

**Health Policy Advisory Committee on
Technology**

Technology Brief

**Enhanced recovery after surgery programs for hip and knee
arthroplasty**

August 2016



**Australian
Safety
and Efficacy
Register
of New
Interventional
Procedures –
Surgical**



**Royal Australasian
College of Surgeons**

HealthPACT
emerging health technology

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This Brief was commissioned by Queensland Health, in its role as the Secretariat of the Health Policy Advisory Committee on Technology (HealthPACT). The production of this Brief was overseen by HealthPACT. HealthPACT comprises representatives from health departments in all States and Territories, the Australian and New Zealand governments and MSAC. It is a sub-committee of the Australian Health Ministers' Advisory Council (AHMAC), reporting to AHMAC's Hospitals Principal Committee (HPC). AHMAC supports HealthPACT through funding.

This brief was prepared by Dr Joanna Duncan from the Australian Safety and Efficacy Register of New Interventional Procedures - Surgical (ASERNIP-S).

Summary of findings

The aim of enhanced recovery after surgery (ERAS) programs is to standardise and optimise pre-, peri- and post-operative care to reduce length of hospital stay (LOS) without sacrificing patient outcomes. No universal orthopaedic ERAS program was identified and there was some variation between published programs. All identified programs; however, provided patient education, standardised analgesia and anaesthesia regimes, and encouraged early patient mobilisation.

Patient outcomes from one systematic review, two randomised controlled trials (RCT) and five non-randomised comparative studies on the use of ERAS programs for hip and/or knee arthroplasty are presented in this Technology Brief. Each of the primary studies compared the ERAS program to existing care procedures. Use of an ERAS program was associated with an average^a reduction in LOS ranging from one to four days. This reduction was reported in all studies, with the exception of one comparative study where a reduction in LOS was observed for patients undergoing knee arthroplasty but not for hip arthroplasty. Quality of life outcomes were reported by one RCT: patients in the ERAS group reported equivalent or higher quality of life measures than those receiving standard care at three- and 12-months post-surgery.

In general, complications arising from surgery were infrequent and equivalent in ERAS and standard care groups. One comparative study observed a significantly higher risk of hip dislocation associated with ERAS and another comparative study observed significantly higher rates of infection associated with ERAS. Mortality rates were equivalent in three comparative studies and no differences in readmission rates were reported by four comparative studies.

There may be cost benefits associated with implementation of ERAS programs, with a single comparative study from New Zealand reporting cost savings per procedure for both hip and knee arthroplasties following ERAS program roll-out.

The variability between ERAS programs needs to be taken into account when considering the results of this Brief. To date, no single program appears to be preferred or has emerged as a 'clinical standard', and no studies comparing different ERAS programs were identified. Determination of the optimum combination of interventions to be included in an ERAS plan, particularly in the Australian setting, would be beneficial and would allow care to be standardised for all patients.

^a Mean or median depending on primary study outcomes

HealthPACT Advice

Within the healthcare system there is a great deal of variation in care and a lack of standardisation of treatment. Enhanced recovery after surgery programs aim to identify pre- and post-surgical factors that may improve the patient's journey through the system, and as a result improve both patients and health system outcomes. From the evidence presented in this Brief, ERAS programs demonstrate positive outcomes in reduced length of stay and may have a major impact on the rehabilitation of selected patients. Although HealthPACT supports the concept of enhanced recovery programs, the introduction of programs such as the ERAS into publically funded clinical practice cannot be supported at this time due to a lack of standardisation.

No further review of the evidence on behalf of HealthPACT is warranted at this time.

Technology, Company and Licensing

Register ID	WP237
Technology name	Enhanced recovery after surgery (ERAS) programs for hip and knee arthroplasty
Patient indication	Patients undergoing hip or knee arthroplasty

Description of the technology

Enhanced recovery after surgery (ERAS) programs are care packages of evidence-based interventions used in multidisciplinary care pathways to improve functional outcomes and promote rapid recovery following surgery.

The first formal peri-operative care program of this nature, called the ERAS Care System, was developed by the ERAS Society to introduce standardised evidence-based care to patients undergoing gastrointestinal surgery.¹

The ERAS Care System is comprised of three parts:

1. ERAS Protocol
2. ERAS Implementation Program
3. ERAS Interactive Audit System

The ERAS Protocol is an evidence-based care protocol developed by the ERAS Society and comprises 20 components (Figure 1) that cover patient care throughout the entire peri-operative process. The protocol was designed to minimise care time while reducing post-operative complications.²

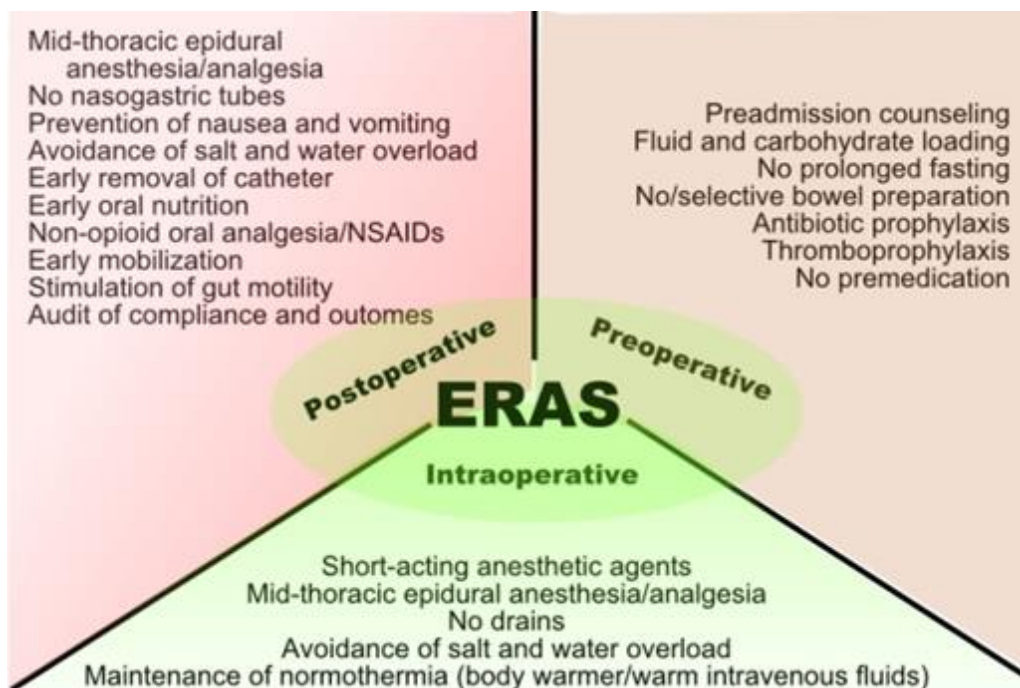


Figure 1 The ERAS Protocol of the ERAS Society for gastrointestinal surgery²

The ERAS Implementation Program is a training and change management program developed for the multidisciplinary peri-operative team to facilitate the implementation of the ERAS Protocol and maintain high levels of compliance.³

The ERAS Interactive Audit System is a software program designed to ensure compliance to the protocol and allow continuous follow-up of patients.⁴ Since its inception the ERAS Care System has been tested and implemented in approximately 40 hospitals throughout Europe.¹

There is no corresponding formalised ERAS program for patients undergoing hip or knee arthroplasty; however, the concept of introducing peri-operative care protocols to minimise hospital stay duration has been adopted at many centres worldwide.⁵

There is no consensus definition for an ERAS program for hip and knee arthroplasty. As part of this Health Technology Brief we conducted an analysis of the components that make up ERAS programs for hip and knee arthroplasty in different centres.

Seven RCTs and 12 comparative studies (Table 15, Appendix 1) were identified that provided a detailed description of the components of the ERAS program used. The results of this analysis illustrates there is no universal 'ERAS' for hip and knee arthroplasty; however, there are common elements to each of the identified programs.

All identified programs included patient education discharge planning, early mobilisation and standardisation of pre- and post- operative analgesia, although variability between programs in the type of analgesia prescribed was noted. Avoidance of epidural anaesthesia was another commonly reported component (79% of programs). All ERAS programs focused on the multidisciplinary management of patients.

Other reported interventions included prophylactic use of antibiotics (32%), anti-emetics (47%), anti-thrombolytic measures (37%), anticonvulsants (21%) and tranexamic acid for bleeding control (32%). Nutrition interventions included preoperative carbohydrate loading (21%), minimisation of fasting (26%) and early resumption of nutrition (37%). Pre-operative screening by a physiotherapist was reported in 32 per cent of programs and screening by a dietician was reported in 26 per cent of studies.

Avoidance of surgical drains (37%), catheters (16%) and sedatives (14%) were also components of some programs.

For the purpose of this Technology Brief ERAS refers to any enhanced recovery program, rather than the program specifically developed by the ERAS Society.

Company or developer

Not applicable.

Reason for assessment

This assessment investigates the impact of ERAS programs on LOS and adverse events for hip arthroplasty and knee arthroplasty procedures. LOS is recognised as a major factor associated with the cost of hip and knee arthroplasty procedures. It was previously thought that any decrease in LOS following arthroplasty would correspond to an increase in postoperative complications.⁶ However, recent evidence suggests that implementation of optimised ERAS programs can reduce LOS without compromising outcomes for patients.⁷

Stage of development in Australia

- | | |
|---|---|
| <input type="checkbox"/> Yet to emerge | <input type="checkbox"/> Established |
| <input type="checkbox"/> Experimental | <input type="checkbox"/> Established <i>but</i> changed indication or modification of technique |
| <input checked="" type="checkbox"/> Investigational | <input type="checkbox"/> Should be taken out of use |
| <input type="checkbox"/> Nearly established | |

Licensing, reimbursement and other approval

No licensing, reimbursement or approval information is relevant to this assessment.

Australian Therapeutic Goods Administration approval

- | | |
|--|-----------------|
| <input type="checkbox"/> Yes | ARTG number (s) |
| <input type="checkbox"/> No | |
| <input checked="" type="checkbox"/> Not applicable | |

Technology type

Program

Technology use

Combination of therapeutic and preventative measures

Patient Indication and Setting

Disease description and associated mortality and morbidity

There are many reasons that patients require hip or knee replacement. The main reason for knee arthroplasty in Australia between September 1999 and December 2014 was osteoarthritis (99% of replacements) osteonecrosis (0.6%) and rheumatoid arthritis (0.3%). Other diagnoses, including fractures and tumours, accounted for less than one per cent.⁸ The primary reason for hip replacement was fracture of the femur neck (95%) followed by osteoarthritis (3%), tumour (1%), failed internal fixation (0.6%), osteonecrosis (0.3%), developmental dysplasia (0.1%) and rheumatoid arthritis (0.1%). Other diagnoses accounted for 0.1 per cent of replacements.⁹

In New Zealand the primary diagnosis leading to hip replacement between January 1999 and December 2014 was osteoarthritis (87%) followed by fracture (4%), avascular necrosis

(3%), developmental dysplasia (2%) and rheumatoid arthritis (1%). Other diagnoses accounted for three per cent of hip replacements.¹⁰ For knee arthroplasty during the same time period the primary diagnoses were osteoarthritis (95%), rheumatoid arthritis (2%) and fracture (1%). Other diagnoses accounted for two per cent of replacements.¹⁰

In Australia hip and knee replacement procedures are both associated with a median LOS of 4 days (range 2-33 days).¹¹ One analysis of 827 total hip or knee arthroplasties performed at a single centre in Victoria, Australia found complications associated with the surgery included: wound complications (9%), surgical site infection (5%), venous thromboembolism (5%), delirium (5%), cardiac complications (2%), respiratory complications (2%), acute kidney injury (2%), pressure ulcers (1%), other infection (1%), gastrointestinal bleed (0.4%), acute urinary retention (0.4%) and bowel obstruction (0.2%).¹¹ Four per cent of patients in this study required readmission to hospital in the first 30-days post-surgery, primarily due to surgical site infection (74%).¹¹ No equivalent New Zealand data was identified.

Number of patients

In the 2013/14 financial year 37,403 hip arthroplasty procedures and 4,185 revision arthroplasty procedures were performed in Australia in public and private hospitals. During the same period 46,756 primary knee arthroplasties and 5,276 revision procedures were performed.¹² Most joint replacement procedures in Australia are performed in the private system (59.7% for hips and 70.3% for knees in 2014)¹³ Demand for joint replacement surgeries in Australia is growing; it is predicted that the number of procedures performed in 2020 will be double relative to 2013.¹¹

In New Zealand 8,344 primary hip arthroplasties and 7,392 primary knee arthroplasties were performed in 2014.¹⁰

Speciality	Orthopaedics, rheumatology and podiatry
Technology setting	General hospital

Impact

Additive and substitution

ERAS programs will likely include some overlap with interventions currently being used in peri-operative care. Some components of an ERAS program will substitute existing procedures, for example substitution of epidural for other forms of spinal anaesthesia. Other components may be additional to existing practices (e.g. patient education programs). These will depend on local practices and composition of an implemented ERAS program.

Current technology

The model of care for peri-operative management of hip and knee arthroplasty patients is not standardised. Consequently, is difficult to summarise current practices in Australia as

they vary between institution and even between patients at the same institution. One study has compared existing practice to ERAS management of patients undergoing joint replacement in Australia and found existing care programs were less likely to include pre-operative assessment by a physiotherapist, occupational therapist and/or dietician.¹⁴ Patients were also less likely to be given clear fluids and oral carbohydrate drinks on the day of surgery and were less often prepared with pre-operative skin wipes. Urinary catheters, surgical drains and epidurals (vs spinal) anaesthesia were more likely used in existing practices, whereas these were discouraged in ERAS program. Thrombosis, nausea and vomiting prophylaxis may not be provided to all patients in existing practice.

International utilisation

Confirmation of the international utilisation of ERAS programs for hip and knee arthroplasty procedures was not possible due to the lack of a standardised program. A number of publications were that describe the use of ERAS in a wide range of countries, and are summarised below. If a publication described the implementation of the program country wide then this has been categorised as widely diffused. If the publication described the introduction of the program to a single region or centre then this has been categorised as limited use. It should be noted that this summary does not attempt to provide a comprehensive list of countries where ERAS programs may have been implemented.

Country	Level of Use		
	Trials underway or completed	Limited use	Widely diffused
Brazil		✓	
Canada		✓	
China		✓	
Denmark			✓
Germany		✓	
New Zealand		✓	
United Kingdom		✓	
United States of America		✓	

Diffusion of technology in Australia

The number of Australian centres using ERAS programs to guide management of hip and knee arthroplasty patients could not be identified. One publication reported the introduction of an ERAS program in three Australian hospitals in Victoria.¹⁴ A report by the NSW Agency for Clinical Innovation highlighted substantial variation in care between patients in NSW and has produced a guideline for peri-operative management of primary hip and knee replacement procedures.¹⁵

Cost infrastructure and economic consequences

Length of hospital stay is a major contributor to the cost of hip and knee arthroplasty procedures. Costs associated with the operation itself are incurred on the day of surgery and are therefore fixed. However, other costs, for example, nursing, supplies, physical therapy and nutrition may be proportional to LOS. It has therefore been hypothesised that reductions in LOS will lead to reductions in the total cost of procedures.¹⁶ Readmission to hospital is also a major contributor to overall costs associated with a service.¹⁶

In Australia hip and knee arthroplasties represent a high volume, high cost class of procedures, and both demand for the surgery and associated costs are increasing.¹¹ The mean total cost for a total hip arthroplasty in Victoria has been estimated at \$22,817 (standard deviation [SD] 12,019), of which \$21,718 (SD 11,957) are inpatient costs. Similarly total knee arthroplasty is estimated to cost \$21,357 (SD 8,902) of which \$21,006 (SD 8,695) are inpatient costs.¹¹

Due to the variability between ERAS programs and existing practices there are no 'set-costs' associated with implementation a program. Some additional costs may be incurred, depending on existing practice, for example if patient education programs need to be set up or if additional medications are required, i.e. for prophylaxis not currently being administered. There may also be cost substitutions, for example converting from epidural to other spinal anaesthesia.

Ethical, cultural, access or religious considerations

No ethical, cultural, access or religious considerations were identified that may limit the use of an ERAS program.

Evidence and Policy

Safety and effectiveness

One systematic review, two RCTs and two comparative studies were identified for inclusion in this Technology Brief. Selection criteria for inclusion were any RCTs with >100 patients and any non-randomised comparative study with > 1,000 patients in the intervention arm that were not included in the systematic review (Stowers et al (2014)). One of each study was identified that discussed the implementation of an ERAS program in Australia and New Zealand, which are included. An overview of the studies is provided in Table 1.

Table 1 Included study characteristics

Study ID Design*	Inclusion criteria	Exclusion criteria	Number of patients Follow-up Lost to follow-up
Stowers et al (2014) ⁵ Systematic review of Level II and III evidence	Peri-operative care interventions comparing enhanced recovery with standard care in the setting of elective THA or TKA.	Unicompartmental procedures, bilateral or simultaneous joint arthroplasty, revision surgery, acute arthroplasty or minimally invasive surgery.	NR (22 studies) NR NR
Gooch et al (2012) ^{17, 18} Level II (RCT) Multicentre (3 centres in Canada)	Patients currently on the waiting list for THA or TKA or waiting for consultation or new referrals to orthopaedic surgeons practicing at the participating centres.	Patients with THA or TKA booked within three months of recruitment, patients not resident in Alberta, patients not referred for degenerative hip or knee disease, patients requiring hip resurfacing, partial knee replacement or revision surgery, patients <18 years of age.	3,434 ERAS: 1,722 Std Care: 1,712 Follow-up = 12 months Lost to follow-up: N = 277
Yang et al (2016) ¹⁹ Level II (RCT) Single centre (China)	Patients aged ≤ 85 years undergoing primary THA. ASA status I-III, no pulmonary or cardiac function limitation, normal haematocrit, no history of pulmonary embolism or DVT within 6 months, normal strength of upper limbs, normal cognitive function adequate home support (responsible adult).	Revision procedure, simultaneous bilateral THA, dysfunction of the ipsilateral knee or ankle delaying weight bearing, hip flexion contracture >30° or leg length discrepancy >2 cm, pathological fracture or primary procedure due to bone tumour.	258 ERAS: 126 Std Care: 127 Follow-up = 90 days Lost to follow-up: N = 8
Glassou et al (2014) ²⁰ Level III-3 (Retrospective comparative study) Multicentre (I: 6 centres, C: All other centres in Denmark)	All patients who had undergone THA or TKA for osteoarthritis and registered in the Danish Hip Arthroplasty Registry or Danish Knee Arthroplasty Registry between January 2005 and September 2011.	Patients with no primary diagnosis and patients who emigrated during the follow-up period.	79,098 ERAS: 17,284 Std Care: 61,814 Follow-up = 90 days Lost to follow-up: N = NR
Khan et al (2014) ²¹ Level III-3 Multicentre (2 Centres in the United Kingdom)	Consecutive patients undergoing THA or TKA between April 2004 and July 2011 at two sites in the Northumbria NHS Foundation Trust.	None reported	6,000 ERAS: 3,000 Standard Care: 3,000 Follow-up = 90 days Lost to follow-up: N = NR
Christelis et al (2015) ¹⁴ Level III-3 Multicentre (3 centres in Australia)	All patients undergoing THA or TKA at one of three public hospitals in Victoria, Australia between March and September 2012 (standard care group) and October 2012 to May 2013 (ERAS group).	None reported	709 ERAS: 297 Standard Care: 412 Follow-up = 6 weeks Lost to follow-up: N = 66
Stowers et al (2016) ²³ Level III-3 Single Centre (New Zealand)	Patients undergoing elective primary THA or TKA surgery.	Patients undergoing bilateral joint surgery, revision surgery, unicompartmental knee replacement and patients with an inability to follow verbal or written instructions.	200 ERAS: 100 Standard Care: 100 Follow-up = 30 days Lost to follow-up: N = 0

ASA: American Society of Anesthesiologists; DVT; deep vein thrombosis; ERAS: enhanced recovery after surgery; RCT: randomised controlled trial; THA: total hip arthroplasty; TKA: total knee arthroplasty.

Stowers et al (2014)⁵

The systematic review by Stowers et al (2014) reported the key components of ERAS programs for patients undergoing total hip arthroplasty (THA) or total knee arthroplasty (TKA) and assessed the impact ERAS programs on hospital length of stay post-surgery. MEDLINE, PubMed, PsychINFO and Cochrane Central Register of Controlled Trials were searched in January 2013 for studies relating to the use of enhanced recovery measures following THA or TKA. No information on the process for study inclusion/exclusion, criteria used or data extraction methodology was reported. The review included 22 studies for the program analysis, the study types were not reported. No quality appraisal of included studies was undertaken and no description of patient characteristics was provided.

Safety

No safety outcomes were reported in this review.

Effectiveness

Results of the mean LOS for patients undergoing an ERAS or control program were presented for nine studies, all of which reported a reduction in LOS associated with use of an ERAS program (Table 2). No statistical analysis of the results was provided.

Table 2 Summary of outcomes reported in Stowers et al (2014)⁵

Study ID	Type of surgery	ERAS Mean LOS (days)	Standard care Mean LOS (days)
Isaac et al (2005)	TKA	3.6	6.6
Larsen et al (2008a and b)	THA and TKA	4.4	8.8
Malviya et al (2011)	THA and TKA	4.8	8.5
Raphael et al (2011)	THA and TKA	2.0	4.8
Wellman et al (2011)	THA	1.7	3.5
Den Hertog et al (2012)	TKA	6.8	13.2
McDonald et al (2012)	TKA	4.0*	6.0*
Scott et al (2013)	THA and TKA	4.0*	5.0*

* Indicates median value reported; LOS: length of stay; THA: total hip arthroplasty; TKA: total knee arthroplasty.

In their review, Stowers et al (2014) narratively discussed each identified component of peri-operative care in the 22 included studies and used these results to develop an evidence-based ERAS program for patients undergoing TKA and THA (Table 3).

Table 3 Proposed ERAS protocol developed by Stowers et al (2014)⁵

Proposed ERAS protocol for THA and TKA
<p>Preoperative care</p> <p>Education, expectation management</p> <p>Discharge planning by occupational therapist, social worker</p> <p>Nutrition screening using the Malnutrition Universal Screening Tool; referral to dietician if at moderate or high risk</p> <p>Premedication: cyclooxygenase-2 selective inhibitors, gabapentin, dexamethasone</p> <p>Intraoperative care</p> <p>Spinal anaesthesia + regional (femoral/saphenous) nerve block or high-volume local anaesthetic</p> <p>Liberal peri-operative intravenous fluids</p> <p>Intravenous prophylactic antibiotics for 24 hours</p> <p>Tranexamic acid</p> <p>Avoidance of surgical drains</p> <p>Postoperative care</p> <p>Early ambulation</p> <p>Early intensive physiotherapy</p> <p>Aspirin, thromboembolic deterrent stockings, and intermittent pneumatic compression devices for venous thromboembolic prophylaxis (for those at low risk)</p> <p>Multimodal, opioid-sparing analgesia regimen</p>

ERAS: enhanced recovery after surgery; THA: total hip arthroplasty; TKA: total knee arthroplasty.

The authors noted the considerable variation in ERAS programs in the identified literature and that the contribution of individual components towards the accelerated discharge time was unclear.

Gooch et al (2012)¹⁷

Gooch et al (2012) reported the results of an RCT on the use of an ERAS program for patients with degenerative joint disorders undergoing THA or TKA. The protocol for the trial is reported in Gooch et al (2009).¹⁸ Components of the ERAS program are described in Table 15 (Appendix 1). Key differences between the ERAS program and standard care regimens were the introduction of patient education, standardisation of medication and treatment protocols and early patient mobilisation with ERAS. Of the 3,434 patients who were randomly assigned, 1,570 underwent surgery during the study timeframe; 504 patients with a standard care protocol (44.8% THA) and 1,066 with an ERAS protocol (42.4% THA). Baseline demographics for the intervention and control groups are presented in Table 4. There were no statistical differences between the two groups at baseline. The primary outcome measures were Western Ontario and McMaster Universities Arthritis Index (WOMAC) score and Short Form (36) Health Survey (SF-36) scores measured at three months and 12 months post-surgery.

Table 4 Baseline characteristics of patients in Gooch et al (2012)¹⁷

Characteristic	ERAS N = 1,066	Standard Care N = 504	p value
Mean age (SD)	69 (10.4)	69.0 (11.1)	0.99
% Male	40	40	0.87
Mean BMI, kg/m ² (SD)	29.4 (5.4)	29.5 (5.6)	0.68
% ASA score ≥ 3	24	22	0.26
Mean WOMAC overall (SD)	44.8 (17.0)	43.3 (16.3)	0.10
Mean SF-36 BP (SD)	28.2 (16.7)	27.4 (16.6)	0.35
Mean SF-36 PF (SD)	27.1 (19.8)	26.1 (20.2)	0.34

ASA: American Society of Anesthesiologists; BMI: body mass index; SD: standard deviation; SF-36 BP: Short Form Health Survey – bodily pain; SF-36 PF: Short Form Health Survey –physical functioning; WOMAC: Western Ontario and McMaster Universities Arthritis Index.

Safety

Adverse events were recorded for the first 30 days post-surgery; no patients were lost to follow-up during this time. A total of 55 adverse events occurred in the ERAS group, a rate of five events per 100 patients. In the standard care group 25 adverse events were observed with a rate of 5 events per 100 patients. Four deaths and eight myocardial infarctions occurred in the ERAS group while none occurred in the standard care group. A detailed safety review concluded that mortality and myocardial infarction rates were within expected ranges compared to provincial administrative data and the Canadian Joint Replacement Registry. More hip dislocations were observed in the ERAS group than in the standard care group or the historical average (1.1%, 0% and 0.7% respectively). These numbers were too low; however, to identify whether the ERAS program significantly increased the risk of dislocation. The authors reported that rates of other adverse events (deep vein thrombosis, fracture, infection, pulmonary embolism, pneumonia, renal failure, stroke, atrial fibrillation and respiratory distress) in both groups were low and consistent with published ranges.

Effectiveness

Effectiveness results are reported in Table 5. There were 177 (17%) and 100 (20%) patients lost to follow-up in the ERAS and standard care groups, respectively, over the duration of the study. Overall WOMAC scores measured at three months and 12 months post-surgery were improved in both the ERAS and control groups compared to baseline. Patients in the ERAS group had significantly higher improvements in WOMAC score compared with those in the standard care group. The treatment effect (adjusted for baseline characteristics) associated with the ERAS program at 12-months post-surgery was 2.5 (95% confidence interval [CI] 1.10 to 4.01, $p = 0.001$). Overall SF-36 physical functioning (PF) and SF-36 bodily pain (BP) scores also improved for both ERAS and standard care groups compared to baseline. There was no significant difference between groups in 12 month SF-36 PF score; ERAS program was associated with an adjusted treatment effect of 1.88 (95% CI -0.34 to

4.06, $p = 0.097$). The ERAS program was associated with significantly higher SF-36 BP scores at 12 months post-surgery, with an adjusted treatment effect of 3.01 (95% CI 0.70 to 5.32, $p = 0.01$). These results indicate that patients being treated under the ERAS program had modest but statistically significant improvements to pain and function in the initial measurement period. Long-term, ERAS patients had small sustained improvements in pain levels compared to patients treated under the traditional care pathway

Table 5 Effectiveness data from Gooch et al (2012)¹⁷

Outcome Mean change from baseline	ERAS (3 months) N = 959	Standard care (3 months) N = 397	ERAS (12 months) N = 919	Standard care (12 months) N = 404
Overall WOMAC score(SD)	36.0 (18.4)	30.9 (18.3)	37.5 (19.2)	34.5 (19.2)
Hip WOMAC score (SD)	41.2 (18.5)	36.2 (18.1)	42.4 (19.2)	39.2 (17.9)
Knee WOMAC score (SD)	32.2 (17.4)	26.4 (17.2)	33.8 (18.3)	30.4 (19.4)
Overall SF-36 PF score(SD)	27.7 (23.7)	23.3 (23.4)	31.2 (25.7)	29.0 (24.7)
Hip SF-36 PF score(SD)	28.5 (25.3)	29.2 (23.6)	33.9 (27.5)	33.6 (24.7)
Knee SF-36 PF score(SD)	27.0 (22.4)	18.4 (22.2)	29.1 (24.1)	25.1 (24.0)
Overall SF-36 BP score(SD)	34.5 (25.0)	28.8 (24.0)	36.8 (26.6)	33.7 (25.0)
Hip SF-36 BP score(SD)	41.5 (25.3)	35.1 (24.0)	41.3 (27.4)	38.2 (24.6)
Knee SF-36 BP score(SD)	29.4 (23.6)	23.6 (22.8)	33.5 (25.5)	29.7 (24.7)

SD: standard deviation; SF-36 BP: Short Form Health Survey – bodily pain; SF-36 PF: Short Form Health Survey –physical functioning; WOMAC: Western Ontario and McMaster Universities Arthritis Index.

Yang et al (2016)¹⁹

Yang et al (2016) aimed to assess the effect of an ERAS program in an RCT of 258 patients undergoing THA. The components of the ERAS program are described in Table 15 (Appendix 1). Key differences between the ERAS and standard care programs were the introduction of compulsory patient education, discharge planning, standardised medication and treatment protocols as well as early mobilisation for patients in the ERAS group. Patient baseline characteristics are reported in Table 6 below; there were no significant differences between the two groups. The primary outcome of the study was the impact of the ERAS program on length of hospital stay; this outcome was defined as the number of nights hospitalised after the procedure.

Table 6 Baseline characteristics of patients in Yang et al (2016)¹⁹

Characteristic	ERAS N = 126	Standard care N = 132	p value
Mean age (SD)	64.2 (9.4)	66.3 (8.6)	0.07
% Male	22	25	0.44
Mean BMI, kg/m ² (SD)	25.2 (4.2)	25.3 (5.0)	0.96
% ASA score \geq 3	8	7	0.07

ASA: American Society of Anesthesiologists; BMI: body mass index; SD: standard deviation.

Safety

Adverse events were recorded for the first 30 days and first 90 days post-surgery (Table 7). The ERAS group had significantly lower rates of nausea, vomiting, cognitive dysfunction and urinary retention than the standard care group. No other differences in adverse events (dizziness, stroke, myocardial infarction, infection, dislocation, fracture or mortality) were found. There was no difference in the number of patients requiring rehospitalisation.

Table 7 Adverse events reported in Yang et al (2016)¹⁹

Adverse event	ERAS 30-days N = 126	Standard care 30-days N = 132	p value
Nausea (%)	3	15	<0.001*
Vomiting (%)	1	8	<0.001*
Dizziness (%)	2	5	0.2
Cognitive dysfunction (%)	3	8	0.02*
Urinary retention (%)	1	5	0.02*

*Results are statistically significant ($p < 0.05$)

Effectiveness

Mean LOS was significantly lower for the ERAS group than for the standard care group (mean 2.1 days (SD 0.5) and 5.8 days (1.8), respectively; $p < 0.001$). Most (83%) patients receiving the ERAS program were discharged by postoperative day two, while 87 per cent in the standard care group were in hospital more than four days after surgery.

Glassou et al (2014)²⁰

The study conducted in Denmark by Glassou et al (2014) reported the results of a retrospective comparison of patients undergoing THA or TKA at one of six centres with an ERAS program compared to results for patients receiving standard care at any other centre. The analysis included 17,284 patients in the ERAS group (9,293 THA, and 7,991 TKA) and 61,814 patients in the standard care group (34,663 THA, and 27,151 TKA). Key components of the ERAS program included patient education, standardisation of medication and treatment and early mobilisation (Table 15, Appendix 1). Patients were divided into three cohorts based on the time period of their operation; those undergoing surgery from: 2005-2007, 2008-2009, and 2010-September 2011. During the initial time period the ERAS program was in its infancy, during the intermediate period six centres implemented a full-scale ERAS program and the during the final time period all six centres optimised the ERAS program. Patient baseline characteristics are presented in Table 8. Patients included in the ERAS group during the initial and intermediate periods were slightly younger and more likely to be male than patients in the standard care group. There was no difference in baseline characteristics between the two groups in the final time period. Patients in the ERAS group were more likely to receive un-cemented or hybrid implants than those in the standard care

group. The primary outcomes of the study were readmission, reoperation and mortality. Length of stay data was also reported.

Table 8 Baseline characteristics of patients in Glassou et al (2014)²⁰

Characteristic	ERAS 2005-2007	Standard care 2005-2007	<i>p</i> value	ERAS 2008-2009	Standard care 2008-2009	<i>p</i> value	ERAS 2010-2011	Standard care 2010-2011	<i>p</i> value
Mean age (SD)	69 (10)	69 (10)	<0.001	68 (10)	69 (10)	<0.001	69 (10)	69 (9)	0.1
% Male	42	40	0.02	42	41	0.1	43	41	0.01
Fixation % THA*	19/59/22	32/47/22	<0.001	10/65/25	19/66/15	<0.001	5/66/29	18/71/11	<0.001
Fixation % TKA*	91/0/9	76/10/14	<0.001	89/3/8	81/6/13	<0.001	91/5/4	77/4/19	<0.001

*Cemented/un-cemented/hybrid. SD: standard deviation; THA: total hip arthroplasty; TKA: total knee arthroplasty.

Safety

Patients were followed-up for 90 days post-surgery. Risk of readmission due to infection was higher in the ERAS cohort than in the standard care cohort during all three time periods, although this was only statistically significant between 2005 and 2007 (Table 9). The most common contributory factor for readmission due to infection was an increased risk of urinary infection. There were no differences in risk of readmission due to thromboembolic event between the ERAS group and standard care group during the initial and intermediate time periods. The ERAS group had a lower risk during the final time period due to reduced risk of deep vein thrombosis. No differences in reoperation risk or mortality were observed between the two groups at any time period.

Table 9 Safety data from Glassou et al (2014)²⁰

Outcome	ERAS 2005-2007	Standard care 2005-2007	<i>p</i> value	ERAS 2008-2009	Standard care 2008-2009	<i>p</i> value	ERAS 2010-2011	Standard care 2010-2011	<i>p</i> value
Readmission: infection risk % (95% CI)	2.6 (2.2-3.0)	2.0 (1.8-2.2)	0.01	2.1 (1.7-2.5)	1.9 (1.7-2.1)	0.4	2.0 (1.7-2.5)	1.9 (1.7-2.2)	0.6
Readmission: thromboembolic risk % (95% CI)	2.0 (1.7-2.4)	2.2 (2.1-2.4)	0.2	2.1 (1.7-2.5)	2.0 (1.8-2.2)	0.8	1.7 (1.3-2.0)	2.2 (2.0-2.5)	0.01
Reoperation: risk % (95% CI)	1.7 (1.4-2.0)	1.6 (1.5-1.8)	0.8	2.0 (1.7-2.4)	1.8 (1.6-2.0)	0.3	1.4 (1.1-1.8)	1.5 (1.3-1.7)	0.5
Mortality: risk % (95% CI)	0.5 (0.3-0.7)	0.5 (0.4-0.6)	0.6	0.5 (0.4-0.8)	0.4 (0.3-0.5)	0.2	0.4 (0.2-0.6)	0.5 (0.4-0.6)	0.4

CI: confidence interval.

Effectiveness

Length of stay was significantly shorter in the ERAS group than the standard care group for all three time periods. In the initial time period median LOS was four days (range^b 2-8 days) compared to six days (range 3-10 days, $p < 0.001$). For the intermediate time period the median LOS in the ERAS group was three days (range 2-9) compared to four days (range 2-7 days, $p < 0.001$). In the final time period median LOS in the ERAS group was 3 days (range 2-5 days) compared to three days (range 2-7 days, $p < 0.001$). The reduction in median LOS in the standard care group over time was attributed to the fact that ERAS programs were being introduced into more centres nationally than the six initially offering ERAS. This is noted as a limitation of the study particularly for data from the final time period.

Khan et al (2014)²¹

Khan et al (2014) reviewed 6,000 consecutive cases of patients undergoing THA or TKA under an ERAS program or standard care. THA and TKA were conducted between April 2004 and April 2008 while ERAS procedures were conducted between May 2008 and July 2011 following the introduction of the ERAS program. The ERAS program comprised standardised medicines and treatment as well as patient education and early mobilisation (Table 15, Appendix 1). Baseline characteristics are reported in Table 10. The ERAS group had a higher proportion of women, a higher proportion of TKA procedures, and patients were more likely to have hypertension ($p < 0.001$), type 2 diabetes ($p < 0.001$) or chronic obstructive pulmonary disease ($p = 0.002$). Other baseline characteristics were the same between groups. Primary outcome measures were median LOS and readmission as well as any adverse events.

Table 10 Baseline characteristics from Khan et al (2014)²¹

Characteristic	ERAS N = 3,000	Standard care N = 3,000	<i>p</i> value
Mean age (SD)	68 ± 10	69 ± 10	0.05
% Male	46	49	0.02
Number TKAs(%)	58	54	0.003

SD :standard deviation; TKA: total knee arthroplasty.

Safety

Patients in the ERAS group were less likely to require blood transfusion (7.6% vs 23%, $p = 0.01$), less likely to suffer a myocardial infarction (0.4% vs 0.9%, $p = 0.03$) or to die in the first 30 days post-surgery (0.2% vs 0.5%, $p = 0.03$). There were no differences between the groups for other safety outcomes.

^b Glassou et al (2014) reported a range from the bottom 10th percentile to the the top 90th percentile rather than minimum and maximum values for all outcomes.

Effectiveness

Median LOS in the ERAS group was three days shorter than in the standard care group (median 3 [range 0 to 82] versus median 6 [range 1 to 125], $p = 0.01$).

Australian and New Zealand implementation of ERAS programs

Christelis et al (2015)¹⁴

Christelis et al (2015) report the implementation of an ERAS program for THA and TKA in three public hospitals in Victoria. This study compared outcome data from patients operated on before ERAS (N = 412, March 2012 to September 2012) to those operated post-ERAS implementation (N = 297, October 2012 to May 2013). Details of the ERAS program are provided in Table 15 (Appendix 1). Successful ERAS implementation required 11 of 16 criteria to be fulfilled. Selected baseline patient characteristics are provided in Table 11. Patients in the standard care group were more likely to be taking opioids or warfarin and patients in the ERAS group were more likely to be taking oral hypoglycaemic medications or non-steroidal anti-inflammatory drugs before surgery. No other differences between the two groups were observed. The primary outcome of the study was length of hospital stay. Secondary outcome measures were adherence to ERAS and adverse events.

Table 11 Baseline characteristics from Christelis et al (2015)¹⁴

Characteristic	ERAS N = 297	Standard care N = 412	p value
Mean age (SD)	67 (10)	68 (11)	0.05
% Male	38	40	0.02
Mean Weight kg (SD)	87 (20)	84 (19)	0.09
Number TKAs(%)	58	54	0.003
% ASA status ≥ 3	42	44	0.6

ASA: America Society of Anesthesiologists; SD: standard deviation; TKA: total knee arthroplasty.

Safety

Safety outcomes were measured in the immediate post-operative period and six weeks post-surgery. All patients were followed-up to discharge. A total of 25 patients (8%) from the ERAS group and 41 patients (10%) from the standard care group were lost to follow-up at six weeks.

No differences in any safety outcomes (mortality, blood transfusion, return to theatre, infection, dislocation or fracture) were observed between the groups and there was no difference in hospital readmission rates.

Effectiveness

Effectiveness outcomes are reported in Table 12. Median length of hospital stay was significantly shorter (approximately one day) for patients undergoing TKA surgery with an

ERAS protocol compared to standard care. No differences in length of stay were observed for patients undergoing THA. Patients in the ERAS group were also observed to have less pain at 24 and 48 hours post-surgery. Patients in the standard care group were treated using a median of eight out of a possible sixteen ERAS interventions compared to a median of twelve in the ERAS group. Overall, patient satisfaction in both groups was high.

Table 12 Effectiveness outcomes from Christelis et al (2015)¹⁴

Outcome	ERAS N = 297	Standard care N = 412	p value
Median overall length of stay, days (IQR)	5.0 (3.8-6.2)	5.0 (4.0-6.8)	0.1
Median THA length of stay, days (IQR)	4.1 (3.0-6.0)	5.0 (4.0-6.7)	0.005
Median TKA length of stay, days (IQR)	5.0 (4.0-6.9)	5.0 (3.5-7.0)	0.99
Median pain at rest. 24 hours (IQR)	4 (2-5)	5 (3-7)	<0.001
Median pain on movement. 24 hours (IQR)	5 (3-7)	6 (4-8)	<0.001
Median pain at rest. 48 hours (IQR)	3 (1-5)	4 (2-6)	<0.001
Median pain on movement. 48 hours (IQR)	5 (2-7)	6 (4-8)	0.001
Successful implementation of ERAS (%)	81	2	<0.001
Median number of ERAS interventions used /16 possible interventions (IQR)	12 (10-13)	8 (7-10)	<0.001

*Outcome measured at 6-weeks post-surgery; ERAS group N = 272 and standard care N = 371 at this time point. ERAS: Enhanced recovery after surgery program; IQR = interquartile range.

Stowers et al (2016)²³

Stowers et al (2016) describe the implementation of the ERAS program derived from their 2014 systematic review⁵ (described above and in Table 15, Appendix 1). A total of 200 patients were included in the study: 100 patients undergoing THA and TKA were prospectively enrolled following implementation of the ERAS program at a single New Zealand centre (August-December 2013). These patients were compared to a historical cohort of 100 patients who underwent THA or TKA prior to ERAS implementation (June-August 2012). Baseline characteristics are reported in Table 13; there were no differences observed between groups. The primary outcomes of the study were LOS and adverse events.

Table 13 Baseline characteristics from Stowers et al (2016)²³

Characteristic	ERAS N = 100	Standard care N = 100	p value
Mean age (SD)	66.7 (9.2)	65.4 (12.5)	0.4
% Male	47	41	0.4
Mean BMI kg/m ² (SD)	34.4 (7.0)	32.5 (6.8)	0.05
Number TKAs (%)	69	61	0.3
% ASA status ≥ 3	31	36	0.2

ASA: American Society of Anesthesiologists; BMI: body mass index; SD: standard deviation; TKA: total knee arthroplasty.

Safety

No differences in safety outcomes (readmission, DVT, infection, pneumonia or myocardial infarction) were observed between the two groups. No differences in return to theatre rates were observed and no deaths were observed in either group.

Effectiveness

Median LOS was shorter by approximately one day for the ERAS group than the standard care group both for patients undergoing either THA or TKA. In the ERAS group, patients undergoing THA had a median LOS of four days (IQR = 2) and those undergoing TKA also had a median LOS of four days (IQR = 2.5). In the standard care group median LOS was five days (IQR = 2, $p < 0.001$) for THA patients and five days (IQR = 3, $p < 0.001$) for TKA patients. Nine key components of the ERAS program were identified; however, only six of these (spinal anaesthesia, foot pumps, thromboembolic stockings, early mobilisation, antiemetic's and non-opioid analgesia) were implemented in 80 per cent or more of patients. Patient education at 'joint camp', catheter removal on post-operative day one and use of tranexamic acid were not successfully implemented in the ERAS group. The standard care group had successful implementation of foot pumps, thromboembolic stockings and standardised analgesia.

Economic evaluation

Stowers et al (2016) included an analysis of costs associated with ERAS program compared with existing care before ERAS program implementation.²³ Procedures performed under the ERAS program were found to be less costly than those performed before ERAS implementation. For THA the mean cost was \$9,937.81 for an ERAS procedure compared with \$12,342.52 for a non-ERAS procedure ($p = 0.057$). For TKA the mean cost of an ERAS procedure was \$11,026.98 compared with \$11,251.68 for a non-ERAS procedure ($p = 0.0326$).^c

Ongoing research

A search of ClinicalTrials.gov and the Australian and New Zealand Clinical Trials Registry identified three clinical trials currently recruiting participants.

Table 14 Registered ongoing clinical trial characteristics

Study Location	Design	Number of patients	Intervention	Primary outcomes	Trial status (Estimated completion date)
ACTRN12615001170516 Australia	Non-randomised comparative trial	330	ERAS principles of care in THR	Quality of Recovery-15 score	Recruiting
NCT01515670	Observational	30,000	Fast-track THA/TKA	Length of hospital stay and surgically	Recruiting

^c AUD = 1.071 NZD, currency conversion performed on 19 May 2016, source XE Currency Converter

Study Location	Design	Number of patients	Intervention	Primary outcomes	Trial status (Estimated completion date)
Denmark	study (cohort)			related readmission.	
NCT01551017 Austria	Observational study (case-control)	80	Fast-track knee arthroplasty	Swelling	Recruiting

THA: total hip arthroplasty; TKA: total knee arthroplasty.

Other issues

There is considerable variation between published ERAS programs THA and TKA, and no single program appears to be recognised as a clinical standard. Determination of the optimal combination of interventions to be included in an ERAS program, particularly in the Australian setting, would be beneficial and would allow for standardised care.

In many of the included studies, some aspects of the ERAS programs were also being implemented in existing practice. It may be that the program effectiveness is underestimated by these studies as existing practice 'catches up' to the ERAS model.

The ERAS Care System developed by the ERAS Society for gastrointestinal surgery includes formal training and audit programs to be used in conjunction with the listed interventions. No equivalent standardised training and auditing programs were identified in the orthopaedic literature. This may be something to consider for future implementation of ERAS programs.

Number of studies included

All evidence included for assessment in this Technology Brief has been assessed according to the revised NHMRC levels of evidence. A document summarising these levels may be accessed via the [HealthPACT web site](#).

Total number of studies	8
Total number of Level II studies	2
Total number of Level III studies	6 (includes 1 systematic review of Level II and III studies)

Search criteria to be used (MeSH terms)

(Enhanced recovery OR fast-track OR fast track OR multimodal OR ERAS)

AND

(Hip OR Knee OR arthroplasty)

Search date

12 May 2016

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Appendix 1 Summary of orthopaedic ERAS programs

Table 15 Summary of orthopaedic ERAS programs

Component*	Stowers et al (2016)	Christelis et al (2015)	Alito et al (2016)	Auyong et al (2015)	Ayalon et al (2011)	Borgwardt et al (2009)	Dwyer et al (2014)	Gooch et al (2009)	Khan et al (2014)	Larsen et al (2008)
Country	New Zealand	Australia	Brazil	USA	USA	Denmark	UK	Canada	UK	Denmark
Type of surgery	THA, TKA	THA, TKA	THA	TKA	TKA	TKA	TKA	THA, TKA	THA, TKA	THA, TKA
Patient education	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Discharge planning	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Pre-medication with anticonvulsant,	✓									
Standardised (opioid sparing) analgesia	✓			✓	✓			✓	✓	✓
Nutrition screening with dietician referral if required	✓	✓						✓		✓
Preadmission review by physiotherapist if required		✓				✓	✓	✓		
Pre-operative carbohydrate loading		✓	✓				✓			
Minimal fast pre-operatively		✓	✓				✓			✓
Avoidance of sedative pre-operatively		✓					✓			
Anti-nausea prophylaxis		✓		✓			✓	✓		✓
Spinal anaesthesia (not epidural)	✓	✓	✓	✓		✓	✓		✓	
Regional or local anaesthesia	✓	✓								
Standardisation of IV fluids	✓	✓	✓	✓						
Prophylactic antibiotics	✓		✓						✓	
Tranexamic acid for bleeding control	✓			✓					✓	
Avoidance of surgical drains	✓		✓			✓		✓	✓	
Active warming		✓								
Avoidance of catheter						✓	✓		✓	
Early mobilisation/physio	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Prophylaxis treatment for thrombosis	✓		✓					✓	✓	
Standardisation of multimodal analgesia	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Early nutrition		✓	✓				✓			
Post-discharge support					✓	✓		✓		

Table 15 cont.

Component*	Machin et al (2013)	Maempel et al (2016)	Malviya et al (2011)	McDonald et al (2012)	Petersen et al (2008)	Raphael et al (2011)	Reilly et al (2005)	Stambough et al (2015)	Yang et al (2016)	% studies including
Country	UK	UK	UK	UK	Denmark	Canada	UK	USA	China	
Type of surgery	THA, TKA	THA	THA, TKA	TKA	THA	THA, TKA	TKA	THA	THA	
Patient education	✓	✓	✓	✓	✓	✓	✓	✓	✓	100
Discharge planning	✓	✓	✓	✓	✓	✓	✓	✓	✓	100
Pre-medication with anticonvulsant,	✓		✓	✓						21
Standardised (opioid sparing) analgesia	✓	✓	✓	✓	✓	✓			✓	68
Nutrition screening with dietician referral if required					✓					26
Preadmission review by physiotherapist if required	✓	✓								32
Pre-operative carbohydrate loading	✓									21
Minimal fast pre-operatively	✓									26
Avoidance of sedative pre-operatively										11
Anti-nausea prophylaxis	✓					✓		✓	✓	47
Spinal anaesthesia (not epidural)	✓	✓	✓	✓	✓	✓		✓	✓	79
Regional or local anaesthesia	✓					✓	✓			26
Standardisation of IV fluids	✓		✓	✓		✓		✓	✓	53
Prophylactic antibiotics		✓		✓					✓	32
Tranexamic acid for bleeding control			✓	✓					✓	32
Avoidance of surgical drains		✓							✓	37
Active warming										5
Avoidance of catheter										16
Early mobilisation/physio	✓	✓	✓	✓	✓	✓	✓	✓	✓	100
Prophylaxis treatment for thrombosis			✓			✓			✓	37
Standardisation of multimodal analgesia	✓	✓	✓	✓	✓	✓	✓	✓	✓	100
Early nutrition					✓	✓	✓		✓	37
Post-discharge support	✓			✓	✓		✓		✓	42

Table notes: interventions have been categorised as preoperative (green), operative (red) or post-operative (blue).