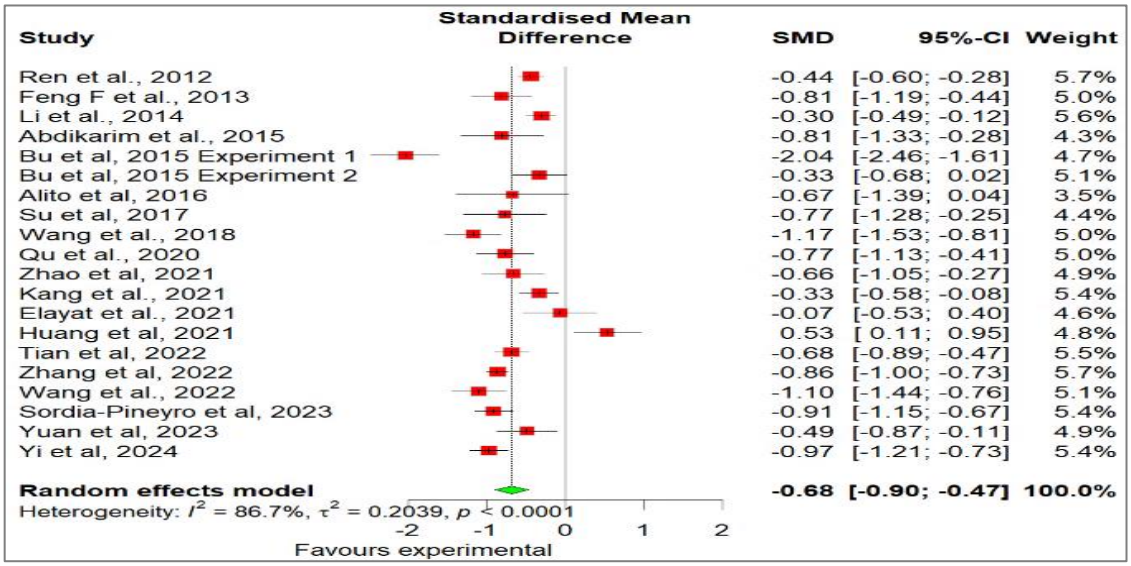

Figure 13 A forest plot of 20 studies reporting postoperative length of hospital stays

The forest plot and sensitivity analysis indicated that two studies(52,66) had a major influence. When these studies are withheld, the pooled analysis of postoperative LOS is decrease from initial pooled SMD = -0.68 [95%CI -0.47 to -0.90] by 0.01 (SMD= -0.67 [95%CI -0.54 to -0.82]) with I^2 = 76.8, as illustrated in *Appendix II, Figure 20.*

The funnel plot indicated some degree of publication bias, although quantitative analysis finding (Egger's test) revealed a non-significant bias estimator of -0.79; p-value = 0.64 for

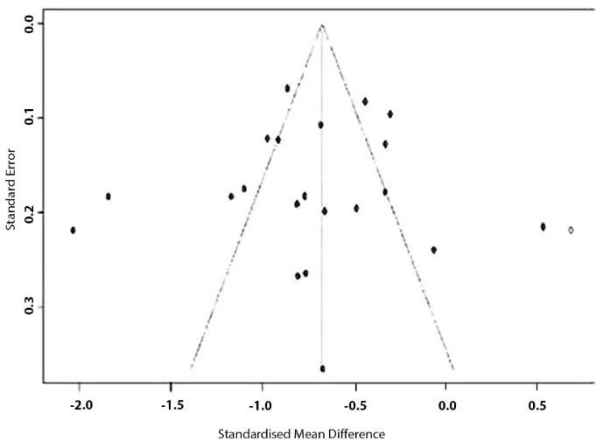

Figure 15 Funnel plot for publication bias in of 20 studies reporting postoperative length of hospital stay

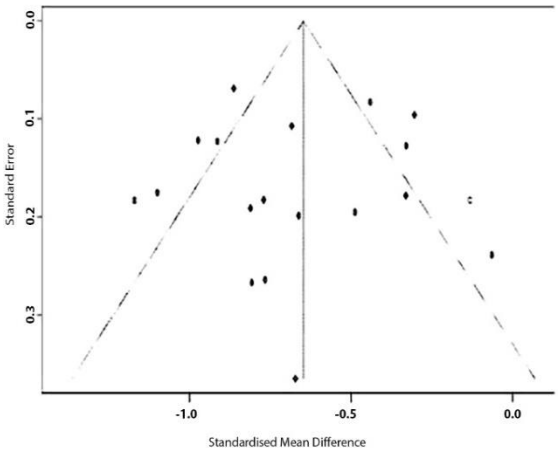

Figure 14 Funnel plot for publication bias in 18 studies reporting postoperative length of hospital stay after removing influential studies

the 21 studies and bias estimator of -0.15; p-value = 0.64 when the two influential studies are left out, as further show figure 12 and 13, respectively. Further more Baujat plot and diagnostic plots indicated that these two studies to had a significant influence on between study heterogeneity *(see Appendix III, Figure 24 & 25, and Appendix V, Figure 26 & 27, respectively*)

Further, to investigate the between study heterogeneity, subgroup analysis which categorized the articles by their study design, and surgical procedure, demonstrated comparable effectiveness of the ERAS protocol across various circumstances (as further illustrated in *Appendix II Figure 17 and 18*, respectively). In relative terms, RCT studies demonstrated SMD of -0. 81(CI95% 0.44 to -0.79) with I^2 of 72.1% while observational studies revealed SMD of -0.67 (95%CI -0.76 to – 96) with I^2 of 16.8%. When looking at subgroup analysis based on surgical specialty, between study heterogeneity is a major concern affecting the reliability of the pooled analysis for abdominal, neurology and spine surgeries while reportable results were observed for orthopedic procedures. Meta-regression analysis for moderators such as surgical type, country economic level, and study design, there was no statistically significant explanation for the between-heterogeneity, each explaining only 16%, 18%, and 12% of heterogeneity, respectively.

Postoperative Readmission

Twenty-three studies(48,50–52,56–60,64,65,67–73,75,76,78) reported postoperative readmission rates. Seven studies(48,50,51,59,60,69,72) demonstrated a similar readmission rate in the two arms. Another eight studies(57,58,64,67,68,75,76,78) presented a lowered readmission rate in the ERAS group compared to the control group, while eight studies(52,56,59,65,70,71,73) showed the contrary. The pooled result revealed a non-significant difference in the occurrence of postoperative readmission between the two groups (RR= 1.11; 95%-CI 0.83 to 1.47, p-value= 0.4872 with I^2=8.4%) as illustrated in figure 14. Asymmetry in the funnel plot was observed and statistically significant publication bias (bias estimator=-1.04; p-value <0.01)) was observed.

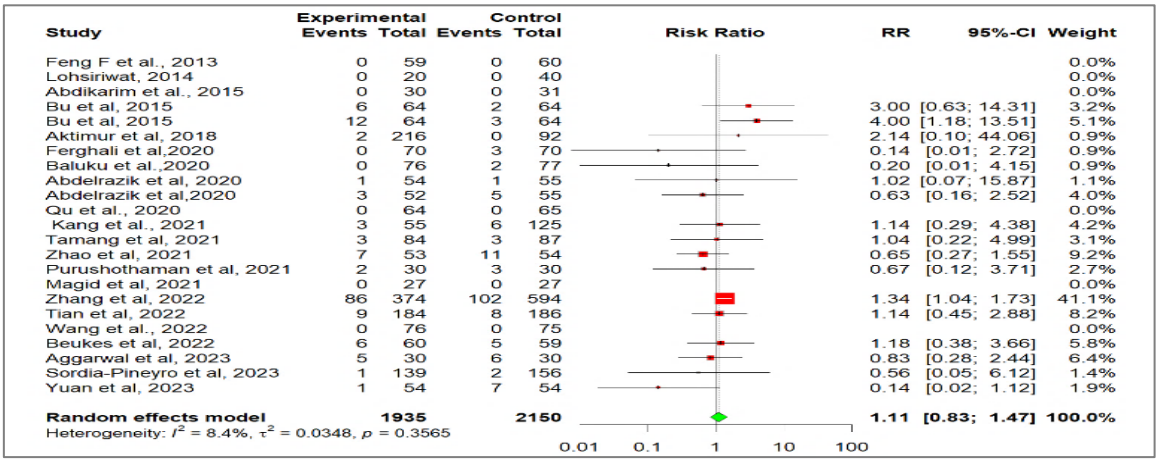

Figure 17 A Forest plot of 23 studies reporting postoperative readmission

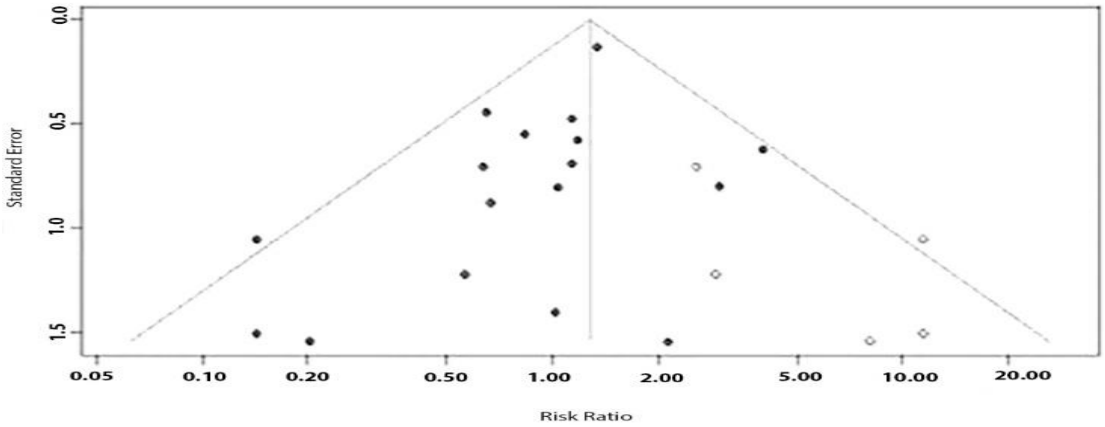

Figure 16 A funnel plot of publication bias in 23 studies reporting postoperative readmission

Postoperative Mortality

Eighteen studies(47–51,56,57,64,66–68,71–73,75–77) reported 30-day postoperative mortality. Of these, the 13 studies (47–51,57,64,66–69,72,73) reported no occurrence of death in both groups, while two studies (56,71) reported an increased death rate in the ERAS group, one study (75) reported similar death rate on both group and one other study(69) reported a higher death rate in the routine care pathway. The findings of pooled analysis resulted in non-significant difference between the two groups (RR=1.00; 95% CI 0.35 to 2.86, P-value = 0.99 and I^2=0%) as illustrated in figure 16. Asymmetry in the funnel plot observed and statistically significant publication bias (bias estimator=-1.04; p-

value <0.01) was observed.

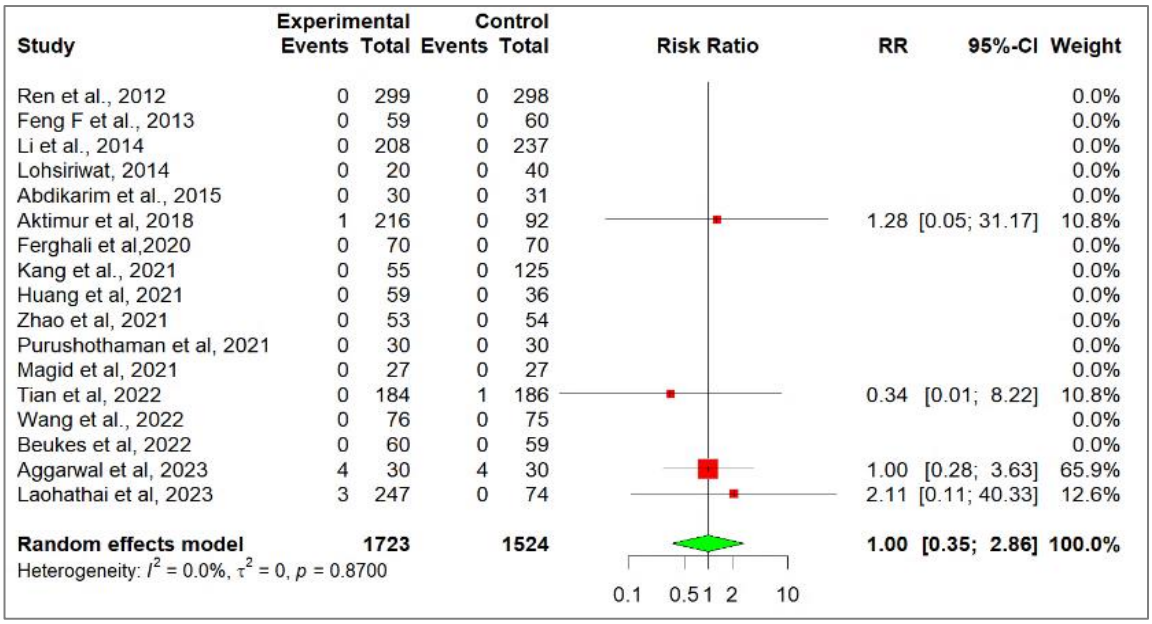

Figure 18 A forest plot of 17 studies reporting postoperative mortality

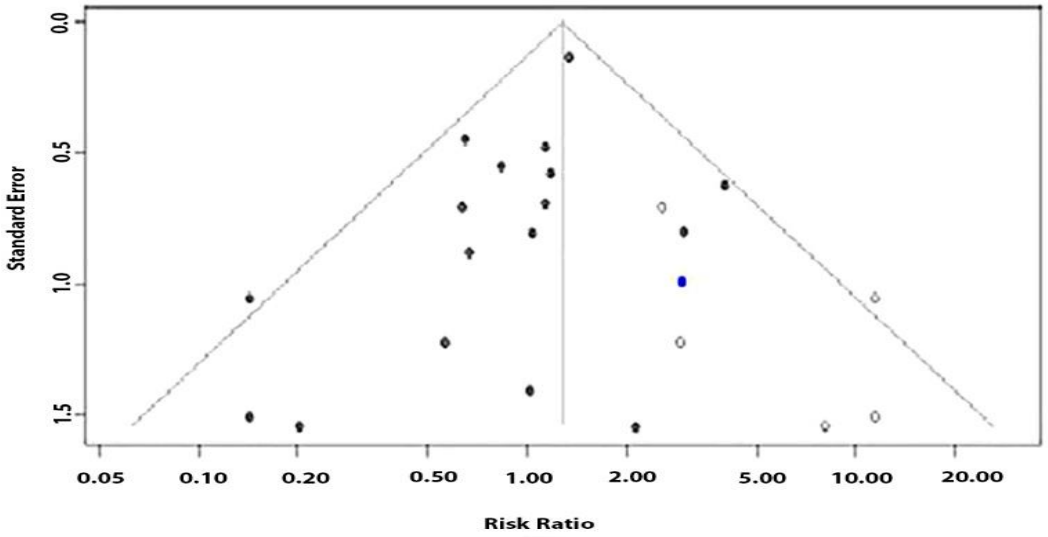

Figure 19 A funnel plot of publication bias 18 studies reporting postoperative mortality

Discussion

The result of this study is based on 35 studies, comparing Enhanced Recovery After Surgery (ERAS) protocol implementation with routine care pathways in LMICs, with majority of the studies originating from upper-middle income countries. The ERAS protocol was implemented across diverse surgical procedures, with abdominal surgeries representing the highest frequency (≈43%). With regard to documented perioperative ERAS protocol elements, postoperative components exhibited the highest report (≈80%). Among all components, preadmission screening and optimization, and fluid management were the least recorded one. In terms of patient outcomes, ERAS implementation showed a substantial reduction in postoperative morbidity (27%) and a lowered postoperative Length of Stay (LOS) by 16 hours when compared to routine care pathways. This study did not find a statistically significant difference between the two groups in terms of patients 30-day postoperative readmission and mortality rates.

The application of ERAS protocol in high income countries has gained a widespread acceptance as standard of care and has transformed their surgical service by speeding up patient recovery. To achieve this same impact in LMICs, the quality improvement initiatives of ERAS should be contextually adapted to these unique settings with the aim of developing well-organized surgical systems (24). This is crucial because the safety of the surgical system is a core indicator of access to surgery in addition to surgical capacity, timeliness, and affordability. Moreover, globally more people die from injury and surgery due to lower quality of care and lack of safety in the available health care, as opposed to lack of availability to care (80). With respect to major surgery eight million lives are lost each year and twice this number is the estimated morbidity while 50 %s of these adverse events and disabilities are preventable (81). Currently LMICs are working to meet the Lancet commission goal of global surgery for 2030 with regard to surgical volume, which expects 5000 procedures per 100000 population (82). Nevertheless, when striving to raise surgical volume in LMICs simultaneously it is essential to improve the appropriateness and quality of care to maximize patient safety (24,83)**.** Within a high-quality health system framework, implementation of evidence-based practices, such as the ERAS protocol, is integral to promote surgical service quality and ultimately improve patient outcomes

(24,80).

Implementing the ERAS protocol is not an easy task as it has multiple elements requiring various disciplines to work synchronously for the best result. In this study, the average perioperative ERAS application rate was 74%, and postoperative ERAS components were the most commonly reported, followed by intraoperative and preoperative components. However, most included studies fail to report their actual adherence to the protocol. While literature advocates an adherence level of 50% or greater to have the beneficial effects of the protocol (20), the theoretical and practical aspects of the ERAS protocol implementation process may differ significantly. This suggests that despite its potential to enhance patient outcomes (84), implementation may be limited due to barriers such as resistance to change, lack of time and resources, and inadequate communication and coordination among departments (85). In Africa, challenges such as poor protocol adherence and, lack of standardization with in hospital procedures, and low numbers of trained staff were also identified as barriers hindering the implementation of the protocol (86). To promote compliance, several strategies can be implemented including capacity building through education, allocating essential resources, and establishing a team to revise existing pathways (87). Additionally, having a multidisciplinary team to oversee ERAS implementation through regular audit is recommended (88). Furthermore, identifying procedure-specific core elements can also simplify the implementation of the entire protocol bundle, particularly in LMICs (89). For instance, in colorectal procedures, it has been determined that five components can function as core ERAS elements sufficient to exert a significant influence on quality of patient outcomes in terms of postoperative morbidity, morality and hospital LOS (90).

This review highlights a key quality indicator of patient health outcome revealing a 27% reduction in postoperative morbidity in ERAS group when compared to traditional perioperative care pathway. Similar finding was observed by Sauro et al (26) meta-analysis indicating reduced postoperative morbidity by 29% in the ERAS groups (RR=0.71, CI 95%; 0.59-0.87) with I^2=78.6. Moreover, other studies have found procedure specific decreased postoperative morbidity in ERAS groups across various surgical specialty namely, emergency abdominal surgery (30) (OR= 0.50, 95%CI 0.38 to 0.66), major

abdominal surgeries (29) (OR= 0.70 95% CI: 0.56-0.86), gynecologic oncology (31) (OR 0.68, 95% CI 0.55–0.83), and caesarian section(32) (RR: 0.50, 95% CI: 0.37 to 0.68) when compared to non-ERAS groups. Correspondingly, in this meta-analysis, the subgroup analysis has revealed gynecologic procedures as having the highest reduction in postoperative morbidity by 60% followed by spine and abdominal procedures. However, the meta-regression model showed a non-significant association between procedure type and postoperative morbidity.

The ERAS effect of reducing postoperative morbidity is beneficial for surgical patients and hospitals, as postoperative morbidity tends to raise hospital costs by 78%, hospital length of stay by 114% and increased consumption of medical resources (91). Moreover, postoperative complications affect patient discharge disposition, by making the patient two times more likely to depend on assistance to return home when compared to patients without complications (92). This in turn could influence patients' productivity and rehabilitation leading to an increased financial burden. In addition, patients with postoperative morbidity have a 26% increased risk for postoperative mortality (93). However, the current review has found a non-significant difference in patient 30-day postoperative mortality rates between the ERAS and non-ERAS groups. This finding goes in line with other meta-analysis that included all types of surgery (26) and specialty specific ones (30,32). This might be attributed to the underestimation of the actual mortality risk when using 30-day postoperative mortality rates; for instance, a higher mortality rate has been observed when assessing 90-day postoperative results (94). Although these results have been observed, the implementation of preoperative screening and suitable interventions, which are fundamental components of the ERAS protocol (23), have been recommended to decrease the subsequent postoperative mortality rate by 1.8%, a statistically significant reduction (95). However, in the present review, preoperative screening and optimization emerged as the least frequently mentioned components of the ERAS protocol, with a reported applicability of approximately 45%.

This meta-analysis observed a 16-hour decreased patient postoperative LOS in the ERAS group when compared to the routine care group. However, the initial I^2 was 86.4%, and when two influential studies were withheld from pooled analysis, the I^2 became 76.4%

with a 0.01 decrement in SMD. This reduction on I^2 while minimal impact on the pooled analysis could be attributed to the variation in surgical specialties, institutional discharge protocols, and methods of effect size measurement. Similarly, Sauro et al. (26) observed a decrease in postoperative LOS in the ERAS group, with a reduction of 2.83 days (95%CI 2.10 to 3.55 days; I^2 = 0%; P < .001). Additionally, meta-analysis by Riad et al. (27) in LMICs indicated decreased postoperative LOS by 2.18 days (95%CI; -4.13, to 0.05, P < 0.01) with I^2 level of 94%. Even though the reduction in postoperative LOS in this current review is lower than other studies, it has nevertheless shown the effectiveness of ERAS in reducing hospital LOS in the LMIC setting. This in turn can reduce healthcare costs, increase hospital inpatient capacity and improve conservation of resources, while enhancing patient satisfaction and quality of life (96,97).

It should be noted that a shorter hospital LOS raises a concern for increased readmission rates, as strict adherence to ERAS metrics may result in premature patient discharge (23). Despite the decrease in postoperative LOS, this study has found that 30-day postoperative readmission rate remains comparable for both the ERAS and routine care pathway groups (RR= 1.11; 95%CI 0.8313 to 1.4735, p-value= 0.4872 with I^2=8.4%). Similarly, Sauro et al. (26) observed a non-significant difference in 30-day postoperative readmission rate (RR =1.04; 95%CI,0.81-1.35; p-value =0.74; I^2 = 0%).

This finding of ERAS patients experiencing decreased postoperative LOS while having a comparable readmission rate could be attributed to key postoperative ERAS protocol components. For example, discharge criteria based on patient physiologic assessment rather than a fixed time-based standard, as well as scheduled post-discharge follow-up (23). These elements are widely recognized as a target intervention to reduce preventable patient readmission (98–100). Approximately 60% of studies included in this review reported the application of ERAS discharge criteria and 50% addressed post-discharge follow-up, indicating room for improvement in the implementation of these elements to ensure safe patient discharge and reduced readmission rates from traditional pathways.

While recognizing the positive impact of ERAS on patient outcomes in LMICs, it is important to consider protocol implementation costs. A study in the United States (101)

indicated that ERAS implementation costs associated with site visits, leadership, personnel, and materials range from $ 1179 to $ 1300 per patient annually. However, the hospital LOS was reduced by 0.7-2.4 days with a corresponding cost reduction of $ 850 to $ 3300 per day, ultimately resulting in net cost savings of $159,720 to $634,720 per year. A systematic review also identified ERAS implementation costs ranging from $57 to $1536, with personnel costs being the most significant (102). When looking into ERAS protocol implementation and patient outcomes, costly ERAS elements were more adapted in high-income countries than in LMICs, significantly influencing LOS between these regions. The mean LOS in high-income countries was 5·85 days compared to 7·17 days in LMICs, $P < 0·001$(103). Yet, in LMICs there was a significant reduction of LOS even though some ERAS elements are not applied. While implementation costs are undeniable, studies from high income countries have offset these costs through reduced direct costs of hospitalization. These findings necessitate ERAS protocol adaptation in LMICs for improved patient outcomes which in turn impacts financial saving and hospital efficiency.

Study Limitation and Strength

Limitation

Variation among included studies by design and surgical procedure type is one of the limitations while considering the generalizability of this study. However, a subgroup analysis was performed to overcome this limitation. As the ERAS protocol has multiple components, various adherence levels to the protocol were observed. This study has provided a description of the applied protocol elements of each study. Most included studies are from upper-middle-income countries, and this could affect the inferentiality of the study. Nevertheless, a subgroup analysis was conducted to address this issue.

Strength

This study evaluated ERAS implementation in LMICs, which is necessary to address the literature gap in this area. Moreover, the subgroup analysis indicated surgical type and countries economical type ERAS protocol implementation status. Additionally, the included studies on data synthesis were of high quality to provide robust results.

Conclusion and Recommendation

Significantly improved patient outcomes related to reduced postoperative complications and length of hospital stay were observed with ERAS application. While postoperative 30-day readmission and mortality rates showed the same differences, the ERAS protocol in LMICs appears promising for enhancing short-term and intermediate hospital outcomes in terms of hospital length of stay and postoperative morbidity, respectively, when compared with routine care of practice. Although the protocol could have costs related to its implementation the net cost could be decreased due to its ability to enhance patients' recovery and reduce hospitalization. Hence, we recommend the application of the ERAS protocol in LMICs.

- For policymakers, we recommend the application of the ERAS protocol as a standard care of practice in LMICs and to establish an ERAS society in LMICs with no society. However, there is a need to modify the protocol according to the need and resource availability.
- To hospitals, we recommend assigning a steering committee that could monitor and evaluate the implementation process of the ERAS protocol.
- For clinicians in perioperative settings, we recommend the application and adherence of the ERAS protocol and team working through a multidisciplinary approach.
- To researchers, we recommend more clinical studies, especially in low-income and lower-middle-income countries, to evaluate the effectiveness and point out ERAS elements that are very efficient and practical to implement according to the surgical specialty. Moreover, when disseminating the results, we recommend authors clearly report both the overall adherence level of protocol and the adherence of each individual element of ERAS protocol. In addition, more studies are needed to answer how much ERAS costs in LMICs settings.

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Annex I: Budget Breakdown

Table 4: Budget requirement in the completion of the study

Budget items	Number of items	Cost per item	Total cash cost	Remarks
Internet	3MB/Sec	990ETB for 7months	6,930 ETB	
Internet accessories	5	2500ETB	12,500 ETB	
Communication	5 Authors	100 ETB air Time	2,500 ETB	
Print	2500 pages	5 ETB	5,000 ETB	
Data extractor	2 Authors	7000	14,000 ETB	
Data cross checker	2 Authors	6000	12,000 ETB	
Quality of study assessor	1 person	7000	7,000 ETB	
Sub total			59,930 ETB	
Contingency	10%		5,993 ETB	
Total			65,923 ETB	

Annex II Work Plan

Table 5: *Work plan elaborating the activities, the time frame and the responsible individual for each activity*

Activities	**Month**						**Responsible individual**
	Nov, 2023-March, 2024	Apr-Sep, 2024	Oct-Dec, 2024	Jan-Feb, 2025	Mar-Apr, 2025	May-July, 2025	
Preparation of protocol							PI and Advisors
Literature Searches							PI and Reviewers
Literature screening							PI and Reviewers
Data collection							PI and Reviewers
Data entry							PI and Reviewers
Follow up of missing information							PI
Analysis							PI with consultation of Biostatistician
Preparation of review report							PI and Advisors
Publication/Dissemination							PI

Annex III: Search Strategy

ERAS filters

"Enhanced Recovery After Surgery" OR "fast-track surgery" OR "fast track surgery FAST" OR "Enhanced Postsurgical Recovery"

Settings- LMICs filters

Deprived Countries OR Deprived Population OR Deprived Populations OR Developing Countries OR Developing Country OR Developing Economies OR Developing Economy OR Developing Nation OR Developing Nations OR Developing Population OR Developing Populations OR Developing World OR LAMI Countries OR LAMI Country OR Less Developed Countries OR Less Developed Country OR Less Developed Economies OR Less Developed Nation OR Less Developed Nations OR Less Developed World OR Lesser Developed Countries OR Lesser Developed Nations OR LMIC OR LMICS OR Low GDP OR Low GNP OR Low Gross Domestic OR Low Gross National OR Low Income Countries OR Low Income Country OR Low Income Economies OR Low Income Economy OR Low Income Nations OR Low Income Population OR Low Income Populations OR Lower GDP OR lower gross domestic OR Lower Income Countries OR Lower Income Country OR Lower Income Nations OR Lower Income Population OR Lower Income Populations OR Middle Income Countries OR Middle Income Country OR Middle Income Economies OR Middle Income Nation OR Middle Income Nations OR Middle Income Population OR Middle Income Populations OR Poor Countries OR Poor Country OR Poor Economies OR Poor Economy OR Poor Nation OR Poor Nations OR Poor Population OR Poor Populations OR poor world OR Poorer Countries OR Poorer Economies OR Poorer Economy OR Poorer Nations OR Poorer Population OR Poorer Populations OR Third World OR Transitional Countries OR Transitional Country OR Transitional Economies OR Transitional Economy OR Under Developed Countries OR Under Developed Country OR under developed nations OR Under Developed World OR Under Served Population OR Under Served Populations OR Underdeveloped Countries OR Underdeveloped Country OR underdeveloped economies OR underdeveloped nations OR underdeveloped population OR Underdeveloped World OR Underserved Countries OR Underserved Nations OR Underserved Population OR Underserved Populations OR TW

Afghanistan OR Albania OR Algeria OR American Samoa OR Angola OR Armenia OR Azerbaijan OR Bangladesh OR Belarus OR Byelarus OR Belorussia OR Belize OR Benin OR Bhutan OR Bolivia OR Bosnia OR Botswana OR Brazil OR Bulgaria OR Burma OR Burkina Faso OR Burundi OR Cabo Verde OR Cape Verde OR Cambodia OR Cameroon OR Central African Republic OR Chad OR China OR Colombia OR Comoros OR Comores OR Comoro OR Congo OR Costa Rica OR Côte d'Ivoire OR Cuba OR Djibouti OR Dominica OR Dominican Republic OR Ecuador OR Egypt OR El Salvador OR Equatorial Guinea OR Eritrea OR Ethiopia OR Fiji OR Gabon OR Gambia OR Gaza OR Georgia OR Georgia Republic OR Ghana OR Grenada OR Grenadines OR Guatemala OR Guinea OR Guinea- Bissau OR Guyana OR Haiti OR Herzegovina OR Hercegovina OR Honduras OR India OR Indonesia OR Iran OR Iraq OR Ivory Coast OR Jamaica OR Jordan OR Kazakhstan OR Kenya OR Kiribati OR Democratic People's Republic of Korea OR Kosovo OR Kyrgyz OR Kirghizia OR Kirghiz OR Kyrgyzstan OR Lao PDR OR Laos OR Lebanon OR Lesotho OR Liberia OR Libya OR Macedonia OR Madagascar OR Malawi OR Malay OR Malaya OR Malaysia OR Maldives OR Mali OR Marshall Islands OR Mauritania OR Mauritius OR Mexico OR Micronesia OR Moldova OR Mongolia OR Montenegro OR Morocco OR Mozambique OR Myanmar OR Namibia OR Nepal OR Nicaragua OR Niger OR Nigeria OR Pakistan OR Palau OR Papua New Guinea OR Paraguay OR Peru OR Philippines OR Principe OR Romania OR Ruanda OR Rwanda OR Samoa OR Sao Tome OR Senegal OR Serbia OR Sierra Leone OR Solomon Islands OR Somalia OR South Africa OR South Sudan OR Sri Lanka OR St Lucia OR St Vincent OR Sudan OR Surinam OR Suriname OR Syria OR Syrian Arab Republic OR Tajikistan OR Tadzhikistan OR Tajikistan OR Tadzhik OR Tanzania OR Thailand OR Timor OR Togo OR Tonga OR Tunisia OR Turkey OR Turkmen OR Turkmenistan OR Tuvalu OR Uganda OR Ukraine OR Uzbek OR Uzbekistan OR Vanuatu OR Venezuela OR Vietnam OR West Bank OR Yemen OR Zambia OR Zimbabwe

Study Design Filters

Randomized controlled trial or RCT or Case Control or Cohort

Annex IV: Data Collection Form

Data collection form for included studies

General Information

Study ID
(e.g. author name, year)

Form completed by			
Study author contact details			
Characteristics of included studies			
Author and year of publication:			
Country			
Start & end dates			
Study funding sources *(including role of funders)*			
Possible conflicts of interest			
Methods	**Design**		
	Aim of study		
	Follow up		
	Adverse event monitoring		
Notes:			
Participants	**Total no. randomized**		
		ERAS	*Routine*
	Age (mean ± SD)		
	Sex (number male)		
	Sex (number female)		
	Surgical specialty type		
	Inclusion criteria		
	Exclusion criteria		
	No. randomized per group	*ERAS*	*Routine*
	No. missing		
	Reasons missing		
Intervention		**Components of ERAS done**	**Components of routine care**
	Preoperative		
	Intraoperative		
	Postoperative		
Note			

Risk of Bias assessment for randomized studies

Domain	Risk of bias			Support for judgment	Location in text or source (pg/fig/table/other)
	Low	High	Unclear		
Random sequence generation (selection bias)	☐	☐	☐		
Allocation concealment (selection bias)	☐	☐	☐		
Blinding of participants and personnel (performance bias)	☐	☐	☐	**Outcome group: All/**	
Blinding of outcome assessment (detection bias)	☐	☐	☐	**Outcome group: All/**	
Incomplete outcome data (attrition bias)	☐	☐	☐	**Outcome group: All/**	
Selective outcome reporting?	☐	☐	☐		
Other bias	☐	☐	☐		

New-Castel Ottawa Quality Assessment scale cohort studies

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability

SELECTION

1) **Representativeness of the Exposed Cohort**
   a) truly representative of the average
   b) somewhat representative of the average
   c) selected group of users eg nurses, volunteers
   d) no description of the derivation of the cohort

2) **Selection of the Non-Exposed Cohort**
   a) drawn from the same community as the exposed cohort
   b) drawn from a different source
   c) no description of the derivation of the non-exposed cohort

3) **Ascertainment of Exposure**
   a) secure record (eg surgical records)
   b) structured interview
   c) written self-report
   d) no description

4) **Demonstration That Outcome of Interest Was Not Present at Start of Study**
   a) yes
   b) no

COMPARABILITY

1) Comparability of Cohorts on the Basis of the Design or Analysis

a) study controls for
b) study controls for any additional factor

OUTCOME

1) **Assessment of Outcome**
   a) independent blind assessment
   b) record linkage
   c) self-report
   d) no description

2) **Was Follow-Up Long Enough for Outcomes to Occur**
   a) yes
   b) no

3) **Adequacy of Follow Up of Cohorts**
   a) complete follow up - all subjects accounted for
   b) subjects lost to follow up unlikely to introduce bias - small number lost - > 10 % (
   c) follow up rate <10%
   d) no statement

Inpatient outcome

Study ID		
	ERAS group	**Routine group**
Length of Stay		
Morbidity Rate		
Types of Morbidity		
Readmission Rate		

Other information

	Description as stated in report/paper	**Location in text or source (pg & ¶/fig/table/other)**
Key conclusions of study authors		
References to other relevant studies		
Correspondence required for further study information (from whom, what and when)		
Notes:		

Appendix I: Supplementary Data on ERAS protocol adherence of all Individual Studies

Table 6: Description of ERAS protocol element compliance by all included studies

ERAS Components	**Ren et al., 2012**	**Feng F et al., 2013**	**Li et al., 2014**	**Lohsiriwat, 2014**	**Abdikarim et al., 2015**	**Bu et al, 2015**	**Alito et al, 2016**	**Su et al, 2017**	**Wang et al., 2018**	**Aktimur et al, 2018**	**Kate et al., 2020**	**Ferghali et al,2020**	**Baluku et al., 2020**	**Abdelrazik et al, 2020**	**Qu et al., 2020**	**Gopakumar et al, 2020**	**Elayat et al., 2021**	**Kang et al., 2021**
Preadmission patient education regarding the protocol	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Preadmission screening and optimization	No	No	Yes	No	No	No	Yes	No	Yes	No	No	No	No	Yes	Yes	Yes	No	No
Fasting and carbohydrate loading guidelines	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
Pre-emptive analgesia	Yes	No	Yes	No	No	No	No	No	No	Yes	Yes	Yes	No	No	Yes	No	Yes	No
Anti-emetic prophylaxis	Yes	No	No	Yes	No	No	No	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	No	No
Intraoperative fluid management strategy	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Standardized anesthesia care	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes	N/A	No
Patient warming strategy	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Management of postoperative fluids	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	No	No	No	Yes	Yes	No	No	No	Yes
Postoperative analgesia and anti-emetic plans	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Plan for opioid minimization	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
Drain and line management	Yes	Yes	Yes	Yes	Yes	Yes	N/A	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Early mobilization strategy	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Postoperative diet and bowel regimen management	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Criteria for discharge	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	No
Tracking of post-discharge outcomes	No	Yes	No	Yes	Yes	Yes	No	Yes	No	Yes	No	Yes	Yes	No	Yes	No	No	Yes
Adherence To ERAS components (%)	13/16	12/16	12/16	11/16	11/16	12/16	8/15	12/16	11/16	12/16	10/16	11/16	13/16	13/16	14/16	12/16	11/15	10/16
Surgical Specialty	Colorecta	Gastrotomy	Colorecta	Colorecta	Gastrotomy	Gastrotomy	Ortho	Gastrotomy	Neuro	Bariatric	Gastrotomy	Gynecology	Obstetric	Gynecology	Neuro	Abd	Neuro	Liver

ERAS Components	**Tamang et al, 2021**	**Elayat et al., 2021**	**Kang et al., 2021**	**Huang et al, 2021**	**Zhao et al, 2021**	**Purushothaman et al, 2021**	**Magid et al, 2021**	**Zhang et al, 2022**	**Tian et al, 2022**	**Wang et al., 2022**	**Beukes et al, 2022**	**Pathrika et al, 2023**	**Aggarwal et al, 2023**	**Sordia-Pineyro et al, 2023**	**Laohathai et al, 2023**	**Yuan et al, 2023**	**Yi et al, 2024**
Preadmission patient education regarding the protocol	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes
Preadmission screening and optimization	No	No	No	Yes	Yes	Yes	No	Yes	Yes	Yes	No	No	No	No	Yes	Yes	Yes
Fasting and carbohydrate loading guidelines	Yes	Yes	Yes	Yes	Yes	N/A	Yes	Yes	Yes	Yes	Yes	No	N/A	Yes	Yes	Yes	No
Pre-emptive analgesia	No	Yes	No	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes
Anti-emetic prophylaxis	No	No	No	No	No	No	Yes	Yes	No	Yes	Yes	No	No	No	No	No	Yes
Intraoperative fluid management strategy	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes
Standardized anesthesia care	Yes	No	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes
Patient warming strategy	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes
Management of postoperative fluids	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	No	No	Yes	Yes	No	Yes	Yes
Postoperative analgesia and anti-emetic plans	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Plan for opioid minimization	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Drain and line management	Yes	Yes	Yes	N/A	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Early mobilization strategy	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Postoperative diet and bowel regimen management	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Criteria for discharge	Yes	Yes	No	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	No	No	No
Tracking of post-discharge outcomes	Yes	No	No	No	Yes	Yes	No	No	No	Yes	No	Yes	Yes	No	Yes	No	No
Adherence To ERAS components (%)	13/16	11/16	8/16	9/15	14/16	10/15	14/16	12/14	12/14	15/16	11/16	8/16	12/16	9/16	12/16	11/16	13/16
Surgical Specialty	Obstetric	Neuro	Liver	ENT	Ortho	Abdominal	Gyneco	Esopha	Gastrotomy	Neuro	Ortho	Gastrotomy	Abdominal	Obstetric	Thoracic	Spine	Spine

Appendix II: Supplementary Data of forest Plot

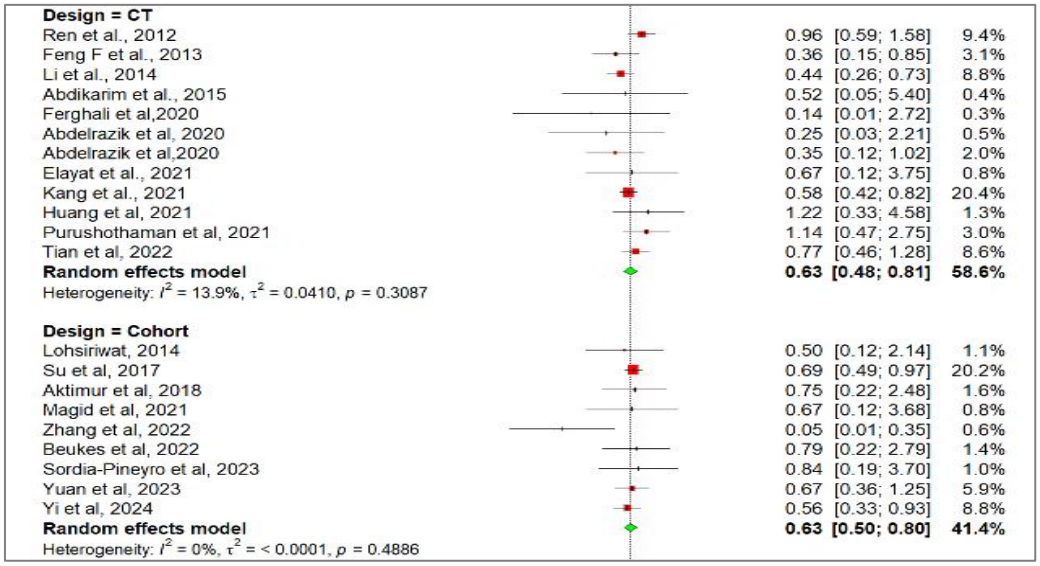

Figure 20 Forest plot for subgroup analysis of postoperative morbidity in terms of study design

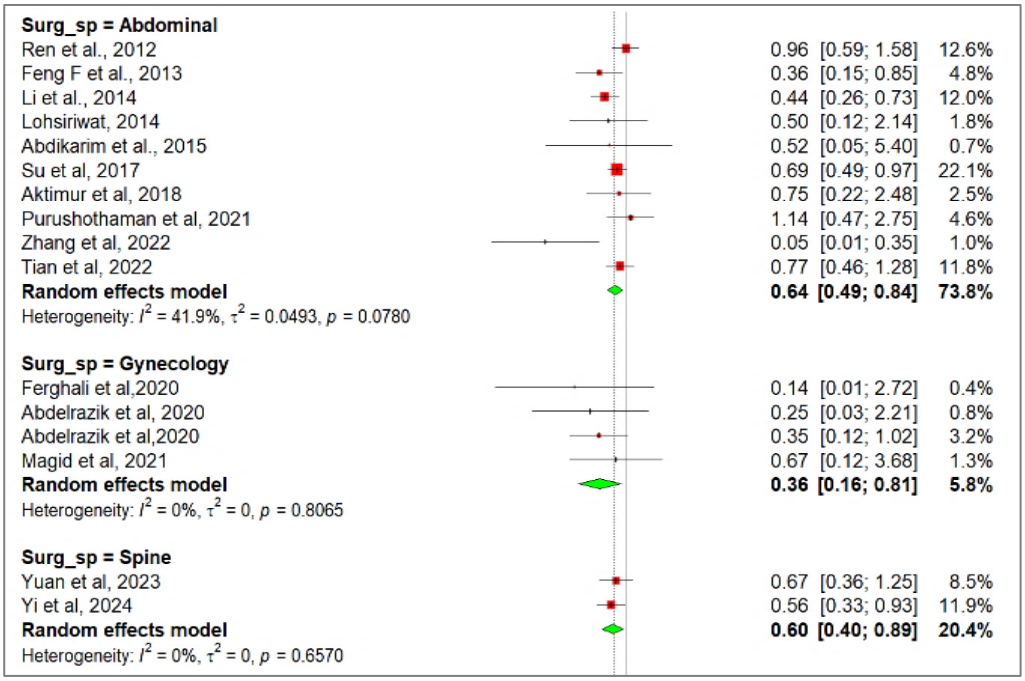

Figure 21 Forest plot of subgroup analysis of postoperative morbidity in terms of surgical specialty

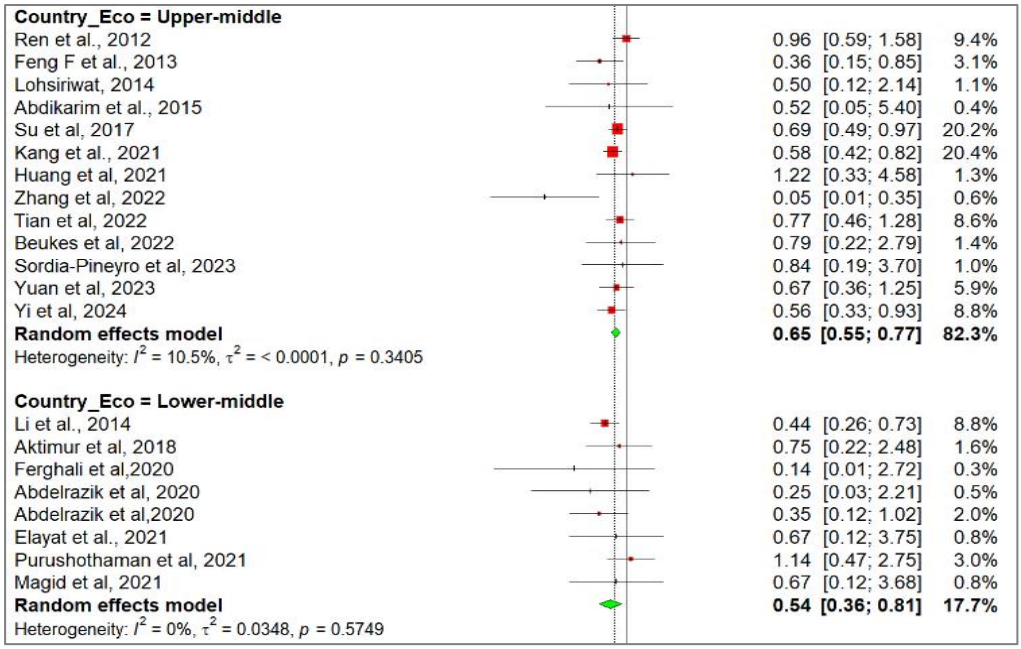

Figure 22 Forest plot of subgroup analysis of postoperative morbidity in terms of countries economic level

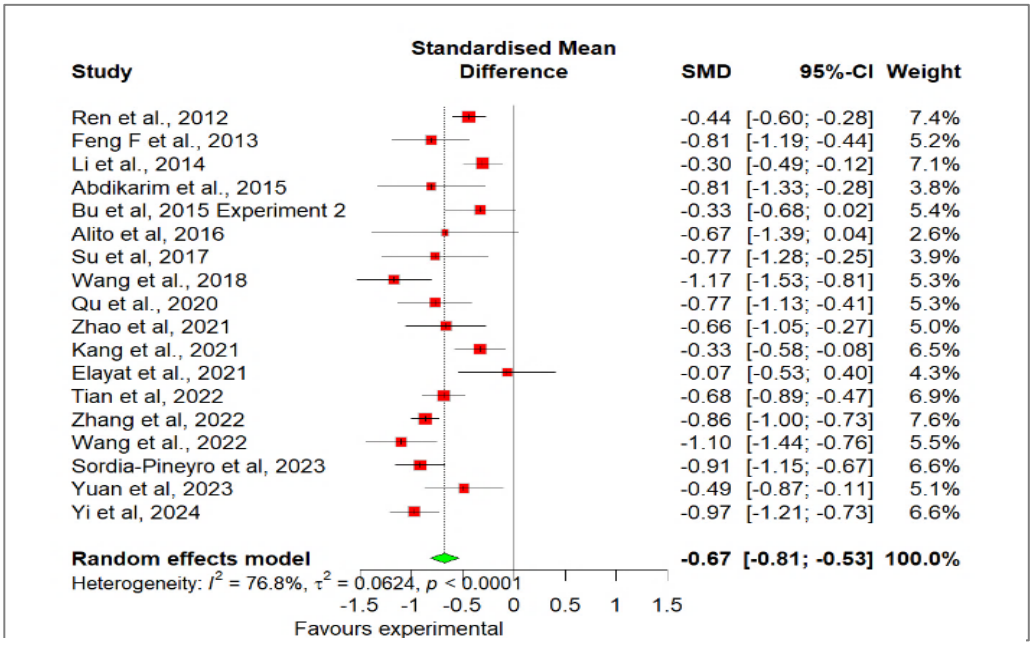

Figure 23 Forest plot of postoperative length of hospital stay after removing influential studies

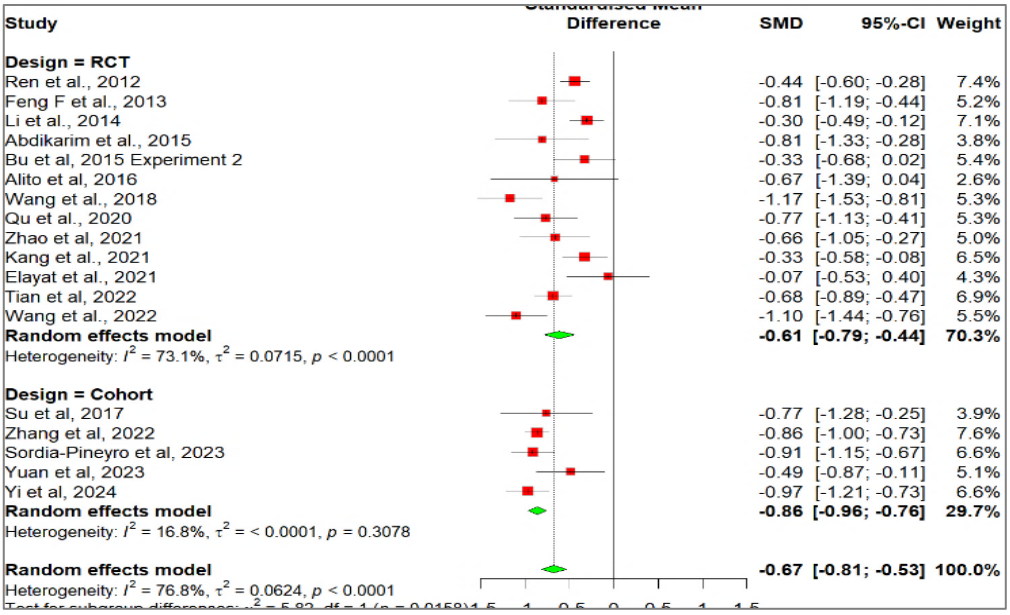

Figure 25 Forest plot of subgroup analysis of postoperative length of hospital stays in terms of study design

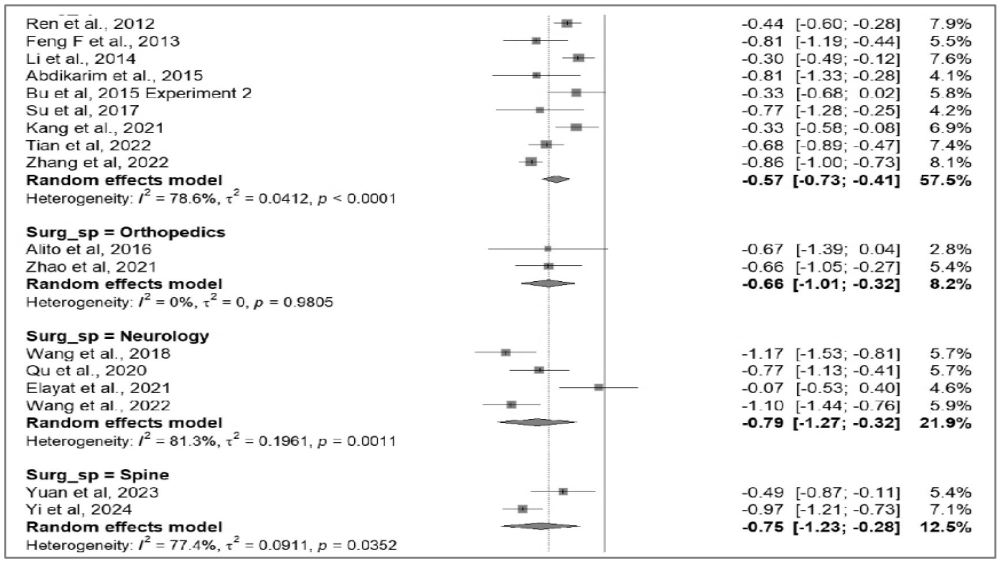

Figure 24 Forest plot of subgroup analysis of postoperative length of hospital stays in terms of surgical specialty

Appendix III: Supplementary Data of Baujat Plot

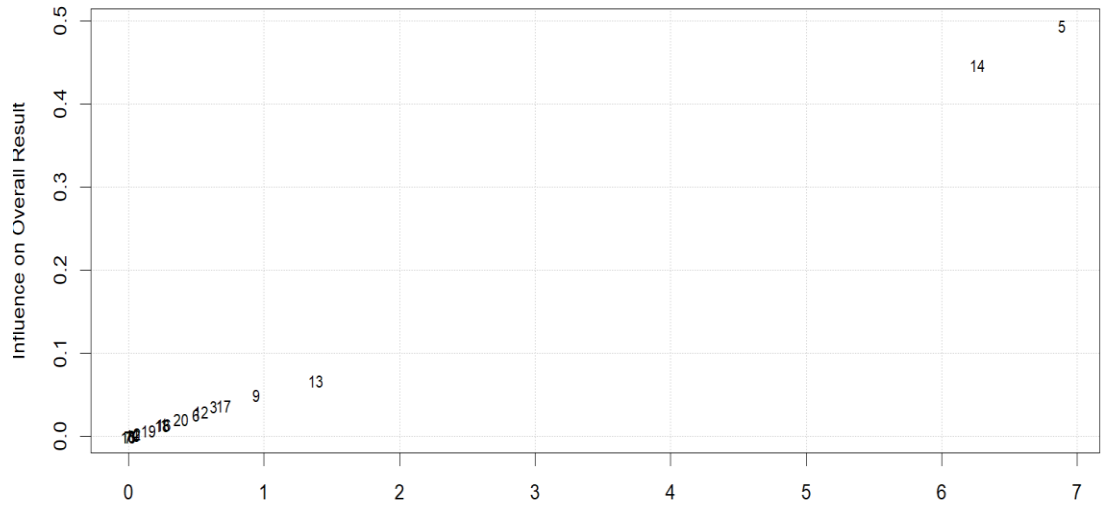

Figure 27 Baujat plot of 20 studies after for postoperative LOS

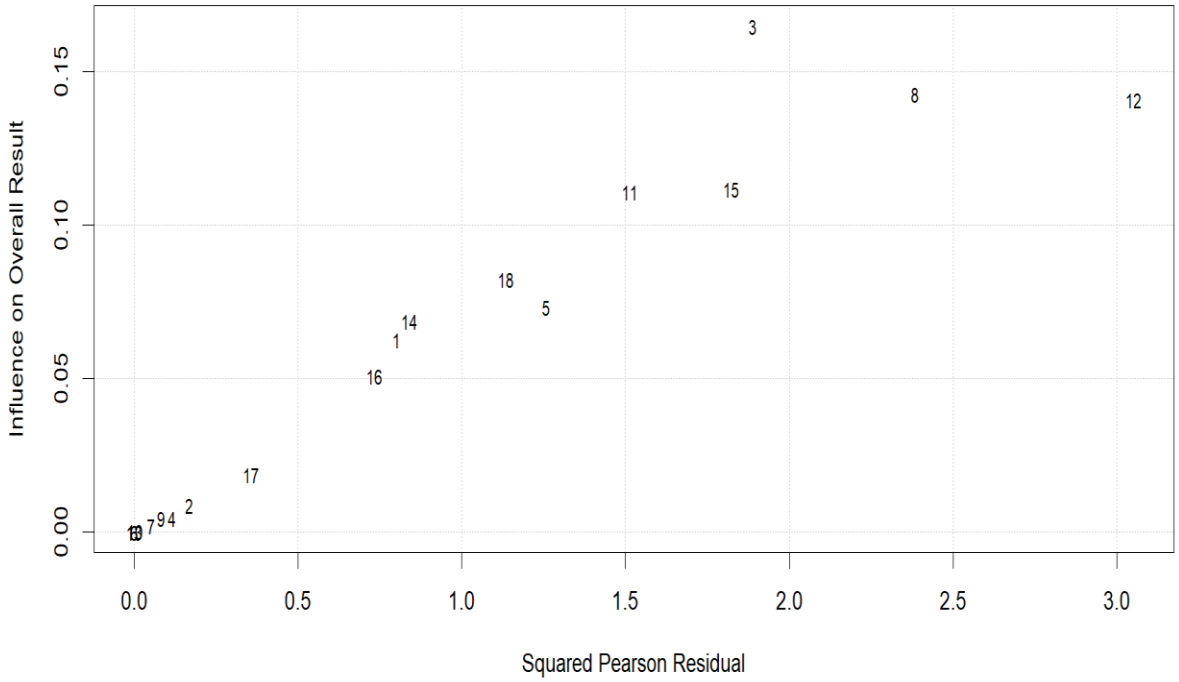

Figure 26 Baujat plot of 18 studies after two influential studies are withheld for postoperative LOS

Appendix IV: Supplementary Data of Influence diagnostic of meta-analysis model

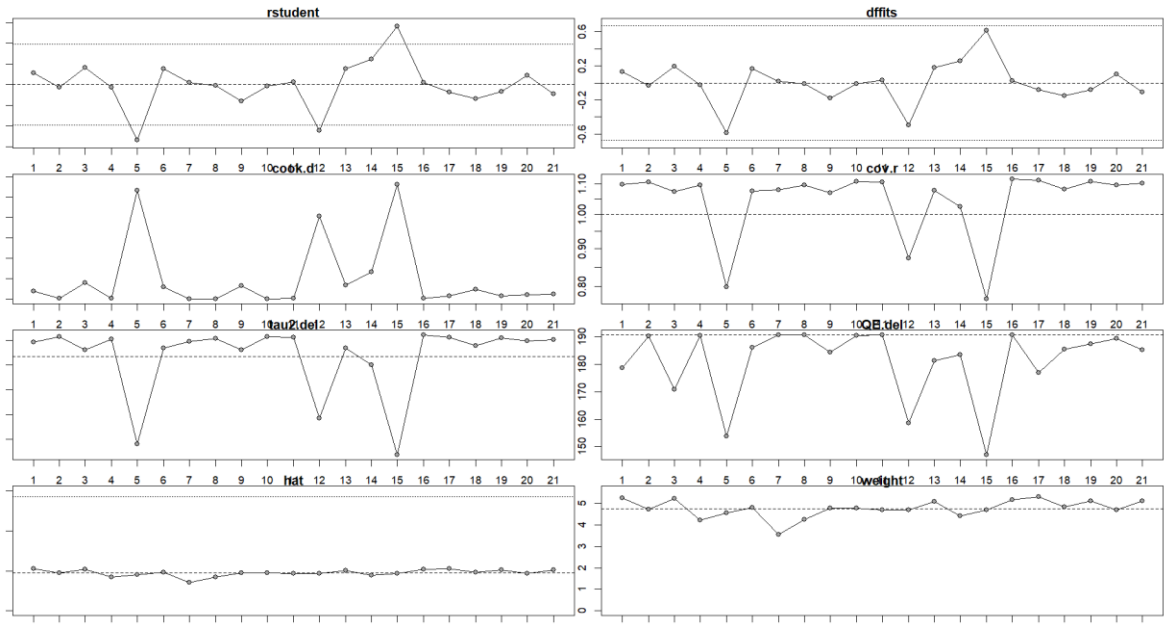

Figure 28 Influence diagnostic of meta-analysis model for postoperative LOS of 20 studies

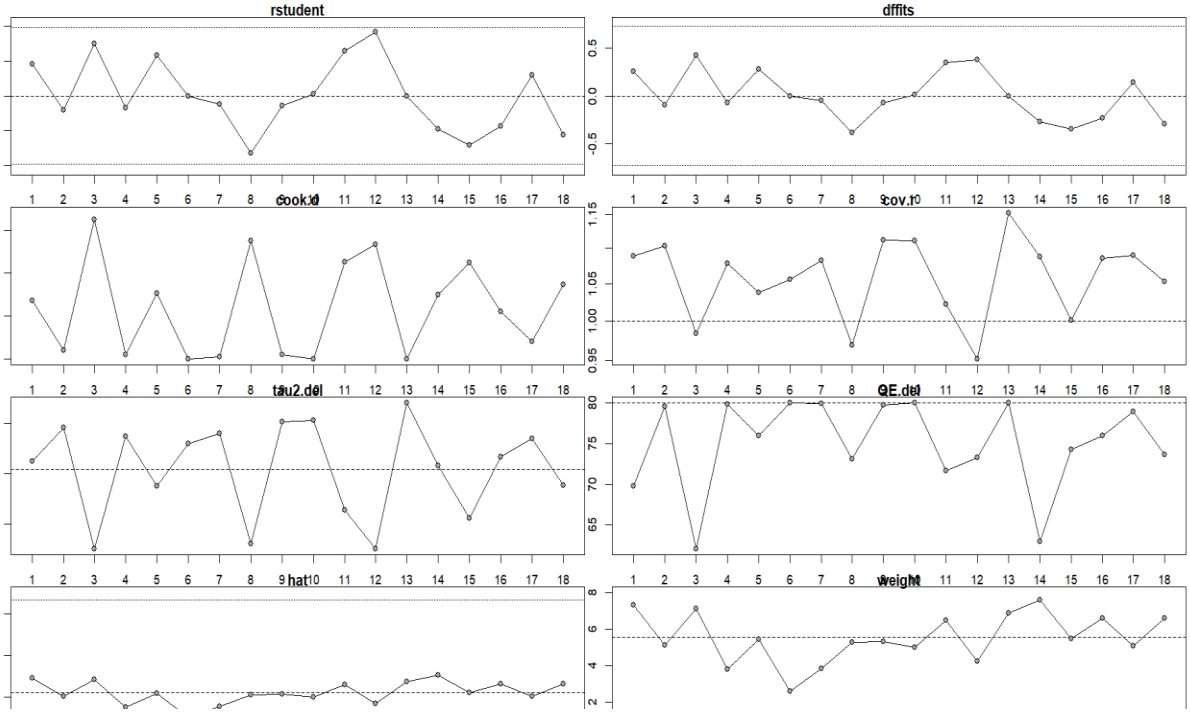

Figure 29 Influence diagnostic of meta-analysis model for postoperative LOS of 18 studies

Appendix V: Supplementary Data of Database Search

Enhanced Recovery After Surgery (ERAS) in Africa,
PubMed Searched PubMed on May 2024

	MESH	Keywords	TextWord
	"Enhanced Recovery After Surgery"[Mesh]	Enhanced Recovery After Surgery OR ERAS OR fast-track surgery OR fast track surgery FAST OR Enhanced Postsurgical Recovery	

Search	Query	Records retrieved
# 7	**"Enhanced Recovery After Surgery"[Mesh]**	1,670
# 6	Enhanced Recovery After Surgery OR ERAS OR fast-track surgery OR fast track surgery FAST OR Enhanced Postsurgical Recovery	15,778
# 8	("Enhanced Recovery After Surgery"[Mesh]) OR (Enhanced Recovery After Surgery OR ERAS OR fast-track surgery OR fast track surgery FAST OR Enhanced Postsurgical Recovery)	15,778
# 11	("Enhanced Recovery After Surgery"[Mesh]) OR ("Enhanced Recovery After Surgery" OR ERAS OR "fast-track surgery" OR "fast track surgery FAST" OR "Enhanced Postsurgical Recovery")	12,448
# 9	"Enhanced Recovery After Surgery"[All Fields] OR "ERAS"[All Fields] OR "fast-track surgery"[All Fields] OR "fast track surgery FAST"[All Fields] OR "Enhanced Postsurgical Recovery"[All Fields]	9, 820
#4	"fast-track surgery"[Title/Abstract] OR "Enhanced Postsurgical Recovery"[Title/Abstract] OR "fast track surgery FAST"[Title/Abstract] OR "ERAS"[Title/Abstract] OR "Enhanced Recovery After Surgery"[Title/Abstract]	9, 176
#2	("Deprived Country*"[Text Word] OR "Deprived Population*"[Text Word] OR "Developing Country*"[Text Word] OR "Developing Economy*"[Text Word] OR "Developing Nation*"[Text Word] OR "Developing Population*"[Text Word] OR "Developing Population*"[Text Word] OR "Developing World"[Text Word] OR "LAMI Country*"[Text Word] OR "Less Developed Country*"[Text Word] OR "Less Developed Economy*"[Text Word] OR "Less Developed Nation*"[Text Word] OR "Less Developed World"[Text Word] OR "Lesser Developed Country*"[Text Word] OR "Lesser Developed Nation*"[Text Word] OR LMIC[Text Word] OR LMICS[Text Word] OR "Low GDP"[Text Word] OR "Low GNP"[Text Word] OR "Low Gross Domestic"[Text Word] OR "Low Gross National*"[Text Word] OR "Low Income Country*"[Text Word] OR "Low Income Economy*"[Text Word] OR "Low Income Nation*"[Text Word] OR "Low Income Population*"[Text Word] OR "Lower GDP"[Text Word] OR "lower gross domestic*"[Text Word] OR	1,961,372

	"Lower Income Country*"[Text Word] OR "Lower Income Nation*"[Text Word] OR "Lower Income Population*"[Text Word] OR "Middle Income Country*"[Text Word] OR "Middle Income Economy*"[Text Word] OR "Middle Income Nation*"[Text Word] OR "Middle Income Population*"[Text Word] OR "Poor Country*"[Text Word] OR "Poor Economy*"[Text Word] OR "Poor Nation*"[Text Word] OR "Poor Population*"[Text Word] OR "Poor World "[Text Word] OR "Poorer Country*"[Text Word] OR "Poorer Economy*"[Text Word] OR "Poorer Nation*"[Text Word] OR "Poorer Population*"[Text Word] OR "Third World"[Text Word] OR "Transitional Country*"[Text Word] OR "Transitional Economy*"[Text Word] OR "Underdeveloped Country*"[Text Word] OR "Underdeveloped nation*"[Text Word] OR "Underdeveloped World"[Text Word] OR "Under Served Population*"[Text Word] OR "Underdeveloped Country*"[Text Word] OR "Underdeveloped economy*"[Text Word] OR "Underdeveloped nation*"[Text Word] OR "Underdeveloped population*"[Text Word] OR "Underdeveloped World"[Text Word] OR "Underserved Country*"[Text Word] OR "Underserved Nation*"[Text Word] OR "Underserved Population*"[Text Word] OR Afghanistan[Text Word] OR Albania[Text Word] OR Algeria[Text Word] OR "American Samoa"[Text Word] OR Angola[Text Word] OR Armenia[Text Word] OR Azerbaijan[Text Word] OR Bangladesh[Text Word] OR Belarus[Text Word] OR Byelarus[Text Word] OR Belorussia[Text Word] OR Belize[Text Word] OR Benin[Text Word] OR Bhutan[Text Word] OR Bolivia[Text Word] OR Bosnia[Text Word] OR Botswana[Text Word] OR Brazil[Text Word] OR Bulgaria[Text Word] OR Burma[Text Word] OR "Burkina Faso"[Text Word] OR Burundi[Text Word] OR "Cabo Verde"[Text Word] OR "Cape Verde"[Text Word] OR Cambodia[Text Word] OR Cameroon[Text Word] OR "Central African Republic"[Text Word] OR Chad[Text Word] OR China[Text Word] OR Colombia[Text Word] OR Comoros[Text Word] OR Comores[Text Word] OR Comoro[Text Word] OR Congo[Text Word] OR "Costa Rica"[Text Word] OR "Côte d'Ivoire"[Text Word] OR Cuba[Text Word] OR Djibouti[Text Word] OR Dominica[Text Word] OR "Dominican Republic"[Text Word] OR Ecuador[Text Word] OR Egypt[Text Word] OR "El Salvador"[Text Word] OR "Equatorial Guinea"[Text Word] OR Eritrea[Text Word] OR Ethiopia[Text Word] OR Fiji[Text Word] OR Gabon[Text Word] OR Gambia[Text Word] OR Gaza[Text Word] OR Georgia[Text Word] OR "Georgia Republic"[Text Word] OR Ghana[Text Word] OR Grenada[Text Word] OR Grenadines[Text Word] OR Guatemala[Text Word] OR Guinea[Text Word] OR "Guinea- Bissau"[Text Word] OR Guyana[Text Word] OR Haiti[Text Word] OR Herzegovina[Text Word] OR Hercegovina[Text Word] OR Honduras[Text Word] OR India[Text Word] OR Indonesia[Text Word] OR Iran[Text Word] OR Iraq[Text Word] OR "Ivory Coast"[Text Word] OR Jamaica[Text Word] OR Jordan[Text Word] OR Kazakhstan[Text Word] OR Kenya[Text Word] OR Kiribati[Text Word] OR "Democratic People's Republic of Korea"[Text Word] OR Kosovo[Text Word] OR Kyrgyz[Text Word] OR Kirghizia[Text Word] OR Kirghiz[Text Word] OR Kyrgyzstan[Text Word] OR "Lao PDR"[Text Word] OR Laos[Text Word] OR Lebanon[Text Word] OR Lesotho[Text Word] OR Liberia[Text Word] OR Libya[Text Word] OR Macedonia[Text Word] OR Madagascar[Text Word] OR Malawi[Text Word] OR Malay[Text Word] OR Malaya[Text Word] OR Malaysia[Text Word] OR Maldives[Text Word] OR Mali[Text Word] OR "Marshall Islands"[Text Word] OR Mauritania[Text Word] OR Mauritius[Text Word] OR Mexico[Text Word] OR Micronesia[Text Word] OR Moldova[Text Word] OR Mongolia[Text Word] OR Montenegro[Text Word] OR Morocco[Text Word] OR Mozambique[Text Word] OR Myanmar[Text Word] OR Namibia[Text Word] OR	

	Nepal[Text Word] OR Nicaragua[Text Word] OR Niger[Text Word] OR Nigeria[Text Word] OR Pakistan[Text Word] OR Palau[Text Word] OR "Papua New Guinea"[Text Word] OR Paraguay[Text Word] OR Peru[Text Word] OR Philippines[Text Word] OR Principe[Text Word] OR Romania[Text Word] OR Ruanda[Text Word] OR Rwanda[Text Word] OR Samoa[Text Word] OR "Sao Tome"[Text Word] OR Senegal[Text Word] OR Serbia[Text Word] OR "Sierra Leone"[Text Word] OR "Solomon Islands"[Text Word] OR Somalia[Text Word] OR "South Africa"[Text Word] OR "South Sudan"[Text Word] OR "Sri Lanka"[Text Word] OR "St Lucia"[Text Word] OR "St Vincent"[Text Word] OR Sudan[Text Word] OR Surinam[Text Word] OR Suriname[Text Word] OR Swaziland[Text Word] OR Syria[Text Word] OR Syria[Text Word] OR "Syrian Arab Republic"[Text Word] OR Tajikistan[Text Word] OR Tadzhikistan[Text Word] OR Tajikistan[Text Word] OR Tadzhik[Text Word] OR Tanzania[Text Word] OR Thailand[Text Word] OR Timor[Text Word] OR Togo[Text Word] OR Tonga[Text Word] OR Tunisia[Text Word] OR Turkey[Text Word] OR Turkmen[Text Word] OR Turkmenistan[Text Word] OR Tuvalu[Text Word] OR Uganda[Text Word] OR Ukraine[Text Word] OR Uzbek[Text Word] OR Uzbekistan[Text Word] OR Vanuatu[Text Word] OR Venezuela[Text Word] OR Vietnam[Text Word] OR "West Bank"[Text Word] OR Yemen[Text Word] OR Zambia[Text Word] OR Zimbabwe[Text Word])	
# 13	(("Enhanced Recovery After Surgery"[Mesh]) OR ("Enhanced Recovery After Surgery" OR ERAS OR "fast-track surgery" OR "fast track surgery FAST" OR "Enhanced Postsurgical Recovery")) AND (("Deprived Country*"[Text Word] OR "Deprived Population*"[Text Word] OR "Developing Country*"[Text Word] OR "Developing Economy*"[Text Word] OR "Developing Nation*"[Text Word] OR "Developing Population*"[Text Word] OR "Developing Population*"[Text Word] OR "Developing World"[Text Word] OR "LAMI Country*"[Text Word] OR "Less Developed Country*"[Text Word] OR "Less Developed Economy*"[Text Word] OR "Less Developed Nation*"[Text Word] OR "Less Developed World"[Text Word] OR "Lesser Developed Country*"[Text Word] OR "Lesser Developed Nation*"[Text Word] OR LMIC[Text Word] OR LMICS[Text Word] OR "Low GDP"[Text Word] OR "Low GNP"[Text Word] OR "Low Gross Domestic"[Text Word] OR "Low Gross National*"[Text Word] OR "Low Income Country*"[Text Word] OR "Low Income Economy*"[Text Word] OR "Low Income Nation*"[Text Word] OR "Low Income Population*"[Text Word] OR "Lower GDP"[Text Word] OR "lower gross domestic*"[Text Word] OR "Lower Income Country*"[Text Word] OR "Lower Income Nation*"[Text Word] OR "Lower Income Population*"[Text Word] OR "Middle Income Country*"[Text Word] OR "Middle Income Economy*"[Text Word] OR "Middle Income Nation*"[Text Word] OR "Middle Income Population*"[Text Word] OR "Poor Country*"[Text Word] OR "Poor Economy*"[Text Word] OR "Poor Nation*"[Text Word] OR "Poor Population*"[Text Word] OR "Poor World "[Text Word] OR "Poorer Country*"[Text Word] OR "Poorer Economy*"[Text Word] OR "Poorer Nation*"[Text Word] OR "Poorer Population*"[Text Word] OR "Third World"[Text Word] OR "Transitional Country*"[Text Word] OR "Transitional Economy*"[Text Word] OR "Underdeveloped Country*"[Text Word] OR "Underdeveloped nation*"[Text Word] OR "Underdeveloped World"[Text Word] OR "Under Served Population*"[Text Word] OR "Underdeveloped Country*"[Text Word] OR "Underdeveloped economy*"[Text Word] OR "Underdeveloped nation*"[Text Word] OR "Underdeveloped population*"[Text Word] OR "Underdeveloped World"[Text Word] OR "Underserved Country*"[Text Word] OR "Underserved	665

	Nation*"[Text Word] OR "Underserved Population*"[Text Word] OR Afghanistan[Text Word] OR Albania[Text Word] OR Algeria[Text Word] OR "American Samoa"[Text Word] OR Angola[Text Word] OR Armenia[Text Word] OR Azerbaijan[Text Word] OR Bangladesh[Text Word] OR Belarus[Text Word] OR Byelarus[Text Word] OR Belorussia[Text Word] OR Belize[Text Word] OR Benin[Text Word] OR Bhutan[Text Word] OR Bolivia[Text Word] OR Bosnia[Text Word] OR Botswana[Text Word] OR Brazil[Text Word] OR Bulgaria[Text Word] OR Burma[Text Word] OR "Burkina Faso"[Text Word] OR Burundi[Text Word] OR "Cabo Verde"[Text Word] OR "Cape Verde"[Text Word] OR Cambodia[Text Word] OR Cameroon[Text Word] OR "Central African Republic"[Text Word] OR Chad[Text Word] OR China[Text Word] OR Colombia[Text Word] OR Comoros[Text Word] OR Comores[Text Word] OR Comoro[Text Word] OR Congo[Text Word] OR "Costa Rica"[Text Word] OR "Côte d'Ivoire"[Text Word] OR Cuba[Text Word] OR Djibouti[Text Word] OR Dominica[Text Word] OR "Dominican Republic"[Text Word] OR Ecuador[Text Word] OR Egypt[Text Word] OR "El Salvador"[Text Word] OR "Equatorial Guinea"[Text Word] OR Eritrea[Text Word] OR Ethiopia[Text Word] OR Fiji[Text Word] OR Gabon[Text Word] OR Gambia[Text Word] OR Gaza[Text Word] OR Georgia[Text Word] OR "Georgia Republic"[Text Word] OR Ghana[Text Word] OR Grenada[Text Word] OR Grenadines[Text Word] OR Guatemala[Text Word] OR Guinea[Text Word] OR "Guinea- Bissau"[Text Word] OR Guyana[Text Word] OR Haiti[Text Word] OR Herzegovina[Text Word] OR Hercegovina[Text Word] OR Honduras[Text Word] OR India[Text Word] OR Indonesia[Text Word] OR Iran[Text Word] OR Iraq[Text Word] OR "Ivory Coast"[Text Word] OR Jamaica[Text Word] OR Jordan[Text Word] OR Kazakhstan[Text Word] OR Kenya[Text Word] OR Kiribati[Text Word] OR "Democratic People's Republic of Korea"[Text Word] OR Kosovo[Text Word] OR Kyrgyz[Text Word] OR Kirghizia[Text Word] OR Kirghiz[Text Word] OR Kyrgyzstan[Text Word] OR "Lao PDR"[Text Word] OR Laos[Text Word] OR Lebanon[Text Word] OR Lesotho[Text Word] OR Liberia[Text Word] OR Libya[Text Word] OR Macedonia[Text Word] OR Madagascar[Text Word] OR Malawi[Text Word] OR Malay[Text Word] OR Malaya[Text Word] OR Malaysia[Text Word] OR Maldives[Text Word] OR Mali[Text Word] OR "Marshall Islands"[Text Word] OR Mauritania[Text Word] OR Mauritius[Text Word] OR Mexico[Text Word] OR Micronesia[Text Word] OR Moldova[Text Word] OR Mongolia[Text Word] OR Montenegro[Text Word] OR Morocco[Text Word] OR Mozambique[Text Word] OR Myanmar[Text Word] OR Namibia[Text Word] OR Nepal[Text Word] OR Nicaragua[Text Word] OR Niger[Text Word] OR Nigeria[Text Word] OR Pakistan[Text Word] OR Palau[Text Word] OR "Papua New Guinea"[Text Word] OR Paraguay[Text Word] OR Peru[Text Word] OR Philippines[Text Word] OR Principe[Text Word] OR Romania[Text Word] OR Ruanda[Text Word] OR Rwanda[Text Word] OR Samoa[Text Word] OR "Sao Tome"[Text Word] OR Senegal[Text Word] OR Serbia[Text Word] OR "Sierra Leone"[Text Word] OR "Solomon Islands"[Text Word] OR Somalia[Text Word] OR "South Africa"[Text Word] OR "South Sudan"[Text Word] OR "Sri Lanka"[Text Word] OR "St Lucia"[Text Word] OR "St Vincent"[Text Word] OR Sudan[Text Word] OR Surinam[Text Word] OR Suriname[Text Word] OR Swaziland[Text Word] OR Syria[Text Word] OR Syria[Text Word] OR "Syrian Arab Republic"[Text Word] OR Tajikistan[Text Word] OR Tadzhikistan[Text Word] OR Tajikistan[Text Word] OR Tadzhik[Text Word] OR Tanzania[Text Word] OR Thailand[Text Word] OR Timor[Text Word] OR Togo[Text Word] OR Tonga[Text Word] OR Tunisia[Text Word] OR Turkey[Text Word] OR	

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Filters #20	Study Type: Observational study, Clinical Trial and Randomized clinical trial	63

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