Systematic Review and/or Meta-analysis

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Enhanced recovery programme after colorectal surgery in high-income and low-middle income countries: a systematic review and meta-analysis

Naim Slim, MBBS, MSc, MRCS[a], Wai Huang Teng, MBChB, MRCS[a], Ealaff Shakweh, MRes, BMBS[b], Helena-Colling Sylvester, MBChB[a], Mina Awad, MBChB, MRCS[a], Rebecca Schembri, MD[a], Shady Hermena, MBBCh[a], Manish Chowdhary, MBBS,[c], Ravi Oodit, MBChB[f], Nader K. Francis, MBChB, PhD,[a,e,d,*]

Background: Enhanced recovery after surgery (ERAS) protocols strive to optimise outcomes following elective surgery; however, there is a dearth of evidence to support its equitable application and efficacy internationally.

Materials and methods: The authors performed a systematic review and meta-analysis of studies on the uptake and impact of ERAS with the aim of highlighting differences in implementation and outcomes across high-income countries (HICs) and low-middle income countries (LMICs). The primary outcome was characterisation of global ERAS uptake. Secondary outcomes included length of hospital stay (LOS), 30-day readmission, 30-day mortality and postoperative complications.

Results: Three hundred thirty-seven studies with considerable heterogeneity were included in the analysis (291 from HICs, and 46 from LMICs) with a total of 110 190 patients. The weighted median number of implemented elements were similar between HICs and LMICs ($P = 0{\cdot}94$), but there was a trend towards greater uptake of less affordable elements across all aspects of the ERAS pathway in HICs. The mean LOS was significantly shorter in patient cohorts in HICs (5·85 days versus 7·17 days in LMICs, $P < 0{\cdot}001$). The 30-day readmission rate was higher in HICs (8·5 vs. 4·25% in LMICs, $P < 0{\cdot}001$, but no overall world-wide effect when ERAS compared to controls (OR 1·00, 95% CI: 0·88—1·13). There were no reported differences in complications ($P = 0{\cdot}229$) or 30-day mortality ($P = 0{\cdot}949$).

Conclusion: Considerable variation in the structure, the implementation and outcomes of ERAS exists between HICs and LMICs, where affordable elements are implemented, contributing towards longer LOS in LMICs. Global efforts are required to ensure equitable access, effective ERAS implementation and a higher standard of perioperative care world-wide.

Keywords: colorectal, ERAS, fast-track surgery, global health, global surgery, health equity

Introduction

Advancements in the quality of perioperative care have improved the outcome of surgery across high-income countries (HICs). However, data from the International Surgical Outcomes Study (ISOS) suggests that the quality of perioperative care is variable across low-middle-income countries (LMICs)[1] and thus there is a need to address these discrepancies if safe surgery is to be practiced in an equitable manner across the globe. Evidence from the Lancet Global Commission has highlighted the significant gap in access to safe and affordable surgical care and anaesthesia between HICs and LMICs[2]. It is likely that this disparity expands across the entire perioperative pathway.

One innovation that has yielded demonstrable improvement in patient outcomes and perioperative care in the last two decades is the introduction of an Enhanced recovery after surgery (ERAS) programme; a multimodal programme designed to optimise outcomes through the implementation of numerous perioperative care elements[3]. ERAS programmes have been shown to decrease

HIGHLIGHTS

- Data comparing the implementation of Enhanced recovery after surgery (ERAS) programmes and effects on patient outcomes across the world, particularly in low-middle-income countries (LMICs), is lacking.
- We found significant variation in the uptake of individual ERAS elements, and a significantly longer length of stay in LMICs, but similar rates of mortality.
- Efforts are needed to understand barriers to implementation of ERAS programmes and patient outcome measurement in LMICs an in order for the benefits of the programme to be sustained across the world.

[a]Department of General Surgery, Yeovil District Hospital, Higher Kingston, Yeovil, Somerset, [b]Department of General Surgery, Northwick Park Hospital, [c]Directorate of Training, Northwick Park Institute of Medical Research, Northwick Park Hospital, [d]The Griffin Institute, Northwick Park and St Mark's Hospital, Harrow, [e]Division of Surgery and Interventional Science, University College London, UK and [f]Division of Global Surgery, University of Cape Town, Cape Town, Western Cape, South Africa

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*Corresponding author. Address: The Griffin Institute, Northwick Park and St Mark's Hospital, Y Block, Watford Road, Harrow, Middlesex, HA1 3UJ Tel.: +441 935 384 244; fax: +441 935 384 653. E-mail: Nader.francis@ydh.nhs.uk (N.K. Francis).

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the rate of postoperative complications, accelerate patient recovery and shorten length of stay (LOS)[4–7]. Originally developed in Denmark in the mid-1990s, specifically for use within colorectal surgery[3], various perioperative care pathways based on the principles of ERAS have been adopted for use routinely in many specialities in HICs. There is; however, a paucity of evidence to support its equitable application and efficacy internationally, particularly in LMICs.

This paper aims to systematically review the global uptake and impact of ERAS across the world. We seek to provide an overview of the contemporary implementation of ERAS interventions in perioperative care across the world, drawing comparison between implementation and outcomes between HICs and LMICs.

Materials and methods

Overview

We performed a systematic review and meta-analysis of studies on the uptake and impact of ERAS in the context of elective colorectal surgery worldwide, with the aim of highlighting differences in implementation and outcomes across the HIC and LMIC's. This review was reported according to The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA, Supplemental Digital Content 1, http://links.lww.com/JS9/A909) and Assessing the methodological quality of systematic reviews (AMSTAR, Supplemental Digital Content 2, http://links.lww.com/JS9/A910) guidelines[8,9].

Search strategy, selection criteria and data extraction

A systematic review was conducted to ascertain the global uptake, nature, implementation and outcomes of ERAS within colorectal surgical practice. We focused on colorectal surgery, the speciality within which ERAS was first implemented and hence likely to have the largest body of global evidence.

A literature search was conducted on the SCOPUS and PubMed databases from January 2010 to December 2020, with the search terms as follows: *Scopus search:* (TITLE-ABS-KEY((enhanced recovery) OR eras OR (rapid recovery) OR multimodal OR multimodal OR (accelerated discharge) OR (early discharge) OR (early rehabilitation) OR (clinical pathway) OR (accelerated pathway) OR (integrated care pathway)) AND TITLE-ABS-KEY(colorectal OR colo-rectal OR (colo-rectal cancer) OR (colorectal cancer) OR CRC OR bowel OR (bowel resection) OR (bowel surgery) OR colon OR proctectomy OR colectomy OR (segmental colectomy)) AND AFFILCOUNTRY (united kingdom)) AND (LIMIT-TO (SRCTYPE,"j")) AND (LIMIT-TO (DOCTYPE,"ar") OR LIMIT-TO (DOCTYPE,"re")) AND (LIMIT-TO (SUBJAREA,"MEDI") OR LIMIT-TO (SUBJAREA,"BIOC")) AND (LIMIT-TO (PUBYEAR,2020) OR (LIMIT-TO (PUBYEAR,2019) OR LIMIT-TO (PUBYEAR,2018) OR LIMIT-TO (PUBYEAR,2017) OR LIMIT-TO (PUBYEAR,2016) OR LIMIT-TO (PUBYEAR, 2015) OR LIMIT-TO (PUBYEAR,2014) OR LIMIT-TO (PUBYEAR,2013) OR LIMIT-TO (PUBYEAR,2012) OR LIMIT-TO (PUBYEAR,2011) OR LIMIT-TO (PUBYEAR,2010)) AND (LIMIT-TO (LANGUAGE,"English")); *Pubmed search:* ((enhanced recovery)[Title/Abstract] OR eras[Title/Abstract] OR (rapid recovery)[Title/Abstract] OR multimodal[Title/Abstract] OR multimodal[Title/Abstract] OR (accelerated discharge)[Title/Abstract] OR (early discharge)[Title/Abstract] OR (early rehabilitation)[Title/Abstract] OR (clinical pathway)[Title/Abstract] OR (accelerated pathway)[Title/Abstract] OR (integrated care pathway)[Title/Abstract]) AND (colorectal[Title/Abstract] OR colo-rectal[Title/Abstract] OR (colo-rectal cancer)[Title/Abstract] OR (colorectal cancer)[Title/Abstract] OR CRC[Title/Abstract] OR bowel[Title/Abstract] OR (bowel resection)[Title/Abstract] OR (bowel surgery)[Title/Abstract] OR colon[Title/Abstract] OR proctectomy[Title/Abstract] OR colectomy[Title/Abstract] OR (segmental colectomy)[Title/Abstract]) Filters: English, from 2010/1/1 - 2020/12/31.

We intentionally reviewed the entire ERAS literature, not limiting the search terms to HIC or LMIC, but using each paper's country of origin to stratify the income class as defined by the United Nations World Economic Situation and Prospects (WESP) report[10].

The inclusion criteria for article selection were: prospective or retrospective study of elective resectional colorectal surgery cases (open, laparoscopic, or robotic), and patients managed within a defined ERAS protocol that reports outcomes. We excluded studies that included nonresectional surgery, noncolorectal cases, emergency cases (where these could not be excluded from the data collection and analysis), case reports, case series with fewer than 10 patients, paediatric surgical cases, editorials, commentaries, narrative reviews, systematic reviews and meta-analyses. Studies conducted across multiple countries or continents were excluded due to the difficulty in ascertaining the country of origin.

Data analysis

A dedicated database was developed to capture and extract information from the included studies. Data pertaining to the following was extracted: author's name, publication date, study design, sampling period, study location, number of patients enroled within an ERAS programme, summary patient baseline demographics, method of surgical access (open, laparoscopic, or robotic), the reported presence (or absence) of ERAS elements as defined by the comprehensive consensus review published by the ERAS society[11] and characterisation of the method used to achieve element implementation (for example, use of the goal-directed method or zero fluid balance method for intraoperative fluid therapy), reported compliance with each element (if reported), and outcome measures including LOS, and complications, readmission and mortality within 30 days. For the purposes of data analysis, the ERAS elements were categorised by whether they were preoperative, intraoperative, or postoperative. Data was independently extracted by seven reviewers (NS, WHT, HCS, MA, RS, SH and MC). The disagreement was resolved by discussion with the senior author (NKF).

The primary outcome of this study is the characterisation of the global uptake of ERAS as defined by the presence of a formal ERAS protocol in a surgical unit, along with the infrastructure and training to implement it. Secondary outcomes include length of hospital stay, 30-day readmission, 30-day mortality and postoperative complications.

Quality assessment

Randomised studies that were included were scored according to the Cochrane Risk of Bias (ROB2) tool[12] by three independent assessors (NS, WHT, ES). Judgements were made on the risk of bias in relation to the randomisation process, deviations from intended interventions, missing outcome data, measurement of the outcomes and selection of the reported result.

Statistical analysis

Meta-analysis was performed for an outcome if more than one study presented relevant data. Only randomised controlled trials (RCTs) were used for meta-analysis to reduce heterogeniety and ensure the reliability of results. The odds ratio (OR) along with the 95% CI was used as an effect estimate for dichotomous outcomes, with OR values of less than or equal to 1 indicating fewer events in HICs (in the case of comparison between HICs and LMICs) or fewer events in the specified region compared to Europe (in the case of regional analysis). In the case of zero events, a 0·5 correction was added to incorporate all available data in the meta-analysis and to maintain analytic consistency. When studies provided only means for continuous variables and sample sizes, a SD was imputed according to Furukawa *et al*.[13]. For studies that reported medians with an interquartile range or range, estimation of the mean and SD was performed with methods described by Luo *et al*.[14]. The summary estimate was computed according to the random effect model as described by DerSimonian and Laird[15]. A conservative random effect model was chosen a priori in consideration of foreseen heterogeneity amongst the array of included studies from various countries. The heterogeneity among studies was tested with the Q statistic and quantified by the I^2 statistic, with I^2 values less than 25%, between 25 and 50% and above 50% indicating low, moderate and high heterogeneity, respectively. The presence of publication bias was investigated visually by means of funnel plots, where the summary estimate of each study, reported as an OR, was plotted against a measure of study precision (standard error). In addition to visual inspection, funnel plot symmetry was tested using Egger's linear regression method. *P*-values $\leq 0{\cdot}05$ were considered to be statistically significant. Statistical analysis was performed with the 'meta' package in *R* [Version 4.0.3, R Foundation for Statistical Computing, Vienna, Austria].

Role of the funding source

There was no funding source for this study.

Results

A total of 24 886 titles were identified with the initial search. One thousand twenty papers were relevant for full-text review, and 337 studies including 110 190 patients ultimately met the inclusion criteria as detailed in Figure 1. The majority of the studies were from HICs, with a total of 291 (86·3%) studies compared to 46 (13·6%) included from LMICs. Sixty-two RCTs (43 from HICs and 19 from LMICs) were included (18·4%), with the remainder being nonrandomised studies. The Cochrane Risk of Bias (ROB2) tool was used to assess the risk of bias in the included RCTs, the results of which are included in the Supplementary Appendix (Supplemental Digital Content 3, http://links.lww.com/JS9/A911).

Global ERAS uptake

The uptake of ERAS elements was reported in 241 studies (82·8%) from HICs and 37 studies (80·4%) from LMICs. The weighted median number of elements implemented was similar in HICs (12·5 elements, IQR: 9–16) and LMICs (14·5 elements, IQR: 7–15) ($\chi^2 = 0{\cdot}08$, $P = 0{\cdot}940$). The reported uptake of individual elements across HICs and LMICs varied considerably, and a summary of this is shown in Figure 2.

Across the preoperative elements, preanaesthetic medication (OR 5·13, 95% CI: 4·81–5·49); prehabilitation (OR 2·91, 95% CI: 2·33–3·64); preoperative feeding (OR 1·94, 95% CI: 1·77–2·12); and preoperative fasting and carbohydrate loading (OR 1·30, 95% CI: 1·22–1·39) were more commonly reported in HICs. Regarding preanaesthetic medication, the use of preoperative analgesia was exclusively described in HICs, and the use of preoperative benzodiazepines did not differ between HICs and LMICs (OR 1·09, 95% CI: 0·82–1·47, $\chi^2 = 0{\cdot}2899$, $P = 0{\cdot}5903$). Preoperative counselling (OR 1·40, 95% CI: 1·32–1·49) and bowel preparation avoidance (OR 1·21, 95% CI: 1·14–1·28) were also more commonly reported in HICs. Preoperative optimisation (OR 0·87, 95% CI: 0·80–0·94) and preoperative nutritional screening (OR 0·52, 95% CI: 0·48–0·56) were elements more commonly reported in LMICs.

Across the intraoperative elements, use of a transverse abdominis plane block (OR 1·69, 95% CI: 1·57–1·76); use of spinal anaesthesia (OR 1·66, 95% CI: 1·34–2·06) and use of epidural blockade (OR 1·47, 95% CI: 1·38–1·56) were more commonly reported in HICs. In addition, use of laparoscopy (OR 1·27, 95% CI: 1·20–1·35) was more prevalent in HICs, and robotic surgery was exclusively described in studies from HICs. With regards to intraoperative fluid therapy, the zero fluid balance approach was more commonly reported in LMICs (OR 0·33, 95% CI: 0·31–0·35) whereas the goal-directed approach was more commonly reported in HICs (OR 1·63, 95% CI: 1·53–1·74). When analysed by region, using Europe as a control, goal-directed fluid therapy (GDFT) was utilised more in North America (OR 1·41, 95% CI: 1·36–1·47, $P < 0{\cdot}001$), and Australia and Oceania (OR 1·15, 95% CI: 1·01 – 1·32, $P = 0{\cdot}03$). Patients in Asia were less likely to have GDFT as part of an ERAS programme (OR 0·64, 95% CI: 0·60 – 0·69, $P < 0{\cdot}001$), and no significant difference was found in the Middle East, North Africa and Greater Arabia (OR 1·23, 95% CI: 0·79–1·95 , $P = 0{\cdot}36$). Antimicrobial prophylaxis (OR 0·90, 95% CI: 0·85–0·95) and use of a standardised anaesthetic protocol (OR 0·62, 95% CI: 0·59–0·64) were elements more commonly reported in LMICs. Avoidance of postoperative nasogastric tubes (OR 1·65, 95% CI: 1·56–1·76) and drains (OR 1·25, 95% CI: 1·18–1·32) were elements more commonly reported in HICs, and prevention of hypothermia (OR 0·51, 95% CI: 0·48–0·54) was more commonly reported in LMICs.

Across the postoperative elements, the following elements were more commonly reported in HICs: postoperative nutritional care (OR 2·36, 95% CI: 2·18–2·56); postoperative fluid and electrolyte therapy (OR 1·60, 95% CI: 1·51–1·70); thromboprophylaxis (OR 1·35, 95% CI: 1·28–1·43); and use of opiate sparing multimodal analgesia (OR 1·23, 95% CI: 1·15–1·31). Specifically, regarding multimodal analgesia, the use of NSAIDs was uniform between HICs and LMICs (OR 0·94, 95% CI: 0·87–1·01, $P = 0{\cdot}08$), as was the use of opioids (OR 1·07, 95% CI: 0·99–1·16). Other pharmacological agents such as lidocaine (OR 1·66, 95% CI: 1·46–1·89) and dipyrone (OR 1·62, 95% CI: 1·10–2·41) were more commonly used in HICs. Furthermore, the use of gabapentinoids, corticosteroids and NMDA receptor antagonists was reported exclusively in studies from HICs. The weighted median number of modes of analgesia that formed part of a multimodal analgesic regimen was two (IQR: 2–3) in HICs versus one (IQR: 1–1) in LMICs ($W = 4078{\cdot}5$, $P < 0{\cdot}001$). Prevention of postoperative nausea and vomiting (OR 0·57, 95%

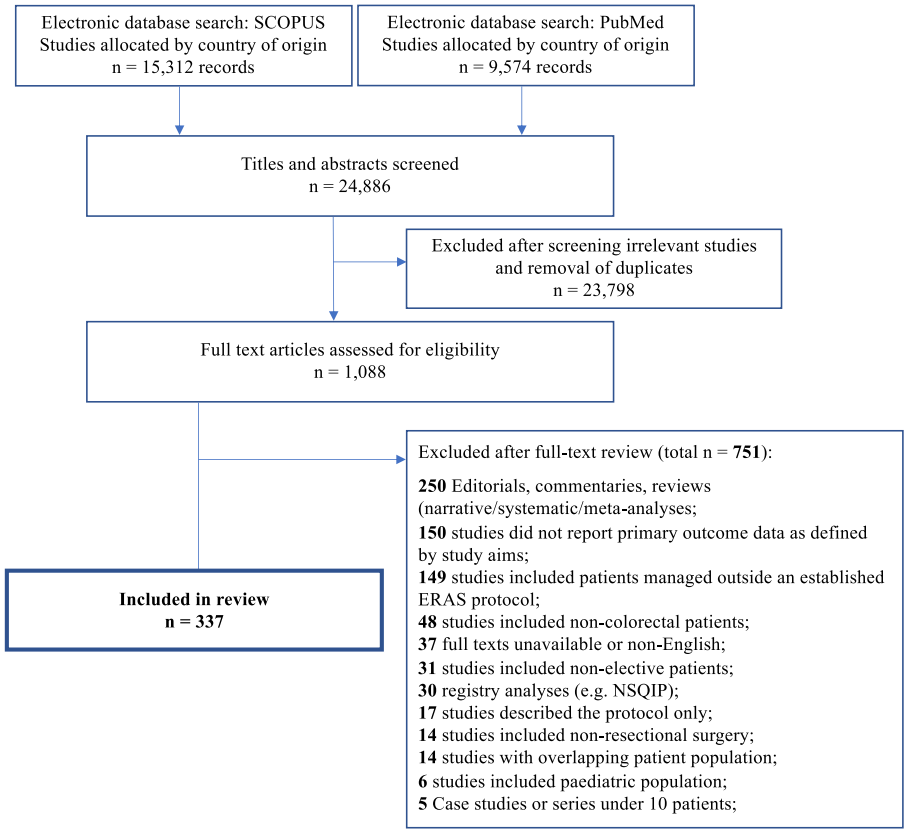


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) diagram showing inculsion and exclusion of articles. ERAS, enhanced recovery after surgery.

CI: 0·53–0·60) postoperative glycaemic control (OR 0·43, 95% CI: 0·38–0·49 and early trial without catheter (OR 0·79, 95% CI: 0·74–0·84) were more commonly reported in LMICs. Measures to prevent postoperative ileus (OR 1·02, 95% CI: 0·96–1·09) and early mobilisation (OR 1·03, 95% CI: 0·94–1·13) were the only elements that did not differ significantly in uptake between HICs and LMICs.

The reporting on patient compliance to an established ERAS protocol and their elements varied considerably in the literature, in terms of the method of reporting (overall compliance, adherence to different elements grouped into preoperative, intraoperative, and postoperative and compliance with individual elements), as well as the parameters by which each study defined the conditions by which compliance was deemed to have been met. Compliance in general was reported in 109 studies from HICs, and 10 studies from LMICs. No significant differences in reported compliance between HICs and LMICs were detected among individual ERAS elements, allowing for the low number of studies that reported compliance in LMICs.

Global outcomes

The LOS was reported in 54 RCTs (37 from HICs and 17 from LMICs). The pooled mean reported LOS was 6·23 days (5·86–6·64), but with significant heterogeneity observed in the included studies ($Q = 5107{\cdot}04$, df = 89, $P < 0{\cdot}001$, $I^2 = 98{\cdot}3\%$). The LOS was significantly shorter in HICs compared to LMICs–5·85 days (5·40–6·29) versus 7·17 days (6·53–7·81) respectively ($Q = 11{\cdot}19$, df = 1, $P < 0{\cdot}001$) (Fig. 3). When analysed by region, LOS was significantly shorter in North America (3·66 days, 3·42–3·90) and longer in Asia (7·34 days, 6·72–7·97) ($Q = 277{\cdot}86$, df = 4, $P < 0{\cdot}001$). A map of the world depicting average LOS within each country is shown in Figure 4.

Complication rates were published in 20 RCTs (13 studies from HICs and 7 from LMICs). The overall reported complication rate was 28·4% (95% CI: 24·3–33·1), with significant heterogeneity ($Q = 440.55$, df = 49, $P < 0{\cdot}001$). The reported complication rate was higher in HICs (35.0%, 95% CI: 30.1–40.6) compared to LMICs (14.4%, 95% CI: 9.46–22.0). Patients undergoing surgery within an ERAS pathway were less likely to experience complications compared to patients on conventional care pathways (OR 0·73, 95% CI: 0·54–0·99, $P = 0.042$), but the effect of ERAS on complication rate did not differ between HICs (OR 0·85, 95% CI: 0·61–1·19) and LMICs (OR 0·65, 95% CI: 0·41–1·04) ($P = 0{\cdot}279$).

The 30-day readmission rate was reported in 27 RCTs (21 from HICs and 7 from LMICs). The pooled rate was 10·1% (95% CI: 8·30–12·37%), with high heterogeneity ($Q = 59{\cdot}13$, df = 26, $P < 0{\cdot}0002$). Readmission rates in HICs were nonsignificantly higher (OR 0·11, 95% CI: 0·09–0·13) compared to LMICs (0·06, 95% CI: 0·04–0·11) ($P = 0{\cdot}085$). ERAS implementation had no overall worldwide effect on 30-day readmissions when compared to controls (OR 1·07, 95% CI: 0·86–1·35), with low heterogeneity ($Q = 2{\cdot}05$, df = 6, $P = 0{\cdot}9147$). There were no discernible differences between HICs and LMICs ($P = 0{\cdot}175$) or regions ($P = 0{\cdot}896$).

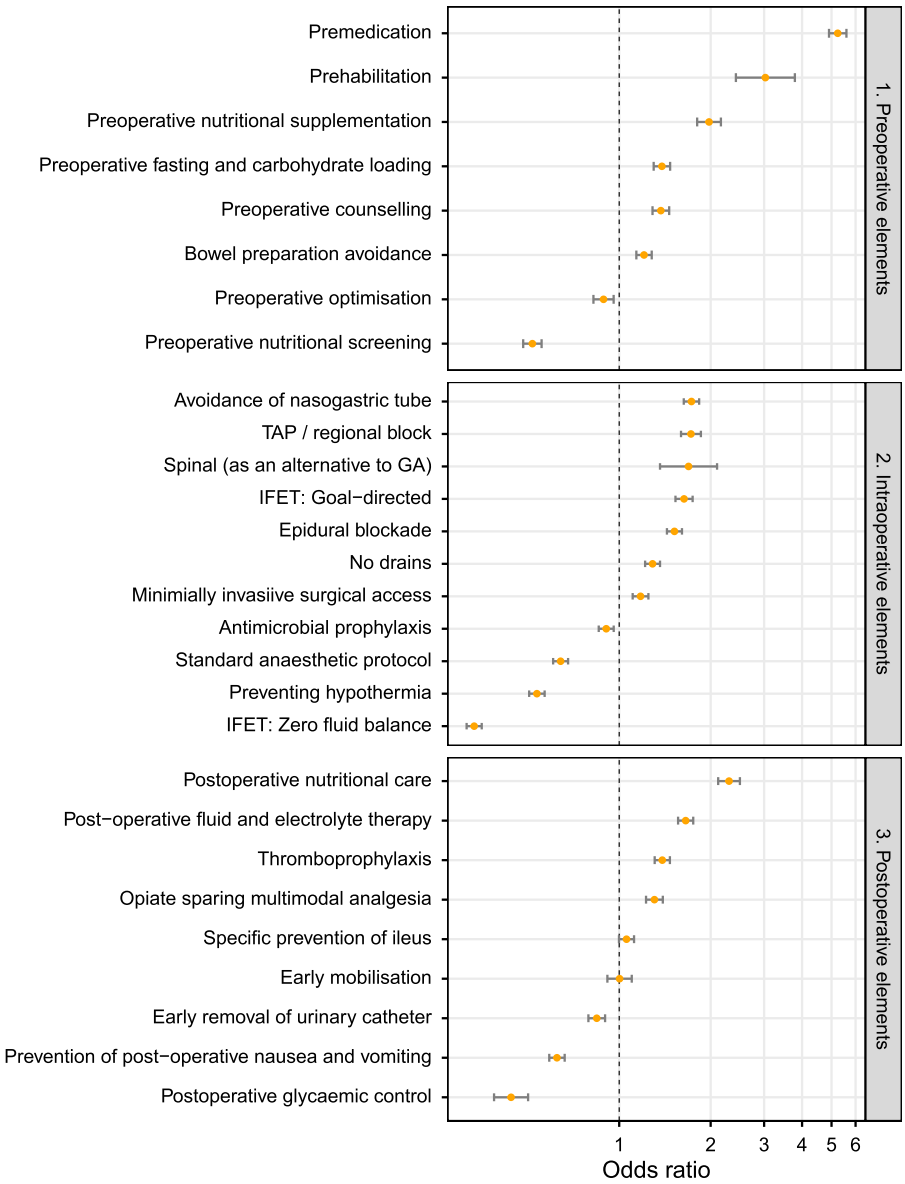


Figure 2. Weighted median number of elements in enhanced recovery after surgery programmes in high-income versus low-middle income countries.

The overall 30-day mortality rate was reported in 42 RCTs (30 from HICs and 12 from LMICs), and the pooled reported rate was 1·8% (95% CI: 1·42–2·28%). There was low study heterogeneity ($Q = 27·33$, df = 41, $P = 0·9499$). Mortality rates in HICs (OR 0·02, 95% CI: 0·015–0·024) and LMICs (OR 0·013, 95% CI: 0·007–0·025) were similar ($P = 0·308$). ERAS implementation had no effect on 30-day mortality when compared to controls (OR 1·41, 95% CI: 0·50–3·97, $P = 0·460$), and there was no difference between HICs and LMICs ($P = 0·631$) or regions ($P = 0·555$).

Discussion

In this study, we aimed to examine the global equality of perioperative care, uptake and impact of ERAS in a pooled analysis of over 110 000 elective colorectal patients undergoing in surgery across 36 countries.

Though the weighted median number of elements implemented in studies was broadly similar between HICs and LMICs and between regions of the world, there were numerous differences with regard to the uptake of individual elements within an established ERAS pathway. Indeed, the only components that featured equally in HICs and LMICs were early mobilisation and prevention of postoperative ileus. Both of these interventions are relatively inexpensive to implement[16,17]. In comparison, many of the elements that were more prevalent in cohorts from HICs, such as prehabilitiation, use of transverse abdominis plane blocks or spinal anaesthesia and use of minimally invasive techniques for surgical access often come with a greater cost and burden on hospital resources[18–20]. The prevalence of mechanical bowel preparation use was greater in LMICs. The role of mechanical bowel preparation in elective colorectal surgery is controversial, and previous guidelines[11] based on evidence from meta-analyses of RCTs[21] stipulate that there is no evidence of increased risk of

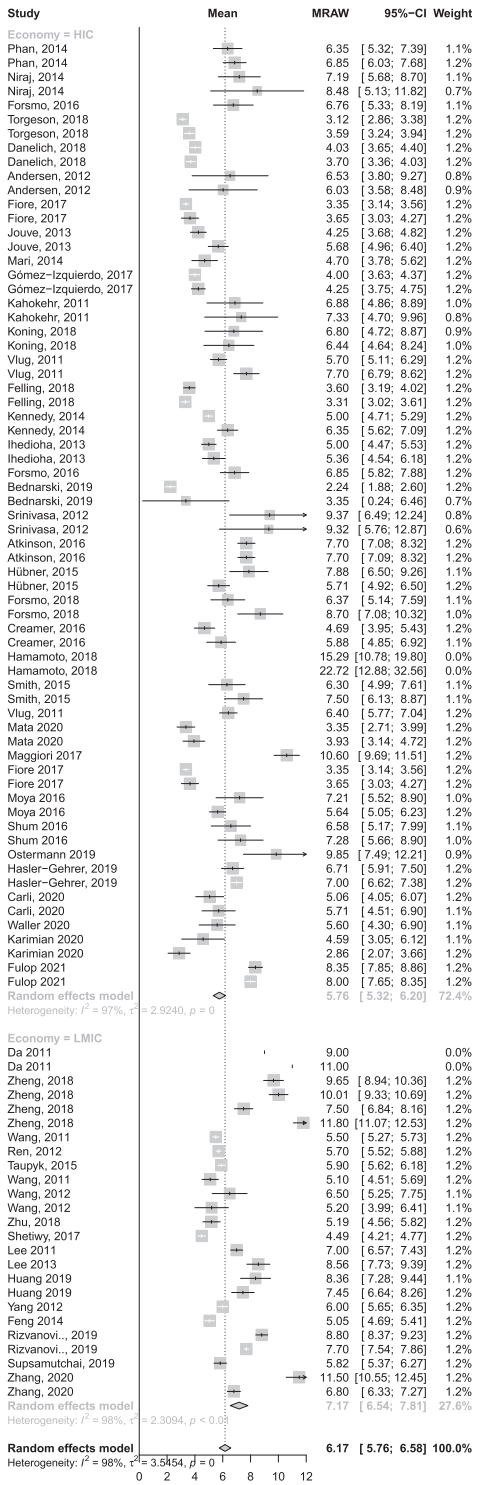


Figure 3. Forest plot comparing length of stay between high-income and low-middle income countries.

anastomotic leakage, and that its use may cause preoperative dehydration and electrolyte abnormalities. Its continued use in LMICs may reflect a delay in uptake of newer guidelines; however, a number of worldwide RCTs are in progress[22] to determine definitively whether bowel preparation with or without oral antibiotics and it is likely that guidance may change again.

Furthermore, differences were detected not just with the presence, or absence of, components within ERAS pathways, but the means by which they were implemented. Two notable elements discussed in this study were the use of GDFT, as opposed to a zero fluid balance approach, as a means to guide intraoperative fluid administration, and the modes of analgesia employed within the multimodal opioid-sparing analgesia element.

The evidence comparing intraoperative fluid management between LMICs and HICs is limited. In our study, we identified that a significantly higher proportion of patients undergo GDFT in HICs compared to LMICs. Judicious fluid management has been shown to be beneficial in the prevention of postoperative complications[23]. Successful implementation of GDFT requires a degree of real-time haemodynamic monitoring[24], which in turn requires equipment and expertise that may be lacking in LMICs. However, the role of GDFT as a routine method of intraoperative fluid monitoring is controversial, and the recent change in guidance favouring a zero fluid balance approach implies that the greater provision of technology, with the associated resource requirement, is not a compulsory prerequesite for the adoption of best practice in LMICs[25].

Multimodal nonopioid analgesia was another element that was shown to have discrepancy in implementation between HICs and LMICs. Whilst patients in HICs and LMICs were equally likely to receive NSAIDs, other medications such as dipyrone and lidocaine were more likely to form part of a multimodal analgesic regimen in HICs. Furthermore, gabapentinoids, NMDA antagonists and steroids were only described as being in use in papers from HICs. The wider array of nonopioid adjuncts, as well as the higher number of analgesic elements included on average, may contribute towards a faster recovery and shorter LOS amongst patients in HICs.

The pooled mean LOS was significantly shorter in studies from HICs. In addition, the LOS was significantly shorter in North America and significantly longer in Asia. Some of the aforementioned disparities in ERAS element implementation may account for this, such as reduced preoperative optimisation or prehabilitation, but it is also likely that there are factors outside of ERAS which may account for the disparities in LOS. Data from the Organisation for Economic Co-operation and Development (OECD) shows that on average, over the last decade, health expenditure per capita was ~28 times higher in the USA ($9255) than in China ($335)[26], but healthcare spend, as a surrogate measure of resource provision, is unlikely to be the sole contributing factor. Issues relating to differing health infrastructure, such as public and private healthcare systems can also be in play. Hospital LOS may be prolonged as a result of factors at an institutional or governmental level[27], which cannot be assessed at the level of a literature review; conversely, patients in HICs staying in private hospitals without health insurance may experience a shorter LOS if aspects of treatment are not covered[28]. Similarly, the 30-day readmission rate was non-significantly higher in HICs. This may be as a result of a degree of reporting bias amongst published studies. Furthermore, there may be barriers to representation to healthcare services that are not accounted for within the scope of the included studies. This difference may also be an indirect consequence of a shorter LOS, which has been identified as a risk factor for postoperative readmission[29].

Interestingly, this evidence synthesis showed no difference in overall mortality between HICs and LMICs. This is likely to be

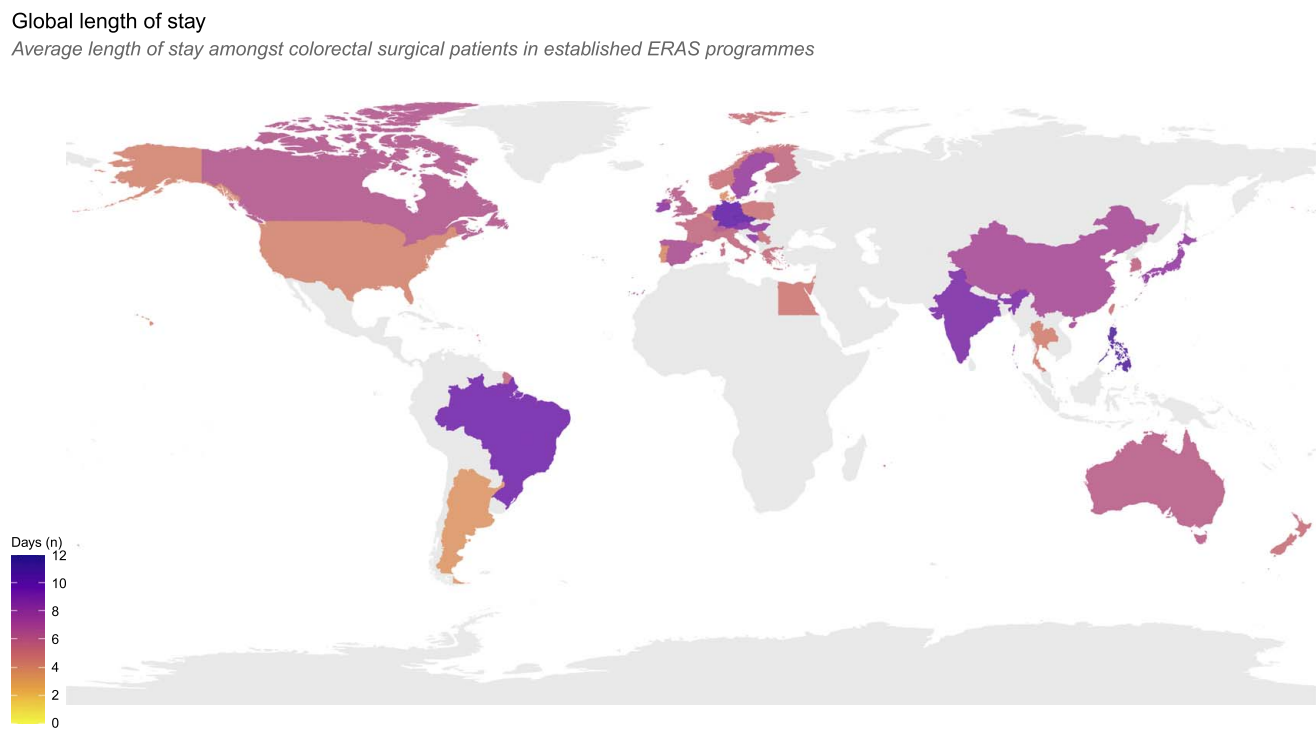


Figure 4. Map of the world depicting average length of stay amongst patients enroled in an enhanced recovery after surgery programme.

due to the selection bias of reporting, as countries or units with very low resources are unlikely to have the opportunity to publish their outcomes. Further population-based studies are warranted to provide more representative data.

To our knowledge, this is the first study to detail the uptake and implementation of ERAS pathways and elements with a focus on a global setting. However, there are some limitations with the generalisability of our results. Firstly, there was a significant over-representation of studies from HICs and a reciprocal under-representation from LMICs. This reflects the current literature gap from LMICs, and further efforts are required to support perioperative research in these countries. Secondly, in pooling the outcome data there was significant heterogeneity, which affects the reliability of the results. Thirdly, we excluded large national-based registry studies, as this may have increased the risk of including patients that would have otherwise been included in institutional papers. We also excluded studies that incorporated populations from multiple countries as it would have made analysis between countries difficult. Exclusion of both of these would inevitably reduce study generalisability; however, this was exclusively an issue amongst HICs, and it was felt there was a sufficient patient population to draw meaningful conclusions from.

The ERAS care pathway provides an ideal platform to standardise perioperative care as exemplified by its implementation across several countries throughout the world. Implementation of evidence-based guidelines, development of well-functioning perioperative teams, and audit and measurement of patient outcomes and compliance are key facets that ultimately reduce complications, LOS and associated healthcare costs. Efforts have begun to support the implementation of ERAS care pathways in LMICs, with recently published guidelines[30] outlining a bespoke ERAS programme designed for the generalist rather than the subspecialist and have taken into consideration contextual healthcare needs but have not, as of yet, taken costs into consideration.

These findings highlight the significant difference in uptake of the ERAS programme in LMICs when compared to HICs. The overall improvement in key outcome measures is seen across LMICs and HICs when conventional care is compared to ERAS benchmarks. There was no difference in complications and mortality rates, readmissions were nonsignificantly lower, and LOS significantly longer in LMICs. Understanding the barriers to implementation of ERAS in LMICs, and developing sustainable solutions is an important next step; the pooling of resources and skills between high-middle income countries and low-middle income countries needs to be prioritised. Global collaboration is required to provide resources for low-middle income countries as implementation of affordable elements in ERAS contributes towards better outcomes.

Ethical approval

Systematic review and meta-analysis only – ethical approval not required.

Consent

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Author contribution

N.S., W.H.T., N.K.F: designed the study; N.S., W.H.T., H.C.S., M.A., R.S., S.H., and M.C.: collected the data; N.S., E.S., and W.H.T: performed the risk of bias assessments; N.S.: analysed the data and generated the figures; W.H.T.: did the literature search; N.S. and N.K.F: interpreted the data and draughted the manuscript; E.S., R.O., and N.K.F.: critically revised the manuscript. All authors had full access to all the data in the study. N.S.: had final responsibility for the decision to submit to publication.

Conflicts of interest disclosure

The authors declare that they have no conflicts of interest.

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Data availability statement

All data pertaining to this research article is available as summarised in the supplementary data pack, or otherwise found in the original published articles included in the review.

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None.

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