Evidence Synthesis Program

Orthopedic Surgery Complication Risk Associated with Smoking Cessation and Use of Nicotine Replacement Therapies

June 2023

U.S. Department of Veterans Affairs
Veterans Health Administration
Health Services Research & Development Service

Recommended citation: Mackey KM, Beech EH, Young S, Parr NJ. Orthopedic Surgery Complication Risk Associated with Smoking Cessation and Use of Nicotine Replacement Therapies: A Systematic Review. Washington, DC: Evidence Synthesis Program, Health Services Research and Development Service, Office of Research and Development, Department of Veterans Affairs. VA ESP Project #09-199; 2023.

AUTHORS

Author roles, affiliations, and contributions to the present report (using the CRediT taxonomy) are summarized in the table below.

Author	Role and Affiliation	Report Contribution
Katherine M. Mackey, MD, MPP	Associate Director & Clinician Investigator, Evidence Synthesis Program (ESP) Coordinating Center, Portland VA Health Care System Portland, OR	Conceptualization, Methodology, Investigation, Formal analysis, Writing – original draft, Writing – review & editing, Supervision
Erin H. Beech, MA	Senior Research Associate, ESP Coordinating Center, Portland VA Health Care System Portland, OR	Conceptualization, Methodology, Investigation, Writing – original draft, Writing – review & editing, Project administration
Sarah Young, MS	Research Associate, ESP Coordinating Center, Portland VA Health Care System Portland, OR	Investigation, Project administration, Visualization
Nicholas J. Parr, PhD, MPH	Associate Director & Research Scientist, ESP Coordinating Center, Portland VA Health Care System Portland, OR	Conceptualization, Methodology, Writing – review & editing

This report was prepared by the Evidence Synthesis Program Coordinating Center located at the **VA Portland Health Care System**, directed by Mark Helfand, MD, MPH, MS and funded by the Department of Veterans Affairs, Veterans Health Administration, Health Services Research and Development.

PREFACE

The VA Evidence Synthesis Program (ESP) was established in 2007 to provide timely and accurate syntheses of targeted health care topics of importance to clinicians, managers, and policymakers as they work to improve the health and health care of Veterans. These reports help:

- Develop clinical policies informed by evidence;
- Implement effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures; and
- Set the direction for future research to address gaps in clinical knowledge.

The program comprises 4 Centers around the US and a Coordinating Center, which are led by VA clinicians and scientists who are recognized leaders in the field of evidence synthesis. The Coordinating Center, located in Portland, Oregon, was created to manage program operations, ensure methodological consistency and quality of products, engage with stakeholders, and address urgent evidence synthesis needs. To ensure responsiveness to VA decision-makers, the ESP is governed by a Steering Committee of health system leadership and researchers. Nominations for ESP reviews are submitted via the program website.

The present report was developed in response to a request from Veterans Health Administration (VHA) National Surgery Office. The scope was further developed with input from Operational Partners (below) and the ESP Coordinating Center review team.

ACKNOWLEDGMENTS

The ESP is grateful to Dawn M. Bravata, MD and the VA's EXTEND QUERI for efforts in analyzing VA data relevant to the report topic; Kathryn Vela, MLIS for literature searching; and the following individuals for their contributions to this project:

Operational Partners

Operational partners are system-level stakeholders who help ensure relevance of the review topic to the VA, contribute to the development of and approve final project scope and timeframe for completion, provide feedback on the draft report, and provide consultation on strategies for dissemination of the report to the field and relevant groups.

Jason M. Johanning, MD, MS
Medical Director
Surgical Quality Improvement Program,
National Surgery Office

Mark Wilson, MD, PhD
Executive Director
National Surgery Office

Peer Reviewers

The Coordinating Center sought input from external peer reviewers to review the draft report and provide feedback on the objectives, scope, methods used, perception of bias, and omitted evidence (see Appendix E for disposition of comments). Peer reviewers must disclose any relevant financial or non-financial conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The Coordinating Center works to balance, manage, or mitigate any potential nonfinancial conflicts of interest identified.

TABLE OF CONTENTS

FIGURES AND TABLES

EVIDENCE REPORT

INTRODUCTION

PURPOSE

The VA Evidence Synthesis Program (ESP) Coordinating Center is responding to a request from the Veterans Health Administration (VHA) National Surgery Office for a review of smoking cessation interventions and use of nicotine replacement therapy (NRT) prior to elective orthopedic surgery and their effects on complication risks. Findings from this review will be used to inform clinical guidance.

BACKGROUND

Professional societies including the American College of Surgeons recommend tobacco cessation prior to undergoing elective surgery[1] to improve overall health and reduce the risk of surgical complications. In the case of elective orthopedic surgery, the American Academy of Orthopaedic Surgeons (AAOS) urges patients to quit smoking prior to surgery, citing tobacco use as a cause of poor wound healing, infection, and worse overall outcomes.[2,3] While society guidelines encourage surgical teams to discuss tobacco cessation with patients prior to surgery, current guidelines do not suggest *requiring* patients to stop tobacco use. However, surgical practice can vary[4] and tobacco cessation or participation in a tobacco cessation program may be required prior to surgery in some settings.[5] Further, patients may also be asked to avoid NRT prior to surgery due to concerns related to nicotine exposure generally (not just with tobacco use). In their Surgical Risk Reduction Toolkit, AAOS suggests testing patients on the day of surgery for cotinine, a blood test that detects nicotine due to cigarette smoking and NRT.[6]

In a 2022 survey,[7] more than 1 million Veterans enrolled in VHA care reported currently using tobacco (defined as cigarette smoking every day or some days), equating to almost 13% of all VHA enrollees. Among Veterans aged 45-64 and older than 65, approximately 16% and 10% reported currently using tobacco, respectively. While VHA widely promotes tobacco cessation and offers medications to help patients quit (NRT, varenicline, and bupropion) as well as a range of counseling options,[8] many Veterans continue to smoke. In 2022, approximately 4% of Veterans who formerly smoked reported successfully quitting in the past year, while approximately 52% of current tobacco users reported unsuccessful quit attempts.[9] Challenges associated with quitting smoking and high rates of unsuccessful quit attempts in the general population are also well described.[10,11]

While requiring tobacco cessation prior to elective orthopedic surgery may lower complication risks, overly restricting the option of surgery also has the potential to worsen outcomes. Patients who are required to quit smoking prior to surgery but are unable to do so may seek out another surgeon with different requirements (delaying care) or ultimately decide to forgo surgery, even when the symptoms that led them to seek surgery in the first place become more severe or functionally limiting.[12] To best determine if tobacco cessation prior to elective orthopedic surgery should be recommended or required, improved understanding of the degree of risk reduction associated with tobacco cessation interventions in the preoperative period is needed. The evidence most often cited to recommend tobacco cessation before surgery compares outcomes between those who never smoked and current or former tobacco users. Less is known

about the difference in risk among those who smoked but quit or reduced their use before surgery and those who continued to smoke their usual amount before surgery. Factors that may mitigate the potential benefits of tobacco cessation before surgery include the length of time and amount that a patient smoked, use of NRT, demographics such as age, comorbidities, the nature of the specific surgery planned, and the duration of tobacco cessation prior to surgery. The aim of this review is to synthesize evidence on the effects of preoperative smoking cessation interventions and use of NRT for reducing complication risk associated with elective orthopedic surgery.

METHODS

PROTOCOL

A preregistered protocol for this review can be found on the PROSPERO international prospective register of systematic reviews (CRD42022372248).

KEY QUESTIONS

The following key questions were the focus of this review:

Key Question 1	What is the effect of pre-surgery smoking cessation/reduction interventions (including NRT) on peri-postoperative complication risk?
Key Question 1a	Does complication risk vary by intervention intensity (*eg*, number of counseling sessions, length of NRT) or duration of smoking cessation prior to surgery?

ELIGIBILITY CRITERIA

Study eligibility criteria are shown in the table below.

Population	Adults undergoing elective orthopedic surgery
Intervention	Smoking cessation/reduction intervention(s) prior to surgery including behavioral or pharmaceutical (*eg*, varenicline, bupropion, NRT) interventions. Interventions delivered intra- or post-operatively were ineligible.
Comparator	Alternate intervention (*eg*, usual care, briefer/less intensive version of intervention, educational materials only, placebo pharmaceutical) or no-treatment comparison (*ie*, no attempt to modify patient smoking habits). Studies without a comparison condition were excluded.
Outcomes	*Perioperative and postoperative complications:* infection, thromboembolism, prosthetic explantation, extended length of hospital stay, hospital readmission, mortality, *etc*
Study Design	Any

DATA SOURCES AND SEARCHES

To identify articles relevant to the key questions, a research librarian searched Ovid MEDLINE, CINAHL, the Cochrane Database of Systematic Reviews, and ClinicalTrials.gov as well as AHRQ and HSR&D through May 2023 using terms for *elective orthopedic surgery* and *smoking cessation* (see Appendix A for complete search strategies). Additional citations were identified from hand-searching reference lists of relevant systematic reviews. We limited the search to published and indexed articles involving human subjects available in the English language.

Study selection was based on the eligibility criteria described above. We excluded studies that examined the effect of smoking on elective orthopedic surgery complications rather than the effect of smoking cessation interventions. We also excluded studies that did not compare elective orthopedic surgery complications between tobacco users who received a smoking cessation intervention and those who received no intervention or an alternate intervention (see Appendix B for a list of excluded studies and reasons for exclusion). Titles, abstracts, and full-text articles

were independently reviewed by 2 investigators. All disagreements were resolved by consensus or discussion with a third reviewer.

DATA ABSTRACTION AND ASSESSMENT

Effect information and population, intervention, and comparator characteristics were abstracted from all included studies. The internal validity (risk of bias) of each included study was rated using the Cochrane risk of bias tools.[13,14] All data abstraction and internal validity ratings were first completed by 1 reviewer and then checked by another; disagreements were resolved by consensus or discussion with a third reviewer.

SYNTHESIS

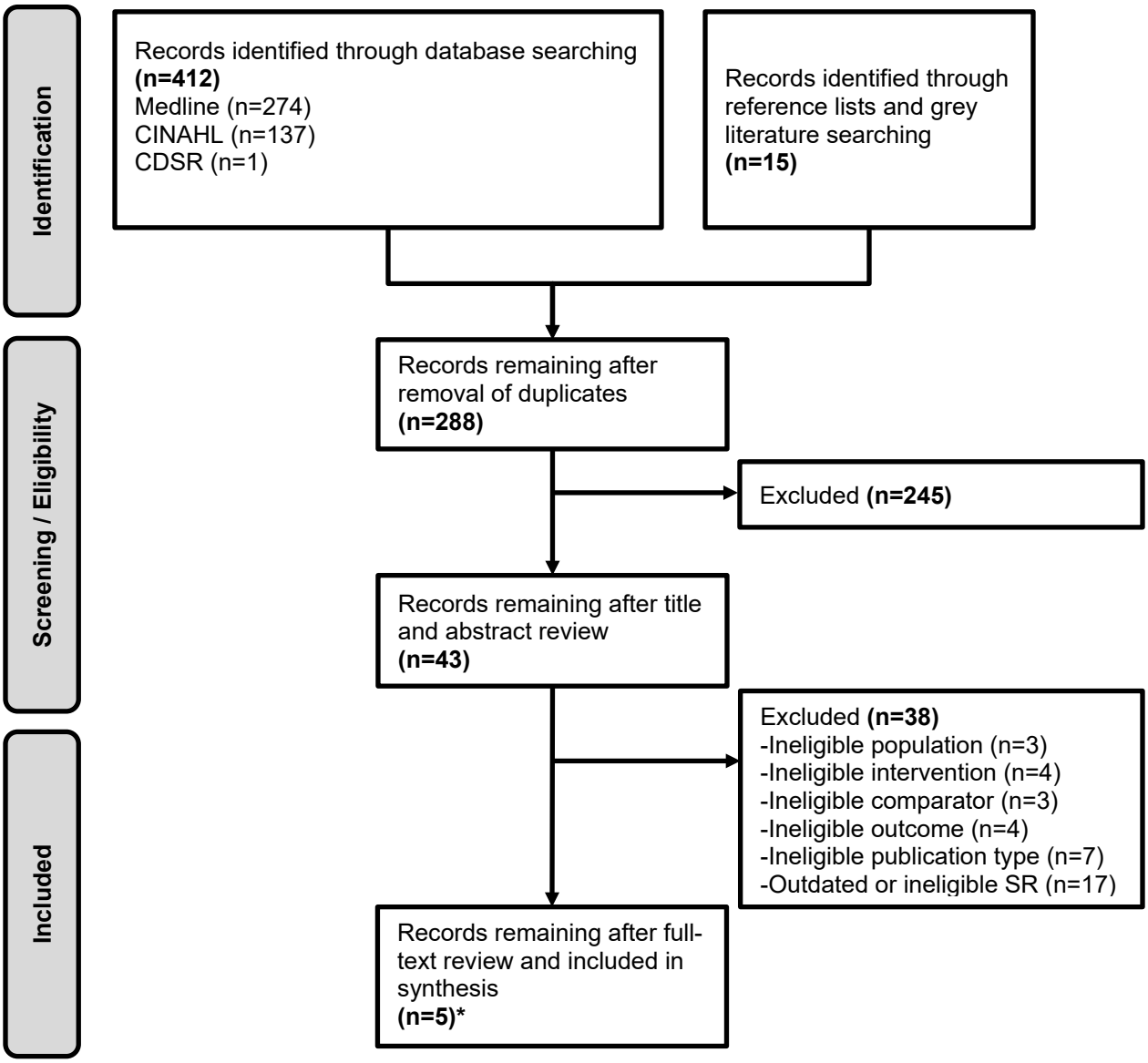
We synthesized available evidence narratively, grouping studies by surgery type. We planned to grade the strength of the evidence for each outcome based on the AHRQ Methods Guide for Comparative Effectiveness Reviews[15] but did not do so because of extensive variation in surgery types and outcomes across included studies.

RESULTS

LITERATURE FLOW

The literature flow diagram (Figure 1) summarizes the results of the study selection process (full list of excluded studies available in Appendix B).

Figure 1. Literature Flowchart



Notes. *4 studies in 5 records
Abbreviations. CDSR=Cochrane Database of Systematic Reviews; CINAHL=Cumulative Index to Nursing and Allied Health Literature; SR=systematic review

LITERATURE OVERVIEW

Our search identified 265 potentially relevant articles. We included 4 studies (in 5 publications): 1 RCT[16,17] and 3 observational studies,[18-20] which are summarized in Table 1. The RCT was conducted in Denmark and the 3 retrospective cohort studies were conducted in the US. Studies varied with respect to the type(s) of surgery that participants underwent. The RCT[16,17] and 1 cohort study[18] included adults who underwent TKA or THA. The other 2 observational studies included patients who underwent spine surgery (single-level anterior cervical discectomy and fusion[19] and single-level lumbar fusion[20]). The RCT included 120 participants, and the sample sizes of the retrospective cohort studies ranged from 201 to 31,935. Mean age of the participants was reported in 2 studies and ranged from 58[18] to 66.[16,17] Only the RCT[16,17] included information characterizing the tobacco use history of the participants, reporting pack years (the number of smoking years multiplied by daily cigarette consumption) and the number of cigarettes participants smoked per day.

Methodological limitations of the RCT included unclear intervention adherence, unclear extent and handling of missing data, and absence of an identified study protocol reporting planned outcomes and analyses. The retrospective cohort studies, 2 of which[19,20] used exact matching, were limited by the potential for bias due to departures from the intended intervention, bias due to confounding, and unclear extent and handling of missing data. One retrospective cohort study[18] was judged to be at serious risk of selection bias because not all eligible patients were offered participation in the smoking cessation intervention. Full details of quality assessments are available in Appendix C.

We did not identify any ongoing clinical trials examining the effect of smoking cessation interventions on complications after elective orthopedic surgery.

Table 1. Characteristics of Included Studies

Study *Study Type*	Sample Size *Follow-up*	Surgery Type	Participant Characteristics	Participant Smoking History	Intervention and Comparator	Risk of Bias Rating
Hip and Knee Replacement						
Moller 2002[16] Moller 2003[17] *RCT*	N=120 *4 weeks*	TKA or THA	Intervention vs Comparison: Mean age: 66 vs 64 Female: 57% vs 58% Race/ethnicity: NR BMI: 27 vs 26 DM: 2% vs 5% Heart disease: 12% vs 15%	Pack years: 35 intervention group vs 37 comparison group; number of cigarettes per day: 15 for both groups	Counseling and NRT 6-8 weeks before surgery vs standard care with little/no information on tobacco risks and no cessation counseling	Some concerns
Herrero 2020[18] *Retrospective Cohort*	N=201 *90 days*	TKA or THA	Intervention vs Comparison: Mean age: 58 both groups Female: 48% both groups AA/Black: 34% vs 38% White: 46% vs 45% Other race: 20% vs 17% BMI: 30 vs 31	NR	Participation in a voluntary smoking cessation program including assessment, education, counseling, and NRT 4-6 weeks prior to surgery vs education and counseling as part of standard preoperative optimization protocols	Serious
Cervical and Lumbar Spine Surgery						
Khalid 2022[19] *Retrospective Cohort*	N=5769 *90 days*	Single-level anterior cervical discectomy and fusion	Total sample: Age >50: 58% Female: 61% Race/ethnicity: NR Obesity: 18% DM: 26% HTN: 54% Heart disease: 13%	NR	Documented NRT, varenicline, and/or cessation counseling at 90 days before surgery vs active tobacco use with no record of NRT, varenicline, and/or cessation counseling 90 days before surgery	Moderate
Khalid 2022[20] *Retrospective Cohort*	N=31935 *30 days, 90 days, or 2.5 years*	Single-level lumbar fusion	Total sample: Age >45: 79% Female: 60% Race/ethnicity: NR Obesity: 22% DM: 28% HTN: 59% Heart disease: 14%	NR	Documented NRT, varenicline, and/or cessation counseling at 90 days before surgery vs active tobacco use with no record of NRT, varenicline, and/or cessation counseling 90 days before surgery	Moderate

Abbreviations. NR=not reported; NRT=nicotine replacement therapy; RCT=randomized controlled trial; THA=total hip arthroplasty; TKA=total knee arthroplasty.

HIP AND KNEE REPLACEMENT

We identified 1 RCT[16,17] and 1 retrospective cohort study[18] evaluating smoking cessation interventions among adult tobacco users prior to THA or TKA. In an RCT[16,17] conducted in Denmark of 120 adults with an average of 35-37 pack-years and current use of 15 cigarettes per day, intervention group participants received counseling and NRT 6-8 weeks before surgery. Compared to participants who received usual care, which consisted of little or no information regarding smoking cessation, intervention group participants had higher rates of quitting tobacco (36% compared to 4%) or reducing their use (14% compared to no participants in the comparison group). Outcomes generally favored the intervention (Table 2). The relative risk of wound-related complications was lower in the intervention group (RR = 0.16, 95% CI [0.05, 0.52]), as was the relative risk of any complication (RR = 0.34, 95% CI [0.17, 0.58]). The proportion of patients needing a secondary surgery (most often due to wound-related complications) was also lower in the intervention group (4% compared to 15%). Rates of respiratory, cardiovascular, renal, and gastrointestinal complications were similar between groups, as were rates of delirium and urinary tract infection. Hospital length of stay was also similar between groups.

The other study[18] we identified of smoking cessation interventions prior to THA or TKA was a retrospective cohort study conducted in the US of 201 adults who were offered participation in a voluntary tobacco cessation program. While all participants received tobacco education and counseling as part of standard preoperative protocols, participants in the cessation program also received NRT as well as 4 pre-operative telephone visits and 2 follow-up visits after surgery with members of the program team (composed of nurse practitioners, licensed clinical social workers, physician's assistants, and physicians). Compared to participants who received care according to standard preoperative protocols, rates of smoking cessation were higher in the intervention group (43% compared to 33%). Rates of infection were lower in the intervention group (7% compared to 13%), although this finding was not statistically significant (Table 2). Hospital length of stay and readmissions were similar between groups. In contrast to the RCT described above, this study did not report on participants' tobacco use history at baseline. The study was also at risk of selection bias because referral to the smoking cessation program was recommended but not required of attending surgeons and not all patients were offered the intervention.

CERVICAL AND LUMBAR SPINE SURGERY

We identified 2 retrospective cohort studies[19,20] evaluating smoking cessation interventions in adult tobacco users prior to spine surgery. Both studies were conducted by the same group of US researchers and used an all-payer claims database to identify patients who had undergone single-level anterior cervical discectomy and fusion[19] or single-level lumbar fusion.[20] In both studies, outcomes were compared between matched samples of former tobacco users on NRT or varenicline and active tobacco users, groups that were identified using a combination of International Classification of Diseases (ICD)-9 and -10 and Current Procedural Terminology (CPT) codes. In the study of adults undergoing anterior cervical discectomy and fusion, which included exact matched populations of 1,923 former and current tobacco users, active tobacco use was associated with *lower* odds of dysphagia (OR = 0.56, 95% CI [0.33, 0.95]) and need for revision surgery (OR = 0.85, 95% CI [0.73, 0.99]) (Table 2). Other outcomes were similar between these groups including risks for hematoma, instrumentation removal, pseudarthrosis, and 30- and 90-day readmission. In the study of adults undergoing lumbar fusion, which

included exact matched populations of 10,645 former and current tobacco users, former tobacco use was associated with lower odds of any postoperative complication compared to active tobacco use (OR = 0.86, 95% CI [0.80, 0.93]) (Table 2). Risks for pseudoarthrosis, need for revision surgery, and 30- and 90-day readmission were similar.

Table 2. Outcomes of Included Studies

Study	Smoking Cessation Rate	Hospital LOS	Postoperative Complication Rate *Mortality*	Readmission Rate	Secondary Surgery or Revision Rate
Moller 2002[16] Moller 2003[17]	Quit: 36% intervention group vs 4% comparison group Reduced use: 14% intervention group vs 0% comparison group	Median 11 days intervention group vs 13 days comparison group, p = 0.41	Relative risk (95% CI) (<1 favors intervention): **Any complication 0.34 (0.17–0.58)**; **Wound-related complications[a] 0.16 (0.05–0.52**) No significant difference between groups for respiratory, CV, renal, GI, complications or delirium or UTI *No deaths in either group*	NR	Need for secondary surgery: 4% intervention group vs 15% comparison group
Herrero 2020[18]	Quit: 43% intervention group vs 33% comparison group	2.47 days intervention group vs 2.62 days comparison group, p = 0.52	Infection rate: 7.3% intervention group vs 12.5% comparison group, p = 0.27	5.8% intervention group vs 4.7% comparison group, p = 0.73	NR
Khalid 2022[19]	NR	NR	OR (95% CI) for matched smoking vs smoking cessation cohort: Composite surgical complications 0.845 (0.705–1.014); **dysphagia 0.559 (0.330–0.947)**; hematoma 1.589 (0.769–3.282); pseudarthrosis 1.034 (0.724–1.479); instrumentation removal 0.750 (0.495–1.136)	OR (95% CI) for matched smoking vs smoking cessation cohort: 30-day readmission 1.000 (0.691–1.447); 90-day readmission 0.932 (0.705–1.231)	OR (95% CI) for matched smoking vs smoking cessation cohort: **Revision surgery 0.846 (0.726–0.988)**
Khalid 2022[20]	NR	NR	OR (95% CI) for matched smoking cessation vs smoking cohort: **Any complication 0.862 (0.804-0.925)**; pseudoarthrosis 1.041 (0.929–1.166)	OR (95% CI) for matched smoking cessation vs smoking cohort: 30-day readmission 1.026 (0.924–1.140) 90-day readmission 1.102 (1.005–1.207)	OR (95% CI) for matched smoking cessation vs smoking cohort: Revision surgery 0.835 (0.694–1.001)

Notes. Boldface indicates statistically significant finding. [a]Wound related complications included hematoma, infection with positive culture, and/or subfascial involvement.

Abbreviations. CV=cardiovascular; GI=gastrointestinal; OR=odds ratio; NR=not reported; NRT=nicotine replacement therapy; THA=total hip arthroplasty; TKA=total knee arthroplasty; UTI=urinary tract infection.

DISCUSSION

Elective orthopedic surgery is common among older adults with a history of tobacco use or who are active tobacco users. Given this common clinical scenario, the evidence base on the effectiveness of preoperative tobacco cessation interventions to mitigate elective orthopedic surgery complication risks is surprisingly small. We identified just 4 studies, 3 of which are observational. The most informative study is an older RCT[16,17] conducted in Denmark of 120 adult tobacco users undergoing TKA or THA who were randomized to counseling and NRT versus usual care in the 6-8 weeks prior to surgery. The trial found that smoking cessation resulted in a lower risk of wound-related complications including infection. Notably, the trial excluded those with a weekly alcohol intake of more than 35 units and participants had a mean body mass index (BMI) of 26-27 and low rates of diabetes (2% in the intervention group and 5% in the control group). The participants included in this trial may be poorly representative of the contemporary US population with a high burden of comorbidities that may independently influence the risk of wound-related and other complications following TKA and THA.

The 3 observational studies we identified contribute little useful information to address the review question. A retrospective cohort study[18] of patients undergoing TKA or THA, which found a lower risk of infection associated with participation in a smoking cessation program, was at risk of selection bias because not all eligible patients were offered the intervention. Further, those who participated in the voluntary smoking cessation program may have had important differences from those who declined the program, and the study did not employ methods to minimize bias due to confounding. The remaining 2 observational studies used an all-payer claims database and had large sample sizes but were not designed to capture participants' lifetime tobacco use history (including duration and severity), use of NRT, actual rate of smoking cessation, or duration of smoking cessation prior to surgery. Understanding these characteristics is important for applying findings of these studies. More critically, these characteristics may be key drivers of complication risk that, if not understood and accounted for when assessing the association between smoking (or smoking cessation) and complication risk, could distort the apparent size and direction of that association.

To provide additional context for this report's findings, we conducted a literature search for systematic reviews on the association between tobacco use and complications following elective orthopedic surgery. While characterizing the relationship between tobacco use and elective orthopedic surgery complications was not a focus of this review, the evidence on this topic provides important background to understand why tobacco cessation before elective orthopedic surgery has generally been recommended. We identified 15 systematic reviews, the results of which are summarized in the table below by surgery type and comparison groups (see Appendix D for review characteristics). The first category listed in each column is considered as the exposure and the second as the comparator (*eg*, in the first column, smoking increases risk of the outcome compared with non-smoking).

Evidence on the association between tobacco exposure and elective orthopedic surgery complications is composed of observational studies (cohorts, case-control studies, and case series) mostly comparing outcomes between groups based on a qualitative assessment of current smoking status (currently smoking or not) without any quantitative assessment of current or past tobacco use. Findings broadly confirm that tobacco use is associated with an increased risk of surgical complications, particularly postoperative infections. However, this body of evidence has

several important limitations when examined in the context of whether to recommend or require tobacco cessation prior to elective orthopedic surgery. As noted by most review authors, primary studies frequently categorize patients as current tobacco users or nonsmokers using different criteria, or do not specify how smoking status was determined. Variability in the definitions of smoking status may not only skew estimates of the association between smoking and complication risk, but also prevents subgroup analyses to determine whether complication risk varies by the length of an individual's smoking history, the severity of use (*ie*, pack years), or the recency of cessation (among patients classified as non-smokers or former smokers)—all important factors to understand when making clinical recommendations.

	Smoking vs Non-smoking	**Current Smoking vs Non-smoking**	**Former Smoking vs Non-smoking**	**Current Smoking vs Former Smoking**
Multiple	2 SRs found significantly increased risk of infection.[21,22]	2 SRs found significantly increased risk of infection.[21,23] 1 SR found no significant difference in revision surgery.[23]	2 SRs found significantly increased risk of infection. [21,23] 1 SR found no significant difference in revision surgery.[23]	1 SR found significantly increased risk of infection.[21]
Hip	1 SR found significantly increased risk of infection.[24]	1 SR found significantly increased risk of infection.[24]	1 SR found significantly increased risk of infection.[24]	
	Smoking vs Non-smoking Only			
Knee	2 SRs found significantly increased risk of infection.[25,26] 1 SR found significantly increased risk of revision surgery.[25]			
Spine	3 SRs found increased risk of infection.[27-29] 1 SR found significantly increased risk of revision surgery.[29] 1 SR found decreased rate of successful spinal fusion.[30] 1 SR found no difference in spinal fusion rate.[29]			

To examine the applicability of this evidence to the VA context, investigators at the VA's EXTEND QUERI analyzed the risk-adjusted association between smoking and TKA complications among VHA patients. A total of 29,104 TKA procedures were included in the analyses, and included Veterans had a mean age of 67. Two-thirds had a BMI of 30 or higher, 33% had diabetes or diabetes-related complications, 18% had coronary atherosclerosis or angina, and 16% had vascular or circulatory disease. Using a combination of health factor data, problem lists from the electronic medical record, and cotinine laboratory levels in the year prior to TKA, 13% of Veterans undergoing TKA were identified as current tobacco users and the remaining populations were classified as not currently using tobacco or having an unknown smoking status. The most common complication among Veterans undergoing TKA was wound infections, though the rate of this complication decreased over time (from 2.8% in FY2018 to 1.6% in FY2022). In risk-adjusted analyses, current smoking status was not associated with higher odds of complications compared with patients not currently using tobacco or having an unknown smoking status (a group that potentially included those who never used tobacco and those who formerly used tobacco).

When considering whether to require tobacco cessation prior to elective orthopedic surgery, perhaps the most critical limitation of foundational evidence on complication risks from smoking is that studies have generally not compared risks between those who smoked but quit or reduced their use in the immediate preoperative period and those who continued to smoke their usual amount prior to surgery. In real-world surgical settings, surgical teams are limited to influencing

perioperative tobacco use and can have no impact on the effects of smoking accumulated over a lifetime. Thus, to make a case for requiring tobacco cessation prior to elective orthopedic surgery, a link must be established between active tobacco use before elective orthopedic surgery and risk reduction attributable to smoking cessation in the perioperative period. As evident in the above table, most studies do not provide this evidence because they do not compare outcomes between current and former tobacco users (and more specifically, between active tobacco users and tobacco users who *recently* quit).

A systematic review[21] of complications following TKA and THA illustrates this issue. The review identified 4 studies with data to compare wound complications between current and former tobacco users. The reported meta-analysis of these studies indicated that current tobacco users had a significantly increased odds of any wound complication compared to former tobacco users (OR = 1.36, 95% CI [1.16, 1.60]). However, each of the 4 studies differed in how former tobacco use was defined. Two studies limited the group of former tobacco users to patients who had stopped smoking at least 1 year before surgery. A third study included former tobacco users who self-reported having quit. The final study required patients to have stopped smoking for only the 30 days prior to surgery. Despite the significant pooled effect, current tobacco users had greater odds of any wound complication only in the 2 studies with former tobacco users who had not smoked for a year or more. In the studies of self-reported former tobacco users (without a time requirement) and patients who could have smoked as recently as 30 days prior to surgery, complication risk did not significantly differ between former and current tobacco users. Other studies have found similar complication risk for current and former tobacco users.[31-33]

Moreover, despite promising results of the included RCT,[16,17] whether short-term tobacco cessation consistently mitigates elective orthopedic surgery complication risks among patients with other independent risk factors for worse outcomes, such as diabetes, is unclear. That the most common post-surgical complication among former and current smokers appears to be wound healing suggests that it may be the lifetime burden of smoking and related comorbidities (*eg*, diabetes) on circulatory health that underlies complication risk. If this is the case, then a brief period of cessation prior to surgery may not be sufficient to alter complication risk.

Importantly, the purpose of this review was not to gauge the overall health benefits of tobacco cessation: available evidence is unequivocal about the harm of tobacco use across the lifespan and the benefits of stopping tobacco use at any age.[34] It also seems clear that patients who have never smoked are, on the whole, at lower risk of complications following elective orthopedic surgery than patients who currently smoke. But in the absence of conclusive evidence establishing that active tobacco users who stop smoking in the *immediate* preoperative period have a reduced risk of surgical complications, whether to require tobacco cessation prior to elective orthopedic surgery may be best determined using shared decision-making and considering the totality of each patient's risk factors and potential benefits of surgery. It is possible that for some patients, requiring tobacco cessation prior to elective orthopedic surgery may be unduly burdensome and may delay improvements to their quality of life without conferring a meaningful reduction in their surgical risks.

LIMITATIONS

Limitations of our review methods include our use of sequential review (rather than dual independent review) for data abstraction and risk of bias assessment.

FUTURE RESEARCH

Existing gaps would best be addressed by an RCT conducted among current tobacco users undergoing elective orthopedic surgery that:

- Describes participants' tobacco use history in detail including the duration and amount of tobacco exposure.
- Describes participants' comorbidities, particularly presence of conditions that may also influence surgical complication risks such as diabetes and describes the severity of such comorbidities.
- Describes in detail the smoking cessation intervention, including the use of NRT and other therapies, and the timing of the intervention relative to surgery.
- Provides data regarding adherence to the smoking cessation intervention in the form of patient interview or objective measures such as cotinine levels.

Additionally, available evidence does not address the question of whether NRT is itself associated with complications following elective orthopedic surgery. In the observational study of adults who underwent anterior cervical discectomy and fusion,[19] participants in the smoking group had a *lower* odds of dysphagia compared to participants in the smoking cessation group, which the study authors speculate could have been due to the irritant effects of nicotine replacement products. A well-conducted trial that captures in detail the extent and duration of participants' tobacco use history as well as their use of nicotine replacement and/or non-nicotine treatment (*eg*, varenicline) relative to the timing of surgery is needed to understand the role of NRT in surgical outcomes (if any).

CONCLUSIONS

Little evidence is available on the impact of smoking cessation interventions on complication risk following elective orthopedic surgery. One RCT reported a lower risk of wound-related complications among patients offered counseling and NRT before undergoing TKA or THA, compared with usual care. Most of the available evidence is drawn from observational studies, which have significant risk of bias. Important questions remain about the degree to which short-term tobacco cessation interventions among active tobacco users mitigate the risk of complications after elective orthopedic surgery – and the extent to which improved patient functionality and quality of life that results from surgery outweigh these risks.

REFERENCES

1. American College of Surgeons. Quit smoking. https://www.facs.org/for-patients/strong-for-surgery/quit-smoking/. Accessed April 11, 2023.
2. American Academy of Orthopaedic Surgeons, American Association of Orthopaedic Surgeons. *Tobacco use and orthopaedic surgery.* 2016.
3. American Academy of Orthopaedic Surgeons. Surgery and smoking. https://orthoinfo.aaos.org/en/treatment/surgery-and-smoking/. Accessed April 11, 2023.
4. Khullar D, Maa J. The impact of smoking on surgical outcomes. *Journal of the American College of Surgeons.* 2012;215(3):418-426.
5. Paulsen K, Carender CN, Noiseux NO, Elkins JM, Brown TS, Bedard NA. What is the fate of total joint arthroplasty patients who are asked to quit smoking prior to surgery? *Arthroplasty Today.* 2023;19:101087.
6. American Academy of Orthopaedic Surgeons. Preoperative risk factors. https://www.aaos.org/quality/quality-programs/quality-toolkits/smoking/. Accessed April 18, 2023.
7. Office of Strategic Planning and Analysis (OSPA), VHA Chief Strategy Office, Veterans Health Administration (VHA), U.S. Department of Veterans Affairs (VA). *2022 survey of veteran enrollees' health and use of health care findings report.* 2022.
8. U.S. Department of Veterans Affairs. Tobacco and health. 2023; https://www.mentalhealth.va.gov/quit-tobacco/index.asp. Accessed April 11, 2023.
9. Wang ZJ, Dhanireddy P, Prince C, Larsen M, Schimpf M, Pearman G. *2021 survey of veteran enrollees' health and use of health care data findings report.* 2021.
10. Borland R, Partos TR, Yong HH, Cummings KM, Hyland A. How much unsuccessful quitting activity is going on among adult smokers? Data from the international tobacco control four country cohort survey. *Addiction.* 2012;107(3):673-682.
11. Chaiton M, Diemert L, Cohen JE, et al. Estimating the number of quit attempts it takes to quit smoking successfully in a longitudinal cohort of smokers. *BMJ Open.* 2016;6(6):e011045.
12. Khullar D, Schroeder SA, Maa J. Helping smokers quit around the time of surgery. *Jama.* 2013;309(10):993-994.
13. Sterne JA, Hernán MA, Reeves BC, et al. Robins-i: A tool for assessing risk of bias in non-randomised studies of interventions. *Bmj.* 2016;355:i4919.
14. Sterne JAC, Savović J, Page MJ, et al. Rob 2: A revised tool for assessing risk of bias in randomised trials. *Bmj.* 2019;366:l4898.
15. Berkman ND, Lohr KN, Ansari M, et al. Ahrq methods for effective health care grading the strength of a body of evidence when assessing health care interventions for the effective health care program of the agency for healthcare research and quality: An update. In: *Methods guide for effectiveness and comparative effectiveness reviews.* Rockville (MD): Agency for Healthcare Research and Quality (US); 2008.
16. Moller AM, Villebro N, Pedersen T, Tonnesen H. Effect of preoperative smoking intervention on postoperative complications: A randomised clinical trial. *Lancet.* 2002;359(9301):114-117.
17. Moller AM, Pedersen T, Villebro N, Norgaard P. Impact of lifestyle on perioperative smoking cessation and postoperative complication rate. *Preventive Medicine.* 2003;36(6):704-709.

18. Herrero C, Tang A, Wasterlain A, et al. Smoking cessation correlates with a decrease in infection rates following total joint arthroplasty. *Journal of Orthopaedics.* 2020;21:390-394.
19. Khalid SI, Eldridge C, Singh R, et al. The impact of smoking and smoking cessation interventions on outcomes following single-level anterior cervical discectomy and fusion procedures. *Clinical Neurology & Neurosurgery.* 2022;219:107319.
20. Khalid SI, Thomson KB, Chilakapati S, et al. The impact of smoking cessation therapy on lumbar fusion outcomes. *World Neurosurgery.* 2022;164:e119-e126.
21. Bedard NA, DeMik DE, Owens JM, Glass NA, DeBerg J, Callaghan JJ. Tobacco use and risk of wound complications and periprosthetic joint infection: A systematic review and meta-analysis of primary total joint arthroplasty procedures. *J Arthroplasty.* 2019;34(2):385-396.e384.
22. Kunutsor SK, Whitehouse MR, Blom AW, Beswick AD, Team I. Patient-related risk factors for periprosthetic joint infection after total joint arthroplasty: A systematic review and meta-analysis. *PLoS ONE [Electronic Resource].* 2016;11(3):e0150866.
23. Singh JA. Smoking and outcomes after knee and hip arthroplasty: A systematic review. *Journal of Rheumatology.* 2011;38(9):1824-1834.
24. Teng S, Yi C, Krettek C, Jagodzinski M. Smoking and risk of prosthesis-related complications after total hip arthroplasty: A meta-analysis of cohort studies. *PLoS ONE [Electronic Resource].* 2015;10(4):e0125294.
25. He Y, Omar M, Feng X, Neunaber C, Jagodzinski M. Impact of smoking on the incidence and post-operative complications of total knee arthroplasty: A systematic review and meta-analysis of cohort studies. *Bosnian Journal of Basic Medical Sciences.* 2022;22(3):353-365.
26. Kong L, Cao J, Meng F, Shen Y. Incidence and risk factors for surgical site infection following total knee arthroplasty: A systematic review and meta-analysis. *Int J Clin Exp Med.* 2016;9(11):20642-20650.
27. Kong L, Liu Z, Meng F, Shen Y. Smoking and risk of surgical site infection after spinal surgery: A systematic review and meta-analysis. *Surgical Infections.* 2017;18(2):206-214.
28. Xing D, Ma JX, Ma XL, et al. A methodological, systematic review of evidence-based independent risk factors for surgical site infections after spinal surgery. *Eur Spine J.* 2013;22(3):605-615.
29. Zheng LM, Zhang ZW, Wang W, Li Y, Wen F. Relationship between smoking and postoperative complications of cervical spine surgery: A systematic review and meta-analysis. *Scientific Reports.* 2022;12(1):9172.
30. Li Y, Zheng LM, Zhang ZW, He CJ. The effect of smoking on the fusion rate of spinal fusion surgery: A systematic review and meta-analysis. *World Neurosurgery.* 2021;154:e222-e235.
31. Kapadia BH, Issa K, Pivec R, Bonutti PM, Mont MA. Tobacco use may be associated with increased revision and complication rates following total hip arthroplasty. *J Arthroplasty.* 2014;29(4):777-780.
32. Sadr Azodi O, Bellocco R, Eriksson K, Adami J. The impact of tobacco use and body mass index on the length of stay in hospital and the risk of post-operative complications among patients undergoing total hip replacement. *J Bone Joint Surg Br.* 2006;88(10):1316-1320.
33. Singh JA. Smoking and outcomes after knee and hip arthroplasty: A systematic review. *J Rheumatol.* 2011;38(9):1824-1834.

34. U.S Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health. *Smoking cessation. A report of the surgeon general.* 2020.
35. Emara AK, Grits D, Samuel LT, Acuna AJ, Rosneck JT, Kamath AF. Hip arthroscopy in smokers: A systematic review of patient-reported outcomes and complications in 18,585 cases. *American Journal of Sports Medicine.* 2021;49(4):1101-1108.
36. Novikov DA, Swensen SJ, Buza JA, 3rd, Gidumal RH, Strauss EJ. The effect of smoking on acl reconstruction: A systematic review. *Physician & Sportsmedicine.* 2016;44(4):335-341.
37. Fan N, Yuan S, Du P, et al. The effects of smoking on clinical and structural outcomes after rotator cuff repair: A systematic review and meta-analysis. *Journal of Shoulder & Elbow Surgery.* 2022;31(3):656-667.