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Surgical Technical Evidence Review for Elective Total Joint Replacement Conducted for the AHRQ Safety Program for Improving Surgical Care and Recovery

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Abstract

Background: Use of enhanced recovery pathways (ERPs) can improve patient outcomes, yet national implementation of these pathways remains low. The Agency for Healthcare Research and Quality (AHRQ; funder), the American College of Surgeons, and the Johns Hopkins Medicine Armstrong Institute for Patent Safety and Quality have developed the Safety Program for Improving Surgical Care and Recovery—a national effort to catalyze implementation of practices to improve perioperative care and enhance recovery of surgical patients. This review synthesizes evidence that can be used to develop a protocol for elective total knee arthroplasty (TKA) and total hip arthroplasty (THA). **Study Design:** This review focuses on potential components of the protocol relevant to surgeons; anesthesia components are reported separately. Components were identified through review of existing pathways and from consultation with technical experts. For each, a structured review of MEDLINE identified systematic reviews, randomized trials, and observational studies that reported on these components in patients undergoing elective TKA/THA. This primary evidence review was combined with existing clinical guidelines in a narrative format. **Results:** Sixteen components were reviewed. Of the 10 preoperative components, most were focused on risk factor assessment including anemia, diabetes mellitus, tobacco use, obesity, nutrition, immune-modulating therapy, and opiates. Preoperative education, venous thromboembolism (VTE) prophylaxis, and bathing/*Staphylococcus aureus* decolonization were also included. The routine use of drains was the only intraoperative component evaluated. The 5 postoperative components included early mobilization, continuous passive motion, extended duration VTE prophylaxis, early oral alimentation, and discharge planning. **Conclusion:** This review synthesizes the evidence supporting potential surgical components of an ERP for elective TKA/THA. The AHRQ Safety Program for Improving Surgical Care and Recovery aims to guide hospitals and surgeons in identifying the best practices to implement in the surgical care of TKA and THA patients.

Keywords

enhanced recovery, total knee replacement, total hip replacement, total joint replacement, patient safety, quality improvement

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Introduction

A multistakeholder partnership between the Agency for Healthcare Research and Quality (AHRQ; funder), the American College of Surgeons (ACS), and the Johns Hopkins Medicine Armstrong Institute for Patient Safety and Quality has developed the Safety Program for Improving Surgical Care and Recovery. This 5-year national effort aims to assist over 750 hospitals in implementing pathways for surgical patients using evidence-based practices. This program will cover 5 surgical areas including colorectal, orthopedics, gynecology, bariatrics, and emergency general surgery. The cornerstone of this project is evidence-based enhanced recovery pathways (ERPs).

ERPs have previously been shown to reduce complications, shorten length of stay (LOS), improve patient satisfaction, and reduce costs for a variety of operations across specialties, including orthopedics.[1-4] The effectiveness of these programs is directly related to a hospitals' ability to promote high compliance with each pathway process. Adherence to these pathways appears to have a dose–response effect on clinical outcomes.[5] Successful and sustainable implementation goes beyond protocol development, requiring integration across patient units, timely feedback of performance data sharing, senior executive support, and ongoing educational sessions.[6] As such, the Safety Program for Improving Surgical Care and Recovery will provide extensive resources beyond the ERP including access to outcome registries, performance benchmarking, educational materials, leadership training, and contemporary implementation science tools.

The foundation on which all of this lies, however, is an evidence-based protocol including best practices for preventing harm and the principles of enhanced recovery. Recognizing that successful and sustainable pathways require transdisciplinary collaboration among surgeons, anesthesia providers, nurses, and other health-care providers, we have split this review into "surgery" and "anesthesia" components. The objective of this article is to review the evidence supporting proposed ERP components relevant primarily to surgeons. This includes a structured review of the literature and existing clinical guidelines. The anesthesia review is being conducted by anesthesiologists and will be published separately (Appendix A). The ultimate goal of these combined reviews is to provide an evidence base that can be used for the development of a total joint (total knee arthroplasty [TKA]/total hip arthroplasty [THA]) ERP.

Methods

The detailed protocol guiding this review has been previously published.[7] Potential components ("bins") of the ERP were identified through review of existing protocols from community hospitals, academic medical centers, integrated healthcare delivery systems, and the expert opinion of technical advisors (Table 1). The focus was on identification of pre- and postoperative practices that can enhance recovery. While a number of operative decisions likely influence patient outcomes, such as approach and technique, these areas fall into the realm of "appropriateness" and were considered beyond the scope of this project. Well-accepted components of ERP pathways, such as the early removal of Foley catheters and adequate skin preparation, were not targeted as the evidence supporting these practices are robust and reported elsewhere.[7,8] We instead focused on procedure-specific and potentially uncertain components. For each bin, we conducted a structured review of the literature. Searches of MEDLINE were conducted between January and August 2017. Search criteria (Appendix B) were generated with the assistance of a research librarian (E.W.). Additional citations were identified through reference mining and from recommendations of our technical experts. Across all bins, articles were included if they utilized a systematic review (SR) with or without meta-analysis (MA), randomized controlled trial (RCT), or observational design and focused on TKA or THA. We focused only on articles that reported outcomes for a specific protocol component, excluding those that studied multiple components simultaneously or those that evaluated entire pathways. Common exclusion criteria were non-SRs, editorials, case reports, articles where the full text was not available, and articles reporting interventions not relevant to US hospitals. The focus of this review was on primary elective TKA/THA for patients with osteoarthritis (OA) or rheumatoid arthritis (RA). Therefore, hip fractures and TKAs/THAs after trauma indications were excluded. A technical review for hip fracture surgery was performed concurrently (separate publication).

Table 1. Improving Surgical Care and Recovery: TKA/THA Protocol Components—Surgery.

Preoperative management
Risk factor assessment
Anemia
Diabetes mellitus
Tobacco use/smoking
Obesity
Malnutrition
Immune modulators
Opiates/drug abuse
Preoperative education
Preoperative bathing/decolonization
Preoperative VTE prophylaxis
Intraoperative management
Drains
Postoperative management
Early mobilization
Continuous passive motion
Extended duration VTE prophylaxis
Early oral alimentation and enhanced nutrition
Discharge planning/discharge criteria

Abbreviations: THA, total hip arthroplasty; TKA, total knee arthroplasty; VTE, venous thromboembolism.

Table 2. Summary of Reviewed TKA/THA Protocol Components, Outcomes, and Literature/Guideline Support.[a]

Component "Bin"	Outcome(s)	Studies	Population Studied	Evidence	Guideline Support
Preoperative management					
Risk factor assessment					
Anemia	↑ Postop transfusion, +/− LOS, infection, mortality; iron, Epo, preop donation → ↓ postop transfusion, +/− LOS, readmission	2 SR, 2 RCT, 9 Obs	TKA/THA	+	NA
Diabetes	↑ Infections (wound, UTI, and respiratory), ↑ pain, ↓ functional improvement	1 SR, 13 Obs	TKA/THA	+++	√√√
Smoking	Cessation → ↓ Complications (wound, CV, and reoperation), ↓ pain	2 RCT, 5 Obs	TKA/THA, spine, other surgical procedures	+++	√
Obesity	↑ Implant failure/reoperation, superficial and deep SSI, DVT, reduced functional scores	5 SR, 23 Obs	TKA/THA	+++	√√√
Malnutrition	↑ LOS, wound complications	9 Obs	TKA/THA	+	NA
Immune modulators	No consistent findings	1 RCT, 5 Obs	TKA/THA	+/−	√
Opiates/drug abuse	↑ Opioid dependence postoperatively	6 Obs	TKA/THA	+	√
Preoperative education	↓ LOS for TKA	4 SR, 6 Obs	TKA/THA	+/−	NA
Preoperative bathing/ decolonization	↓ SSI	1 RCT, 3 Obs	TKA/THA	+++	√√√
Preoperative VTE prophylaxis	No difference in VTE vs postoperative initiation	2 SR, 5 RCT	TKA/THA	+/−	√
Intraoperative management					
Drains	No benefit; may ↑ complications/costs	2 SR, 3 RCT, 7 Obs	TKA/THA	−	√√√
Postoperative management					
Early mobilization	↓ LOS	1 SR, 1 RCT	TKA/THA	+++	√√√
Continuous passive motion	No effect	1 SR, 2 RCT	TKA	−	√√√
Extended duration VTE prophylaxis	↓ Overall VTE rate, ↓DVT	5 SR, 1 RCT	TKA/THA	+	√
Early oral alimentation and enhanced nutrition	No effect	1 SR	HFS	+/−	NA
Discharge planning/ discharge criteria	No consistent findings	1 SR, 1 RCT, 7 Obs	TKA/THA	+/−	NA

Abbreviations: CV, cardiovascular; DVT, deep vein thrombosis; EPO, erythropoietin; HFS, hip fracture surgery; LOS, length of stay; Obs, observational study; RCT, randomized clinical trial; SR, systematic review; SSI, surgical site infection; THA, total hip arthroplasty; TKA, total knee arthroplasty; UTI, urinary tract infection; VTE, venous thromboembolism.

[a]Evidence grading: +++, consistent evidence across studies showed benefit (interventions) or impact (risk assessment); +, evidence was either mixed with the majority favoring benefit/impact or little evidence existed in only one direction; +/−, evidence either did not exist or existed in both directions without one direction being favored; −, evidence showed no effect of a given practice or the intervention's harms outweighed its benefits. Consistency with clinical guidelines: √√√, all guidelines supported a given practice or the guidelines cited strong evidence of support; √, some, but not all, guidelines supported a given practice or guidelines cited weak evidence or expert opinion.

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagrams were recorded for each bin (example reported in Appendix C). After title and abstract screen, full texts were retrieved and assessed according to predefined inclusion/exclusion criteria. Included studies were evaluated in a hierarchical fashion. For example, if a contemporary well-conducted SR/MA was available, this would serve as the foundation for the evidence synthesis. This SR/MA was updated with more recent RCTs or observational studies. If an SR/MA did not exist, the evidence synthesis was focused on available RCTs and/or observational studies. Given the rapid evolution of ERPs, we favored newer studies, with most included studies published after the year 2000. Finally, clinical guidelines from national and international organizations were incorporated into the review, when available. Results are presented in a narrative format.

Results

For each component, we provide the rationale, a review of the primary evidence, a summary of available guidelines (when available), and our overall conclusion as it relates to the development of an ERP. Table 1 lists the 16 protocol components evaluated in this review. Table 2 summarizes the evidence reviewed for each component, the strength and consistency of the evidence, and its concordance with guidelines. Table 3

Table 3. Summary of Guidelines Supporting the Reviewed Components.[a]

Component "Bin"	Procedure	Society	Year[b]	Recommendation/Statement
Preoperative management				
Risk factor assessment				
Anemia	Not available			
Diabetes	TKA	AAOS	2015	Patients with diabetes mellitus are at increased risk of complications (moderate evidence)
Smoking	THA	AAOS	2017	Tobacco users are at increased risk of complications (limited evidence)
	Surgery	ACS SSI	2016	Cessation 4-6 weeks before surgery reduces risk of SSI and is recommended for all current smokers
Obesity	THA	AAOS	2017	Obese patients may achieve lower clinical scores but a similar level of patient satisfaction and relative improvement in pain and function after surgery (moderate evidence)
	THA	AAOS	2017	Obese patients are at increased risk of dislocation, superficial wound infection, and blood loss (limited evidence)
	TKA	AAOS	2015	Obese patients have less improvement in outcomes (strong evidence)
Malnutrition	Not available			
Opiates/drug abuse	TKA	AAOS	2015	Patients with select chronic pain conditions (eg, low-back pain) have less improvement in patient-reported outcomes (moderate evidence)
Immune modulators	TKA/THA	ACR/AAHKS	2017	For patients with rheumatoid arthritis, continue conventional agents (eg, methotrexate) and hold biologic agents (eg, TNF-α inhibitors)
Preoperative education	Not available			
Preoperative bathing/ decolonization	Ortho	WHO	2016	Nasal carriers of *Staphylococcus aureus* should receive intranasal mupirocin +/− chlorhexidine body wash (strong recommendation)
	Surgery	WHO	2016	Patients should bathe prior to surgery with plain or antimicrobial soap; inadequate evidence to assess chlorhexidine (conditional recommendation)
	Surgery	CDC SSI	2017	Patients should bathe prior to surgery with plain or antimicrobial soap at least the night before the operation (strong recommendation); optimal timing/number of applications/use of chlorhexidine unclear
	Ortho	ACS SSI	2017	Nasal carriers of *Staphylococcus aureus* should receive intranasal mupirocin +/− chlorhexidine body wash
Preoperative VTE prophylaxis	Ortho	CHEST	2012	No preference preoperative versus postoperative initiation; however, if using LMWH, therapy should be initiated >12 hours before or after surgery compared to <4 hours before or after surgery
Intraoperative management				
Drains	TKA	AAOS	2015	There is no benefit to the use of drains with respect to complications or patient outcomes (strong evidence)
Postoperative management				
Early mobilization	THA	AAOS	2017	Postoperative physical therapy can improve early function (moderate evidence)
	TKA	AAOS	2015	Rehabilitation started on the day of TKA reduces length of stay (strong evidence) and improves pain and function (moderate evidence)
Continuous passive motion	TKA	AAOS	2015	Continuous passive motion after TKA does not improve outcomes (strong evidence)
Extended duration VTE prophylaxis	TKA/THA	AAOS	2011	Recommend use of pharmacologic agents and/or mechanical compressive devices for VTE prophylaxis, but they make no recommendation regarding which strategy or the duration of therapy
	TKA/THA	CHEST	2012	Recommend therapy over no therapy; dual (pharmacologic and mechanical) over single; LMWH over fondaparinux, DOAC (apixaban, dabigatran, and rivaroxaban), UFH, VKA, or ASA; and therapy should be continued for up to 35 days
	THA	NICE	2016	

(continued)

Table 3. (continued)

Component "Bin"	Procedure	Society	Year[b]	Recommendation/Statement
				Combined mechanical and pharmacologic prophylaxis; any of the following are acceptable with start times in parenthesis: dabigatran (1-4 hours), fondaparinux (6 hours), LMWH (6-12 hours), rivaroxaban (6-10 hours), UFH if renal impairment (6-12 hours) and continue for 28-35 days; timing based on manufacturer recommendations
	TKA	NICE	2016	Same as above but continue for 10-14 days
Early oral alimentation and enhanced nutrition	Not available			
Discharge planning/discharge criteria	Not available			

Abbreviations: AAHKS, Association of Hip and Knee Surgeons; AAOS, American Academy of Orthopedic Surgeons; ACR, American College of Rheumatology; ASA, aspirin; CDC, Centers for Disease Control; CHEST, The American College of Chest Physicians; DOAC, direct oral anticoagulant (eg, apixaban, dabigatran, and rivaroxaban); LMWH, low-molecular-weight heparin (eg, enoxaparin); NICE, National Institute for Health and Care Excellence; Ortho, orthopedic operations; SSI, surgical site infection; THA, total hip arthroplasty; TKA, total knee arthroplasty; TNF, tumor necrosis factor; UFH, unfractionated heparin; VKA, vitamin K antagonist (eg, warfarin); WHO, World Health Organization; VTE, venous thromboembolism.

[a]Adapted from American Academy of Orthopedic Surgeons,[9] American College of Rheumatology/American Association of Hip and Knee Surgeons,[10] American College of Surgeons and Surgical Infection Society,[8] Centers for Disease Control and Prevention surgical site infection,[11] CHEST,[12] and National Institute for Health and Care Excellence.[13]

[b]Year includes published date or date guidelines were last updated, whichever is later.

provides details regarding the guideline recommendations for each component.

Preoperative Management

Risk factor assessment: Preoperative anemia

Rationale. Anemia is common[14] and may predispose patients to postoperative transfusion resulting in adverse clinical outcomes. Correction of anemia may prove beneficial prior to TKA/THA by reducing risk of transfusion.

Evidence. The literature search identified 170 articles, of which 13 met the inclusion criteria and were specific to total joint replacement: 2 SRs, 2 RCTs, and 9 observational studies. One SR[14] and 4 observational studies[15-18] show that preoperative anemia is associated with increased postoperative transfusion rate. However, the relationship with postoperative clinical outcomes (ie, LOS, mortality) is less clear. For example, 1 National Surgical Quality Improvement Program study[16] found higher odds of 30-day mortality after TKA in patients with preoperative anemia but not in THA, while another study found no difference in mortality for either operation up to 1 year postoperatively.[15] The most frequently used definition of anemia is the World Health Organization (WHO)[19] classification using a hemoglobin <13 g/dL (men) and <12 g/dL (women). Two SRs,[14,20] 1 RCT,[21] and several observational studies[22-26] have shown iron (oral and intravenous) supplementation, erythropoietin, and preoperative autologous donation are effective in reducing postoperative allogenic transfusion; however, the benefit on clinical outcomes (ie, LOS and mortality) is unclear. Routine use of these strategies does not appear to benefit nonanemic patients.[22,23]

Summary and recommendations. All patients undergoing elective joint replacement should be screened for anemia, and if identified, appropriate evaluation and treatment prior to surgery should be coordinated with the patients' care team, including their primary care provider.

Risk factor assessment: Diabetes mellitus

Rationale. Diabetes mellitus (DM) is prevalent in those undergoing elective joint replacement[27,28] and may adversely affect outcomes. Preoperative optimization of diabetes may prove beneficial prior to TKA/THA for improving clinical outcomes.

Evidence. The literature search identified 126 articles, of which 14 met the inclusion criteria and were specific to total joint replacement: 1 SR and 13 observational studies. For TKA, 10 observational studies addressed preoperative DM and its relationship with outcomes,[29-38] with 2 large studies (>10 000 patients) showing increased risk of mortality (odds ratio [OR]: 2.99[30] and hazard ratio: 1.49[31]). These studies also found increased risk of postoperative pain,[33,35,36] functional limitations,[37] and periprosthetic infections.[31,34,38] For THA, 1 SR/MA[28] found an increased risk of surgical site infection (SSI; OR: 2.04), urinary tract infection (UTI; OR: 1.43), and respiratory tract infection (OR: 1.95). Three observational studies corroborated these findings.[31,36,39] In both TKA and THA, studies demonstrated a dose–response curve between severity of DM (variably defined, eg, insulin dependent, with complications, hemoglobin [HbA_{1c}] level) and probability of adverse outcomes.

There is some evidence to support increased risk of complications (primarily SSI) with $HbA_{1c} > 7$[40] (within 1 year prior to surgery), $HbA_{1c} > 8$[41] (within 4 weeks prior to surgery), and fasting blood sugar >200 mg/dL (within 4 weeks prior to surgery).[41] We identified no studies that addressed the impact of

preoperative optimization of DM prior to undergoing elective TKA/THA on clinical outcomes. The American Academy of Orthopedic Surgery (AAOS) found moderate evidence that patients with DM are at an increased risk of complications.[9]

Summary and recommendations. Preoperative DM is associated with worse postoperative outcomes including wound complications, postoperative infections (UTI, respiratory), pain, functional impairment, and possibly mortality. Diabetes mellitus should be screened for and identified prior to undergoing joint replacement surgery and should be optimized through consultation with primary care or endocrinology. No clear cutoff value (or method) has been established, and for now, decisions about surgical management in diabetic patients should be individualized.

Risk factor assessment: Smoking/tobacco use

Rationale. Smoking and other tobacco use may increase the risk of adverse postoperative events, including wound healing complications, pulmonary complications, and other infections.

Evidence. The literature search identified 11 articles, of which 5 met the inclusion criteria and were specific to total joint replacement; 2 additional studies were retrieved via recommendation of the technical experts for a total of 7 included studies[42-48]: 2 RCTs and 5 observational studies.

One trial randomized patients scheduled for TKA/THA to weekly meetings and nicotine replacement.[45] Sixty percent of intervention recipients stopped smoking compared to 7% of controls. Those who decreased smoking >50% had lower rates of postoperative complications (18% vs 52%, $P < .01$). A second RCT in a mixed surgical population also found reduced complications (21% vs 41%, $P = .03$) among those who partially or completely stopped smoking perioperatively.[46] Additional observational evidence found increased complications among smokers[43,47] and that smokers who quit for surgery may benefit from greater reductions in pain and improved wound healing.[42,44]

The AAOS guidelines found limited evidence that smokers are at an increased risk of complications.[41] The ACS SSI guidelines recommend cessation of smoking 4 to 6 weeks prior to surgery to reduce the risk of SSI.[8]

Summary and recommendations. Smoking is associated with increased risk of postoperative complications. Preoperative interventions can help patients with cessation and can improve postoperative outcomes. Patients should abstain for at least 4 to 6 weeks preoperatively and postoperatively; this can be facilitated through counseling and nicotine replacement therapy.

Risk factor assessment: Obesity

Rationale. Obese patients may be at increased risk of adverse events and longer recovery following TKA/THA. Strategies to promote weight loss may prove beneficial.

Evidence. The literature search identified 372 articles, of which 28 met the inclusion criteria and were specific to total joint replacement: 5 SRs and 23 observational studies. For TKA, 3 SRs/MAs[49-51] found higher rates of implant failure, 3 SRs/MAs[49,51,52] found higher rates of SSI, and 1 SR/MA found higher rates of deep infection.[49] Further, 1 SR/MA found lower functional scores postoperatively,[49,50] and 1 SR/MA found higher rates of deep vein thrombosis (DVT). Additional observational studies corroborated these findings[53-60] and suggested obese patients may be at increased risk of acute kidney injury (AKI) perioperatively.[55,61] Similar findings were identified for THA including several observational studies showing increased rates of implant failure,[53,57,62] SSI,[53,55,59,60,62,63] AKI, and DVT. There appears to be a dose–response relationship with significant increases in adverse events among the morbidly obese (body mass index [BMI] >40).

One SR evaluated nonsurgical weight loss prior to joint replacement and actually found higher rates of complications and readmissions in the cohort that lost $\geq$5%.[64] One observational study of patients undergoing TKA/THA following bariatric surgery found no difference in rates of complications between those who had undergone bariatric surgery and matched patients who had not.[65]

For THA, the AAOS guidelines found that obese patients have worse absolute outcome scores (moderate evidence) and increased risk of dislocation and wound infection (limited evidence).[9] For TKA, the AAOS guidelines found strong evidence that obese patients have less outcome improvement than nonobese patients.[9]

Summary and recommendations. Obese patients, especially those with a BMI >40, are at increased risk of adverse outcomes and often experience delayed and dampened functional recovery. These risks should be discussed with patients and incorporated into individualized decision-making. There is insufficient data to support specific use of surgical or nonsurgical weight loss prior to undergoing joint replacement.

Risk factor assessment: Malnutrition

Rationale. Malnourished patients may be at increased risk of complications. Optimization of nutrition prior to elective TKA/THA may reduce adverse events.

Evidence. The literature search identified 179 articles, of which 9 met the inclusion criteria and were specific to total joint replacement (all observational).[66-74] The included studies associated preoperative nutritional status with postoperative outcomes. Nutritional parameters varied and included serum markers (eg, albumin, lymphocyte count), nutrition surveys, and anthropomorphic (ie, body measurement) data. Outcome measures were heterogeneous and included SSI, wound complications, and LOS. Results were mixed with 1 negative study,[66] 3 with increased LOS,[67,69,73] and 4 with increased rates of wound complications.[68,71,72,74] However, individual markers of malnutrition were not consistently tied to outcomes; for example, 1 study found transferrin levels associated with wound complications but not lymphocyte count or albumin,[71] while another study found anthropomorphic data associated with wound complications but not biochemical markers.[72] No

studies were identified that evaluated an intervention to optimize preoperative nutrition prior to TKA/THA.

Summary and recommendations. There is no consistent evidence regarding who should be screened for malnutrition or what measure should be used to assess malnutrition prior to TKA/THA. Malnourished patients may be at increased risk of complications including increased LOS and wound complications, but no studies have addressed nutrition optimization prior to surgery.

Risk factor assessment: Immune-modulating therapy

Rationale. Patients undergoing joint replacement for RA are often on immune-modulating drugs including steroids, conventional agents (eg, methotrexate [MTX]), and newer biologic/synthetic agents (eg, tumor necrosis factor α inhibitors). There is concern that these patients are at increased risk of complications.

Evidence. The literature search identified 424 articles, of which 6 met the inclusion criteria: 1 RCT and 5 observational studies. One RCT randomized elective orthopedic patients (including 121 TKA/THA) to continue MTX through the perioperative period.[75] In adjusted analysis, there was no independent effect of MTX on postoperative outcomes. However, patients in this trial were on a variety of medications, and multivariate analysis did find strong associations between steroids, penicillamine, cyclosporine, and hydroxychloroquine and adverse outcomes. Five observational studies[76-80] found no independent effect of immune-modulating therapy on wound or medical complications; however, these studies have methodologic limitations. None of these studies addressed the timing of discontinuation of agents nor did they address the ramifications of discontinuing therapy on rheumatoid symptoms. A collaboration between the American College of Rheumatology (ACR) and the Association of Hip and Knee Surgeons (AAHKS) recently released guidelines on this topic, including a comprehensive assessment of the literature—the majority of which was not specific to orthopedic operations.[10] In brief, for patients with RA, they recommend perioperative continuation of conventional agents and holding biologic agents.

Summary and recommendations. There is limited evidence to guide clinicians on the perioperative management of immune-modulating drugs for TKA/THA. Recent guidelines from the ACR/AAHKS recommend continuing conventional agents and holding biologic agents in the perioperative period.

Risk factor assessment: Opiate use

Rationale. Pain is a dominant manifestation of OA and may increase the risk of developing opiate dependence. In all, 7% to 23% of THA patients and 10% to 34% of TKA patients have persistent pain following surgery.[81] Understanding the relationship between preoperative opioid dependence and postoperative outcomes may assist with setting patient expectations.

Evidence. The literature search identified 9 articles, of which 3 met the inclusion criteria; 3 additional studies were retrieved via recommendation of the technical expert for a total of 6 included studies (all observational). Multiple observational studies have associated preoperative opioid use with negative postoperative outcomes.[81-85] Large studies in patients undergoing TKA and THA have found that patients on preoperative opioids will often remain opioid dependent postoperatively and may be less satisfied with their clinical outcomes.[82,85] For example, a cohort study of over 6000 patients found that 14% of patients prescribed preoperative narcotics remained on narcotics postoperatively, compared to 3% of patients not prescribed opiates preoperatively.[82] The risk factors for persistent use included younger age, concomitant back pain, diabetes, use of hypnotics, and longer/higher use of opioids preoperatively.[85] A small pilot study of 41 patients found that those who could successfully wean themselves of opioids prior to TKA/THA had greater improvements in patient-reported outcomes than those who did not wean (Western Ontario and McMaster Universities Arthritis Index 43.7 vs 17.8, $P < .01$).[86]

The AAOS guidelines found moderate evidence that patients with select chronic pain conditions (eg, low-back pain) may have less improvement in patient-reported outcomes following TKA.[9]

Summary and recommendations. The current evidence suggests that a fraction of patients on opioids preoperatively will be able to completely stop postoperatively, and of those who do, the time to cessation will be prolonged. Early evidence suggests that patients who can successfully wean themselves from opioids before surgery may have better outcomes than those who cannot. Information about long-term opioid use should be incorporated into discussions with patients before surgery.

Education/bootcamps

Rationale. Preoperative education may improve patient outcomes through improved informed consent and adherence to postoperative protocols.

Evidence. The literature search identified 248 articles, of which 10 met the inclusion criteria and were specific to total joint replacement: 4 SRs and 6 observational studies. Four SRs addressed preoperative education prior to joint replacement including a recent Cochrane SR/MA.[87-90] Educational interventions were heterogeneous and included written and in-person materials, presented either inpatient or prior to admission. Pedagogies included audiovisual, written, and plastic models. Sessions were typically run by physiotherapists or nurses. Across multiple analyses, the only positive finding of the Cochrane review was a reduction in LOS for TKA (2 studies, 1.86 days). They found no benefit in pain, function, adverse events, and quality of life (QOL).

Summary and recommendations. While there is minimal objective evidence that preoperative education has a significant impact on measured postoperative outcomes, their inclusion is important for informed consent and shared decision-making, and educational efforts convey minimal risk. They are recommended to be incorporated into the ERP.

Bathing/Staphylococcus aureus decolonization

Rationale. Preoperative bathing and *Staphylococcus aureus* decolonization may reduce the risk of postoperative SSI.

Evidence. The literature search identified 37 articles, of which 3 met the inclusion criteria; 1 additional observational study was provided to us from a technical expert for a total of 4 studies (1 RCT and 3 observational). One RCT focused on preoperative bathing and 3 observational studies addressed *Staphylococcus aureus* decolonization.[91-94] The RCT compared chlorhexidine cloths to soap and water in patients undergoing TKA/THA and found lower rates of periprosthetic infection in the chlorhexidine cohort (OR: 8.15 for control vs chlorhexidine); however, the statistical significance was borderline ($P = .049$, 95% confidence interval: 1.01-65.6), and the authors calculated a treatment effect as opposed to traditional intent-to-treat effect, reducing external validity. The observational pre–post studies, including a large multicenter study, found reduced SSI rates following the implementation of a screening/treatment program for *S aureus* colonization. An additional large observational study found reduced SSI rates following implementation of a universal decolonization procedure (without screening).[94]

Multiple organizations have issued guidelines related to preoperative bathing and decolonization including the ACS, Centers for Disease Control and Prevention, and the WHO.[8,11,95] The consensus is that preoperative bathing with either plain or antimicrobial soap the night before surgery is beneficial. Further, especially in orthopedic patients, decolonization of nasal carriers of *Stapholococcus aureus* (whether methicillin resistant or not) is recommended. These guidelines have not identified compelling evidence for the use of preoperative chlorhexidine cloths over soap and water.

Summary and recommendation. Patients undergoing elective joint replacement should bathe the night before surgery with soap and water. The evidence supporting the use of chlorhexidine wipes over soap and water is limited. The carriers of *Staphylococcus aureus* should be identified and a decolonizing regimen should be prescribed prior to undergoing surgery. Universal decolonization regimens have some observational support.

Preoperative VTE prophylaxis

Rationale. Chemical venous thromboembolism (VTE) prophylaxis is recommended for all patients undergoing elective total joint replacement. Questions remain however about whether VTE prophylaxis should be initiated preoperatively (focus of this section) and for how long prophylaxis should be continued postoperatively (focus of upcoming section titled extended duration VTE prophylaxis). Intraoperative stasis may contribute to the development of VTE; therefore, preoperative prophylaxis may reduce this risk, but potentially at the expense of increased bleeding.

Evidence. The literature search identified 235 articles, of which 7 met the inclusion criteria and were specific to total joint replacement: 2 SRs and 5 RCTs. A 2002 SR showed no difference in major bleeding and VTE rates comparing preoperative and postoperative low-molecular-weight heparin (LMWH) strategies in patients undergoing THA. Further, while they found that patients started on therapy perioperatively (ie, within 2-4 hours before or after surgery) did have slightly lower VTE rates (10.0% vs 15.3%), they also experienced much higher rates of major bleeding (3.5% vs 0.9%).[96] Subsequent RCTs have randomized patients to preoperative versus postoperative regimens but using different agents, rendering direct comparisons difficult.[97,98] Finally, a recent large registry study found no difference in bleeding, thromboembolic events, or complications when comparing preoperative and postoperative LMWH regimens.[99]

The American College of Chest Physicians (CHEST) guidelines for orthopedic VTE management do not favor preoperative or postoperative initiation but do recommend that therapy be started at least 12 hours before or after surgery as opposed to <4 hours before or after surgery.[12]

Summary and recommendations. While chemical VTE prophylaxis is recommended for all patients undergoing elective joint replacement, there is no convincing evidence favoring preoperative or postoperative initiation. There is evidence that immediate perioperative administration (within 2-4 hours before or after surgery) may increase bleeding disproportionately to the VTE risk reduction. Upcoming section titled extended duration will address extended duration of VTE prophylaxis.

Intraoperative Management

Drains

Rationale. Prophylactic drain placement may reduce hematoma formation and prevent wound infection.

Evidence. The literature search identified 212 articles, of which 12 met the inclusion criteria and were specific to total joint replacement: 2 SRs, 3 RCTs, and 7 observational studies. A Cochrane SR in 2007 for patients undergoing major orthopedic operations, including TKA/THA, found no difference in wound infections, hematoma, dehiscence, or reoperations with the routine placement of closed suction drains.[100] A recent SR in patients undergoing TKA found no difference in LOS, postoperative function, or postoperative hemoglobin levels.[101] These findings have been corroborated in additional RCTs[102,103] and observational studies.[104-106] The AAOS guidelines found strong evidence against the routine use of drains.[9]

Summary and recommendations. There is no evidence supporting the routine use of drains in patients undergoing elective joint replacement.

Postoperative Management

Early mobilization/ambulation

Rationale. Early mobilization may improve postoperative outcomes but potentially at the expense of wound disruption.

Evidence. The literature search identified 283 articles, of which 2 met the inclusion criteria and were specific to total joint replacement: 1 SR and 1 RCT. One SR/MA[107] compared

patients undergoing TKA/THA mobilized on postoperative day 0 (4 of 5 studies) or day 1 compared to controls (day 2 or later). Early mobilization reduced LOS by 1.8 days, with secondary outcomes (function, QOL, adverse events, patient satisfaction) no different or favoring early mobilization. One additional RCT[108] randomized 119 THA patients to day of surgery mobilization versus day after surgery. This study was limited to nonobese, limited complexity (ASA score 2 or less) patients under the care of a single surgeon. They found an increased proportion of intervention patients were discharged at 48 or 72 hours, but no difference in mean LOS. Neither the SR nor the RCT explicitly describes the effect of early mobilization on rates of wound disruption. The AAOS guidelines found moderate (THA) and strong (TKA) evidence in favor of early mobilization for improving LOS and function.[9]

Summary and recommendations. Mobilization of patients on postoperative day 0 appears to be effective and safe. For the majority of patients, mobilization should begin within 24 hours of surgery unless a significant contraindication exists.

Continuous passive motion

Rationale. Passive mobilization of the knee following surgery may improve functional outcomes following TKA.

Evidence. The literature search identified 125 articles, of which 3 met the inclusion criteria and were specific to TKA: 1 SR and 2 RCTs. One SR/MA[109] identified 24 RCTs that compared continuous passive motion (CPM) to standard postoperative care. Usage varied between studies ranging from 1.5 to 24 hours per day for 1 to 17 days, with treatment initiation between the first and fourth postoperative day. They found a small improvement in short-term range of motion (2 degrees) and decreased rate of subsequent surgical manipulations, but no difference in pain, medium/long-term function, QOL, adverse events, or LOS. Two RCTs have been published since this review,[110,111] neither of which found benefit with respect to range of motion or QOL. The AAOS guidelines found strong evidence against the routine use of CPM in TKA.[9]

Summary and recommendations. Continuous passive motion has been studied extensively. There is no evidence of consistent benefit for range of motion, function, QOL, or LOS. Continuous passive motion is likely not as beneficial as alternative modalities such as early mobilization and physiotherapy.

Extended duration VTE thromboprophylaxis

Rationale. Chemical VTE prophylaxis is recommended for all patients undergoing elective total joint replacement. Questions remain however about whether VTE prophylaxis should be initiated preoperatively or postoperatively (focus of previous section titled preoperative VTE prophylaxis) and for how long prophylaxis should be continued postoperatively (focus of this section). In 2012, CHEST guidelines recommended extended duration prophylaxis for patients undergoing major orthopedic operations.[12]

Evidence. The literature search identified 1942 articles, of which 6 met the inclusion criteria and were specific to total joint replacement: 5 SRs and 1 RCT. A 2016 Cochrane review[112] synthesized a large number of contemporary RCTs (referred to as "trials" below); to this, we added 4 additional SRs[113-116] and 1 additional RCT[117] that have been published since the Cochrane literature search concluded.

Heparins. Within the Cochrane review, 6 trials compared LMWH to placebo (ie, no extended prophylaxis), with evidence of reduced composite VTE (combining DVT and pulmonary embolus, symptomatic and asymptomatic) and asymptomatic DVT.

Vitamin K antagonists. Within the Cochrane review, 1 trial compared warfarin to placebo and showed reduced composite VTE. An additional trial in the Cochrane review compared LMWH to a warfarin derivative and found no difference in total VTE.

Two additional studies addressed vitamin K antagonists (VKAs). A 2015 RCT[117] compared fixed low-dose warfarin to variable warfarin (ie, targeting an International Normalized Ratio [INR]) and fondaparinux and found no difference in VTE. A network SR/MA of 94 RCTs[114] assessed 12 different prophylaxis strategies and concluded that variable warfarin conveyed the *highest* risk of DVT.

Direct oral anticoagulants (eg, rivaroxaban, apixaban). Within the Cochrane review, 2 trials evaluated rivaroxaban versus placebo, both showing reduced symptomatic DVT and one showing reduced composite VTE. Five of the included trials compared direct oral anticoagulants (DOACs) to heparins (predominantly LMWH) demonstrating reduced composite VTE.

Two additional studies addressed DOACs. An SR/MA[115] of 18 RCTs found reduced composite VTE for DOACs compared to LMWH. The network SR/MA of 94 RCTs[114] also concluded that DOACs had the lowest risk of asymptomatic and symptomatic DVT compared to other prophylaxis strategies. Limited evidence exists comparing DOACs to one another.

Aspirin. A recent SR/MA focused exclusively on ASA.[116] The quality of included studies limited conclusions, but they did not find any evidence to support the use of aspirin over other agents.

Timing and duration. No studies evaluated the optimal first dose timing. The RCTs typically follow manufacturer's guidelines, although lessons from various studies indicate that the safety of DOACs may be improved by delaying the first postoperative dose for at least 6 hours after surgery. Eligibility for inclusion in the Cochrane review required a minimum duration of therapy of 35 days. Contemporary RCTs differ with respect to therapy duration, but most are between 4 and 5 weeks.

Bleeding. The Cochrane review did not find increased rates of major or clinically relevant bleeding when comparing heparin to placebo, warfarin to placebo, DOAC to placebo, or DOAC to heparin; 1 trial within the review did find higher rates of major bleeding in warfarin compared to heparin (in THA only).

The network SR/MA similarly found no statistical difference in major hemorrhage comparing LMWH to VKA, ASA,

or DOACs.[114] One SR did find statistically different rates of bleeding between different DOACs.[115]

Guidelines. The AAOS guidelines recommend the use of chemical and/or mechanical prophylaxis but do not recommend one chemical strategy over another nor do they make specific reference to duration of therapy.[9] CHEST guidelines recommend chemical prophylaxis, ideally combined with mechanical prophylaxis, with LMWH preferred over fondaparinux/DOACs/unfractionated heparin (UFH)/VKA/ASA.[12] CHEST guidelines further recommend continuing therapy for up to 35 days (TKA or THA). Finally, National Institute for Health and Care Excellence guidelines recommend dual (chemical and mechanical) prophylaxis with no preference between DOACs, LMWH, fondaparinux, and UFH for 28 to 35 days (THA) or 10 to 14 days (TKA).[1]

Summary and recommendations. Extended duration of pharmacologic prophylaxis appears to be safe and effective at reducing total VTE. While heparins (namely, LMWH), warfarin, aspirin, and DOACs are all effective in preventing VTE, there is some comparative evidence that DOACs may be the most efficacious. Little comparative data directly compare DOACs to one another. No consensus exists regarding optimal duration of therapy, although 4 to 5 weeks is a common target.

Early oral alimentation and enhanced nutrition

Rationale. Prolonged fasting can harm patients recovering from major surgery; early enteral nutrition may improve patient outcomes.

Evidence. The literature search identified 52 articles, of which none met the inclusion criteria. One SR in hip fracture surgery is summarized below.

No studies addressed early alimentation or enhanced postoperative nutrition in patients undergoing elective joint replacement. One SR in patients undergoing hip fracture surgery[118] found that oral multinutrient feeds (eg, Boost, Ensure, Sustagen) may reduce complications (eg, pressure sores). They found no support for nasogastric feeds, vitamin/mineral supplementation, or high protein intake. One study included in the SR showed that dietetic assistants may reduce mortality but had no effect on complications. Patients undergoing elective surgery are likely at reduced risk of complications or nutrition-mediated mortality, so these benefits may not apply.

Summary and recommendations. No evidence exists to guide postoperative nutrition in patients undergoing elective joint replacement. In hip fracture surgery, there is no benefit of nasogastric feeds, high protein intake, or vitamin/mineral supplementation. Patients should be fed a regular (or comorbidity appropriate) diet as soon as they are able to tolerate following surgery.

Discharge planning/discharge criteria

Rationale. Early identification of patients at risk of nonhome discharge may allow swifter placement and improve patient outcomes.

Evidence. The literature search identified 529 articles, of which 9 met the inclusion criteria: 1 SR, 1 RCT, and 7 observational studies. Two studies have developed indices to predict discharge based on preoperative variables (eg, age, QOL) with reasonable sensitivity/specificity.[119,120] One study found functional assessments completed after admission could predict timing of discharge.[121] The literature associating discharge location with patient outcomes has significant limitations due to the number of settings (eg, home health, acute and subacute rehab, skilled nursing) and lack of standardized outcome measurement. For example, discharge to inpatient rehabilitation may reduce risk of readmission[122] but may also result in smaller gains in physical QOL measures.[123,124] Patients receiving home health may reach goals more quickly than patients receiving subacute rehabilitation,[125] while discharge to a skilled nursing facility (SNF) may be associated with higher readmission rates.[126] Finally, one RCT randomized THA patients to an enhanced discharge intervention including education and home visits for wound care and medical therapy.[127] While small ($n = 50$), this study found significant cost savings as well as possible improvements in objective funtional measures.

Summary and reccomendations. Discharge planning is an important component of any ERP. Discharge planning should begin well before surgery and involve a multidisciplinary approach including physical therapists, case managers, and social workers. There is insufficient evidence to guide identification strategies or to conclude which settings are best suited to optimize patient outcomes.

Discussion

A vast and growing body of literature exists to help guide clinicians as they implement ERPs in elective joint replacement. Institutions that have introduced ERPs have been able to improve patient outcomes including reduced complications and shorter LOS.[1-4] This ultimately translates to lower costs[128,129]—a factor especially relevant to orthopedic surgeons in the era of episode-based payments. This review includes 16 surgical components potentially relevant to developing a total joint ERP, supported through primary literature, clinical practice guidelines, and/or expert consensus. While the level of support varies in its strength from one bin to the next, there is clear evidence that a number of interventions can improve patient outcomes.

Many of the interventions outlined in this review should be a part of a comprehensive evaluation and discussion with patients before surgery. While the ultimate goal should be reducing adverse events and enhancing recovery, setting appropriate expectations for patients and their families is critical. Screening for anemia, DM, obesity, tobacco use, and opiate dependence can identify cohorts who may have increased risk of transfusion, postoperative infections, wound complications, reoperations, chronic opioid use, and possibly, higher mortality. The literature supporting and optimizing these criteria is, unfortunately, limited, but there is some evidence that correcting preoperative anemia, encouraging smoking cessation

through education and nicotine replacement, and opiate weaning prior to surgery can mitigate risk. These assessments should be considered a part of comprehensive preoperative evaluation and included as a part of the ERP.

Key ERP components beyond the preoperative risk assessment include those related to SSI prevention, VTE reduction, and enhancing mobility. Preoperative bathing with soap and water should be routine, and protocols should be developed to screen/decolonize those individuals colonized with *Staphylococcus aureus*. Routine use of drains should be discouraged. Mobilizing patients as soon as possible appears to decrease LOS and should be incorporated into an ERP in lieu of CPM. Chemical VTE prophylaxis should begin either 12 hours prior to or 12 hours following surgery and should be continued for 4 to 5 weeks postoperatively. Finally, it should be acknowledged that practices beyond those discussed here are also likely beneficial to perioperative care. Examples of these practices include guideline-based administration of prophylactic antibiotics (with discontinuation at the end of the procedure), intraoperative skin prep with an alcohol-based solution, and early discontinuation of Foley catheters.[7,8,130]

In summary, this study provides a review for 16 possible components of an ERP for total joint replacement. Importantly, 7 of these components fall under the category of preoperative evaluation and optimization. The other 8 components represent multidisciplinary processes of care that are evidence-based best practices. Combined with the anesthesia components (reported separately, Appendix A), consistent delivery of the complete ERP will provide patients with the best opportunity for a swift and complete recovery.

Conclusions

This review of 16 surgical bins for enhanced recovery in total joint replacement represents one component of AHRQ Safety Program for Improving Surgical Care and Recovery. Participating hospitals will also be provided state-of-the-art guidance in translating these evidence-based practices into their own clinical settings, with the ultimate goal of improving perioperative care at the national level.

Appendix A

Table A1. Reviewed TKA/THA Protocol Components, Including Anesthesia.

Preoperative management
Risk factor assessment
Anemia
Diabetes mellitus
Tobacco use/smoking
Obesity
Nutrition
Immune modulators
Opiates/drug abuse
Preoperative education
Preoperative bathing/decolonization
Preoperative VTE prophylaxis
Immediate preoperative management
Carbohydrate loading and reduced fasting[a]
Multimodal preanesthesia medications[a]
Multimodal postoperative nausea and vomiting prophylaxis[a]
Intraoperative management
Drains
Antibiotic prophylaxis[a]
Standard intraoperative anesthesia pathway[a]
Tranexamic acid[a]
Fluids/goal-directed fluid therapy[a]
Glycemic control[a]
Multimodal postoperative nausea and vomiting prophylaxis[a]
Standard intraoperative analgesic pathway
Postoperative management
Standard postoperative multimodal analgesic regimen[a]
Glycemic control[a]
Early mobilization
Continuous passive motion
Extended duration VTE prophylaxis
Early oral alimentation and enhanced nutrition
Discharge planning / discharge criteria

Abbreviations: THA, total hip arthroplasty; TKA, total knee arthroplasty; VTE, venous thromboembolism.
[a]Protocol component is reported in separate, anesthesia-focused, article.

Appendix B

Table B1. MEDLINE Search Terms.

	Search Terms		
Component "Bin"	Operation	Bin	Qualifiers
Preoperative management			
Anemia	(("Hip Fractures"[Mesh] OR "Intertrochanteric Fractures"[tiab] OR "Subtrochanteric Fractures"[tiab] OR "Intertrochanteric Fracture"[tiab] OR "Subtrochanteric Fracture"[tiab] OR "hip fracture"[tiab] OR "hip fractures"[tiab])) OR ((Arthroplasty, Replacement, Knee[Mesh]) OR "knee replacement"[tiab]) OR "knee arthroplasty"[tiab]) OR "knee replacements"[tiab]) OR "knee arthroplasties"[tiab]) OR "total knee"[tiab]) OR Arthroplasty, Replacement, Hip [Mesh]) OR "hip replacement"[tiab]) OR "hip arthroplasty"[tiab]) OR "hip replacements"[tiab]) OR "hip arthroplasties"[tiab]) OR "total hip"[tiab]) OR "hip prosthesis implantation"[tiab]) OR "hip prosthesis implantations"[tiab])	anemia[tw]	(preop*[tw] OR pre-op*[tw]) AND English[lang]
Diabetes	("Arthroplasty, Replacement, Hip"[Mesh] OR "Arthroplasty, Replacement, Knee"[Mesh] OR "Hip Fractures"[Mesh] OR "Arthroplasty, Replacement, Hip"[all fields] OR "Arthroplasty, Replacement, Knee"[all fields] OR "Hip Fractures"[all fields] OR "prosthetic joint"[all fields])	("Diabetes Mellitus"[Mesh] OR "Diabetes Mellitus, Type 2"[Mesh] OR "Hemoglobin A, Glycosylated"[Mesh] OR "Hemoglobin A, Glycosylated/analysis"[Mesh] OR "Hyperglycemia"[Mesh] OR "hyperglycemia/complications"[mesh terms] OR "blood glucose"[mesh terms] OR "Diabetes complications/blood"[mesh terms] OR "diabetes mellitus/blood"[mesh terms] OR "Diabetes Mellitus"[all fields] OR "Diabetes Mellitus, Type 2"[all fields] OR "Hemoglobin A, Glycosylated"[all fields] OR "Hyperglycemia"[all fields] OR "glycemic markers"[all fields] OR "blood glucose"[all fields])	("Preoperative Period"[Mesh] OR "Preoperative Care"[Mesh] OR "Preoperative Period"[all fields] OR "Preoperative Care"[all fields] OR "outcome"[all fields]) AND English[lang]
Smoking		("Smoking"[Mesh] OR "Smoking Cessation"[Mesh] OR "Tobacco Smoke Pollution"[Mesh] OR "Smoking"[all fields] OR "Smoking Cessation"[all fields] OR "Tobacco Smoke Pollution"[all fields])	
Obesity	("Arthroplasty, Replacement, Knee"[Mesh] OR "knee replacement"[tiab] OR "knee replacements"[tiab] OR "knee arthroplasty"[tiab] OR "knee arthroplasties"[tiab] or "total knee"[tiab] OR "Arthroplasty, Replacement, Hip"[Mesh] OR "hip replacement"[tiab] OR "hip replacements"[tiab] OR "hip arthroplasty"[tiab] OR "hip arthroplasties"[tiab] OR "total hip"[tiab] OR "hip prosthesis implantation"[tiab] or "hip prosthesis implantations"[tiab] OR "Arthroplasty, Replacement"[Mesh] OR "total joint arthroplasty"[tiab] OR "total joint"[tiab]")	("Body Mass Index"[mesh] OR "body mass index"[tiab] OR "overweight"[mesh] OR "overweight"[tiab] OR "obesity"[mesh] OR "obesity"[tiab] OR "obesity, morbid"[mesh] or "morbid obesity"[tiab])	
Nutrition	(Arthroplasty, Replacement, Knee[Mesh]) OR "knee	("nutrition"[tiab]) OR "Nutritional Status"[Mesh]	NA
Immune modulators	replacement"[tiab]) OR "knee arthroplasty"[tiab]) OR "knee replacements"[tiab]) OR "knee arthroplasties"[tiab]) OR "total knee"[tiab]) OR Arthroplasty, Replacement, Hip [Mesh]) OR	(("Antirheumatic Agents"[Mesh]) OR ("Tumor Necrosis Factor-alpha/antagonists and inhibitors"[Mesh])) OR "Immunosuppressive Agents"[Mesh]	NA

(continued)

Table B1. (continued)

Component "Bin"	Search Terms		
	Operation	Bin	Qualifiers
Opiates/Drug Abuse	"hip replacement"[tiab]) OR "hip arthroplasty"[tiab]) OR "hip replacements"[tiab]) OR "hip arthroplasties"[tiab]) OR "total hip"[tiab]) OR "hip prosthesis implantation"[tiab]) OR "hip prosthesis implantations"[tiab]	("opiate dependent"[tiab]) OR "opioid dependent"[tiab]) OR "opiate dependence"[tiab]) OR "Opioid-Related Disorders"[Mesh]	NA
Education		Patient Education as Topic[mesh] OR "pre-operative education"[tiab] OR "preoperative education"[tiab]	NA
Bathing/decolonization		bath*[tw] OR clean*[tw] OR clorhex*[tw]	preop*[tw]
VTE prophylaxis		"Thromboembolism"[Mesh] OR "thromboembolism"[tw] OR "thromboprophylaxis"[tw]	"Preoperative"[tw] OR "intraoperative"[tw]
Intraoperative			
Drains	Arthroplasty, Replacement, Hip"[All Fields] OR "Arthroplasty, Replacement, Knee"[All Fields] OR "Hip Fractures"[All Fields] OR "Arthroplasty, Replacement, Hip"[All Fields] OR "Arthroplasty, Replacement, Knee"[All Fields] OR "Hip Fractures"[All Fields] OR "prosthetic joint"[All Fields]	"drain"[All Fields]	English [lang]
Postoperative			
Early mobilization	Arthroplasty, Replacement, Knee[Mesh]) OR "knee replacement"[tiab]) OR "knee arthroplasty"[tiab]) OR "knee replacements"[tiab]) OR "knee arthroplasties"[tiab]) OR "total knee"[tiab]) OR Arthroplasty, Replacement, Hip [Mesh]) OR "hip replacement"[tiab]) OR "hip arthroplasty"[tiab]) OR "hip replacements"[tiab]) OR "hip arthroplasties"[tiab]) OR "total hip"[tiab]) OR "hip prosthesis implantation"[tiab]) OR "hip prosthesis implantations"[tiab]	("early ambulation"[tw]) OR "early mobilization"[tw]	NA
Continuous passive motion		"Motion Therapy, Continuous Passive"[Mesh] OR "continuous passive motion"[tiab] OR "CPM therapy"[tiab] OR "CPM therapies"[tiab]	NA
VTE thromboprophylaxis		"Thromboembolism"[Mesh] OR "thromboembolism"[tw] OR "thromboprophylaxis"[tw]	NA
Early oral alimentation and enhanced nutrition	(("Hip Fractures"[Mesh] OR "Intertrochanteric Fractures"[tiab] OR "Subtrochanteric Fractures"[tiab] OR "Intertrochanteric Fracture"[tiab] OR "Subtrochanteric Fracture"[tiab] OR "hip fracture"[tiab] OR "hip fractures"[tiab])) OR (Arthroplasty, Replacement, Knee[Mesh]) OR "knee replacement"[tiab]) OR "knee arthroplasty"[tiab]) OR "knee replacements"[tiab]) OR "knee arthroplasties"[tiab]) OR "total knee"[tiab]) OR Arthroplasty, Replacement, Hip [Mesh]) OR "hip replacement"[tiab]) OR "hip arthroplasty"[tiab]) OR "hip replacements"[tiab]) OR "hip arthroplasties"[tiab]) OR "total hip"[tiab]) OR "hip prosthesis implantation"[tiab]) OR "hip prosthesis implantations"[tiab])	nutrition"[tiab] OR "feeding"[tiab] OR "alimentation"[tiab] or "enteral"[tiab]	("Postoperative Period"[Mesh]) OR ("postoperative"[tiab] OR "postop"[tiab] OR "post-operative"[tiab] OR "post-op"[tiab])
Discharge planning/ discharge criteria	("Arthroplasty, Replacement, Hip"[Mesh] OR "Arthroplasty, Replacement, Knee"[Mesh] OR "Hip Fractures"[Mesh] OR "Arthroplasty, Replacement, Hip"[all fields] OR "Arthroplasty, Replacement, Knee"[all fields] OR "Hip Fractures"[all fields] OR "prosthetic joint"[all fields])	("Patient discharge"[Mesh] OR "Patient discharge"[all fields])	English[lang]

Appendix C

Example PRISMA Flow Diagram and Inclusion/Exclusion Criteria for Each Reviewed Component

Operation: Joints (total hip arthroplasty [THA]; total knee arthroplasty [TKA])
Bin: Pre/perioperative management of immune-modulating drugs (biologics, disease-modifying drugs, etc)
Inclusion Criteria:

Patients: Adult patients undergoing elective TKA or THA for rheumatoid arthritis

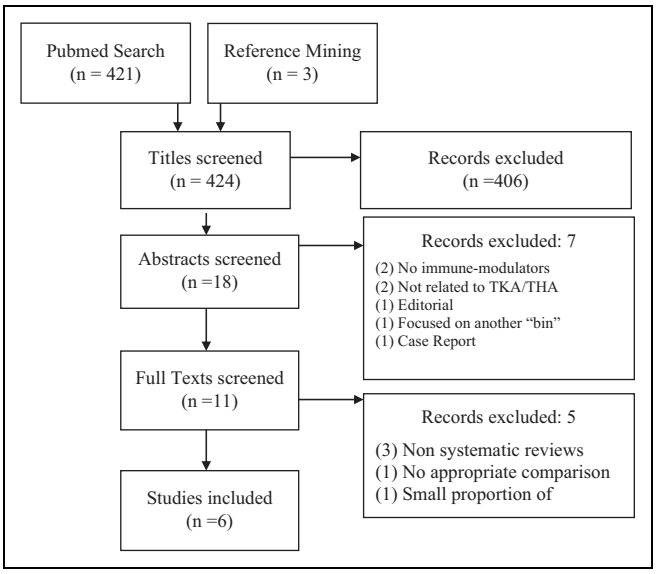
Intervention: Patients on immune-modulating drugs

Comparisons: Patients on alternative therapies or not on immune-modulating drugs

Outcome(s): Postoperative outcomes

Study Design(s): Systematic reviews, randomized controlled trials, observational studies

Exclusion Criteria: Non-English, nonsystematic reviews, editorials, case reports, articles focused only on NSAIDs/COX2 inhibitors or corticosteroids.



Authors' Note

The opinions expressed in this document are those of the authors and do not reflect the official position of Agency for Healthcare Research and Quality or the US Department of Health and Human Services. Elizabeth C. Wick is currently affiliated to Department of Surgery, University of California San Francisco, San Francisco, CA, USA.

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