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

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The findings and conclusions in this document are those of the author(s) who are responsible for its contents and do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs. No investigators have any affiliations or financial involvement (eg, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.

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.

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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.

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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.

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EXECUTIVE SUMMARY

Key Findings

- Little evidence is available on the impact of smoking cessation interventions on complication risk following elective orthopedic surgery.
- One randomized controlled trial (RCT) reported a lower risk of wound-related complications among patients offered counseling and nicotine replacement therapy (NRT) before undergoing total knee arthroplasty or total hip arthroplasty, compared with usual care. Findings from 3 observational studies are at substantial 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 whether reduction in risk varies according to the duration and severity of tobacco use, timing of cessation relative to surgery, and/or use of NRT.
- Whether to require tobacco cessation in the immediate preoperative period 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 delay improvements to their quality of life without conferring a meaningful reduction in their surgical risks.

In a 2022 survey, 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. Professional societies including the American College of Surgeons recommend tobacco cessation prior to undergoing elective surgery to improve overall health and reduce the risk of surgical complications. In the case of elective orthopedic surgery, the American Academy of Orthopaedic Surgeons urges patients to quit smoking prior to surgery, citing tobacco use as a cause of poor wound healing, infection, and worse overall outcomes.

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. 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 aim of this review was to synthesize evidence on the effectiveness of preoperative smoking cessation interventions and use of nicotine replacement therapy (NRT) at reducing complication risk associated with elective orthopedic surgery.

From 265 potentially relevant articles, 1 randomized controlled trial (RCT) and 3 observational studies met eligibility criteria. The most informative study was an older RCT conducted in Denmark of 120 adult tobacco users undergoing total knee arthroplasty (TKA) or total hip arthroplasty (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). Without data from other trials, it is unknown whether a similar intervention would lead to the same benefit in populations with a higher burden of comorbidities.

The 3 observational studies we identified contribute little useful information to address the review question. A retrospective cohort study 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.

An additional limitation of available evidence is a lack of information on whether nicotine exposure in the form of NRT is an independent risk factor for worse outcomes. Participants in the smoking cessation groups of all 4 included studies were offered NRT, although no study reported whether or to what extent participants used NRT. In a study of adults undergoing anterior cervical discectomy and fusion, active tobacco use was associated with *lower* odds of dysphagia, which the authors speculated could have been due to the irritant effects of nicotine replacement products among participants in the smoking cessation group. However, no conclusions can be drawn regarding the effect of NRT based on this study. 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 other medications relative to the timing of surgery is needed to understand the effects of NRT on surgical outcomes (if any).

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. 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.

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 surgery¹ 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 vary⁴ 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](https://www.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	<i>Perioperative and postoperative complications:</i> 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

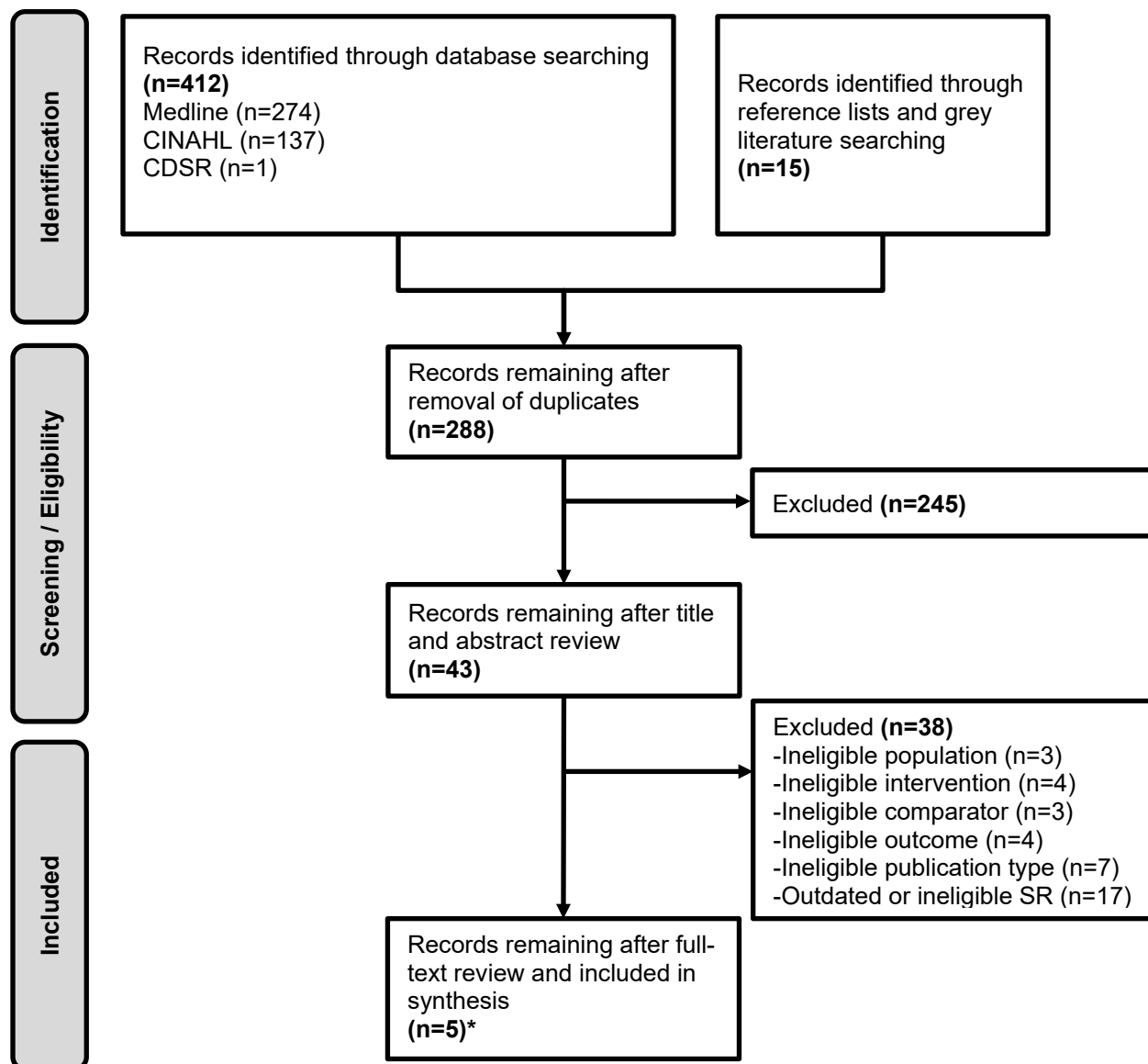
We synthesized available evidence narratively, grouping studies by surgery type. We planned to grade the strength of the evidence for each outcome based on the AHRQ Methods Guide for Comparative Effectiveness Reviews¹⁵ but did not do so because of extensive variation in surgery types and outcomes across 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 study¹⁸ included adults who underwent TKA or THA. The other 2 observational studies included patients who underwent spine surgery (single-level anterior cervical discectomy and fusion¹⁹ and single-level lumbar fusion²⁰). 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 58¹⁸ 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 study¹⁸ 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
<i>Hip and Knee Replacement</i>						
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 <i>Retrospective Cohort</i>	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
<i>Cervical and Lumbar Spine Surgery</i>						
Khalid 2022 ¹⁹ <i>Retrospective Cohort</i>	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 <i>Retrospective Cohort</i>	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 study¹⁸ 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 study¹⁸ 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 fusion¹⁹ 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 <i>Mortality</i>	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 <i>No deaths in either group</i>	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. ^aWound 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 study¹⁸ 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 review²¹ 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.

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APPENDIX A: SEARCH STRATEGY

SYSTEMATIC REVIEWS

1. Search for systematic reviews			
Date Searched: 10-20-22; updated 05-19-23			
A. Bibliographic Databases:	#	Search Statement	Results
MEDLINE: Systematic Reviews Ovid MEDLINE(R) ALL 1946 to October 19, 2022	1	exp Orthopedic Procedures/ OR (orthop?edic procedure\$ OR orthop?edic surger\$ OR orthop?edic operation\$ OR arthroplast\$ OR hip replacement\$ OR knee replacement\$ OR spine fusion\$ OR carpal tunnel\$ OR spine decompression\$ OR rotator cuff OR meniscectom\$ OR meniscal repair OR anterior cruciate ligament OR ACL OR finger replacement\$ OR joint replacement\$ OR joint implantation\$ OR ankle replacement\$ OR elbow replacement\$ OR shoulder replacement\$ OR spine surgery OR lumbar surgery OR spondylodes\$).ti,ab,kw.	452810
	2	Smoking Cessation/ OR exp "Tobacco Use Disorder"/ OR Smoking/ OR (smoking cessation OR nicotine patch OR nicotine polacrilex OR nicotine inhalant\$ OR nicotine device\$ OR nicotine nasal spray OR nicotine replacement\$ OR nicotine lozenge\$ OR smoking habit\$ OR smoking behavior\$ OR nicotine addiction\$ OR nicotine dependence\$ OR (nicotine disorder\$) OR (tobacco disorder\$) OR (smoking adj1 (quit OR quitting OR stop OR stopping or giving up))).ti,ab,kw.	190965
	3	1 and 2	1106
	4	(systematic review.ti. or meta-analysis.pt. or meta-analysis.ti. or systematic literature review.ti. or this systematic review.tw. or pooling project.tw. or (systematic review.ti,ab. and review.pt.) or meta synthesis.ti. or meta-analy*.ti. or integrative review.tw. or integrative research review.tw. or rapid review.tw. or umbrella review.tw. or consensus development conference.pt. or practice guideline.pt. or drug class reviews.ti. or cochrane database syst rev.jn. or acp journal club.jn. or health technol assess.jn. or evid rep technol assess summ.jn. or jbi database system rev implement rep.jn. or (clinical guideline and management).tw. or ((evidence based.ti. or evidence-based medicine/ or best practice*.ti. or evidence synthesis.ti,ab.) and (((review.pt. or diseases category/ or behavior.mp.) and behavior mechanisms/) or therapeutics/ or evaluation studies.pt. or validation studies.pt. or guideline.pt. or pmcbook.mp.)) or (((systematic or systematically).tw. or critical.ti,ab. or study selection.tw. or ((predetermined or inclusion) and criteri*).tw. or exclusion criteri*.tw. or main outcome measures.tw. or standard of care.tw. or standards of care.tw.) and ((survey or surveys).ti,ab. or overview*.tw. or review.ti,ab. or reviews.ti,ab. or search*.tw. or handsearch.tw. or analysis.ti. or critique.ti,ab. or appraisal.tw. or (reduction.tw. and (risk/ or risk.tw.) and (death or recurrence).mp.)) and ((literature or articles or publications or publication or bibliography or bibliographies or published).ti,ab. or pooled data.tw. or unpublished.tw. or citation.tw. or citations.tw. or database.ti,ab. or internet.ti,ab. or textbooks.ti,ab. or references.tw. or scales.tw. or papers.tw. or datasets.tw. or trials.ti,ab. or meta-analy*.tw. or (clinical and studies).ti,ab. or	584041

		treatment outcome/ or treatment outcome.tw. or pmcbook.mp.))) not (letter or newspaper article).pt.	
	5	3 and 4	59
	6	limit 5 to english language	59
CDSR: Protocols and Reviews	1	(Orthopedic Procedures).kw	14
EBM Reviews - Cochrane Database of Systematic Reviews 2005 to October 19, 2022	2	(orthopedic procedure\$ OR orthopedic surger\$ OR orthopedic operation\$ OR arthroplast\$ OR hip replacement\$ OR knee replacement\$ OR spine fusion\$ OR carpal tunnel\$ OR spine decompression\$ OR rotator cuff OR meniscectom\$ OR meniscal repair OR anterior cruciate ligament OR ACL OR finger replacement\$ OR joint replacement\$ OR joint implantation\$ OR ankle replacement\$ OR elbow replacement\$ OR shoulder replacement\$ OR spine surgery OR lumbar surgery OR spondylodes\$).ti,ab,kw.	149
	3	1 OR 2	149
	4	(Smoking Cessation OR "Tobacco Use Disorder" OR Smoking).kw.	122
	5	(smoking cessation OR nicotine patch OR nicotine polacrilex OR nicotine inhalant\$ OR nicotine device\$ OR nicotine nasal spray OR nicotine replacement\$ OR nicotine lozenge\$ OR smoking habit\$ OR smoking behavio?r\$ OR nicotine addiction\$ OR nicotine dependence\$ OR (nicotine disorder\$) OR (tobacco disorder\$) OR (smoking adj1 (quit OR quitting OR stop OR stopping or giving up))).ti,ab,kw.	124
	6	4 OR 5	140
	7	3 AND 6	1

2. Search for current systematic reviews

Date Searched: 10-20-22

B. Non-bibliographic databases	Evidence	Results
AHRQ: evidence reports, technology assessments, U.S Preventative Services Task Force Evidence Synthesis	http://www.ahrq.gov/research/findings/evidence-based-reports/search.html Search: (orthopedic surgery OR arthroplasty OR replacement) AND smoking	0
CADTH	https://www.cadth.ca Search: (orthopedic surgery OR arthroplasty OR replacement) AND smoking	0
HTA: Health Technology Assessments (UP TO 2016)	http://www.ohsu.edu/xd/education/library/ See CDSR search	0
EPPI-Centre	http://eppi.ioe.ac.uk/cms/Default.aspx?tabid=62	0

	Use browser search function [CNTL + F] for keyword search Search: smoking	
NLM	http://www.ncbi.nlm.nih.gov/books Search: (orthopedic surgery OR arthroplasty OR replacement) AND smoking	0
VA Products - VATAP, PBM and HSR&D publications	A. http://www.hsrd.research.va.gov/research/default.cfm B. http://www.research.va.gov/research_topics/ Search: (orthopedic surgery OR arthroplasty OR replacement) AND smoking	0
ClinicalTrials.gov (searched 05-19-23)	https://www.clinicaltrials.gov/ Search: (orthopedic surgery OR arthroplasty OR joint replacement OR finger replacement OR shoulder replacement OR ankle replacement OR elbow replacement OR knee replacement OR ACL) AND smoking Smoking Cessation Study Surgeon-Patient Communication: A Randomized Controlled Trial Evaluating the Impact of an Orthopaedic Related Smoking Cessation Discussion After Fracture Surgery Let's STOP Now Trial: Smoking in Trauma Orthopaedic Patients The Impact of Orthopaedic Smoking Cessation Education on Cigarette Abstinence Self-Efficacy: A Randomized Controlled Trial Smoking Cessation Intervention in Acute Orthopedic Surgery	5
3. Search for systematic reviews currently under development (includes forthcoming reviews & protocols) Date Searched: 10-20-22		
D. Under development:	Evidence:	Results:
AHRQ topics in development (EPC Status Report)	Email Charli Armstrong Charlotte.Armstrong1@va.gov Emailed on 10-20-22	0
PROSPERO (SR registry)	http://www.crd.york.ac.uk/PROSPERO/ (orthopedic surgery OR arthroplasty OR replacement) AND smoking cessation	0

PRIMARY STUDIES

4. Search for primary literature		
Date searched: 11-03-22; updated 05-19-2023		
MEDLINE [Ovid MEDLINE(R) ALL 1946 to November 02, 2022]		
#	Search Statement	Results
1	exp Orthopedic Procedures/ OR (orthop?edic procedure\$ OR orthop?edic surger\$ OR orthop?edic operation\$ OR arthroplast\$ OR hip replacement\$ OR knee replacement\$ OR spine fusion\$ OR carpal tunnel\$ OR spine decompression\$ OR rotator cuff OR meniscectom\$ OR meniscal repair OR anterior cruciate ligament OR ACL OR finger replacement\$ OR joint replacement\$ OR joint implantation\$ OR ankle replacement\$ OR elbow replacement\$ OR shoulder replacement\$ OR spine surgery OR lumbar surgery OR spondylodes\$).ti,ab,kw.	452810
2	Smoking Cessation/ OR (smoking cessation OR nicotine patch OR nicotine polacrilex OR nicotine inhalant\$ OR nicotine device\$ OR nicotine nasal spray OR nicotine replacement\$ OR nicotine lozenge\$ OR smoking behavio?r\$ OR (smoking adj1 (quit OR quitting OR stop OR stopping or giving up))).ti,ab,kw.	54598
3	1 and 2	236
4	limit 3 to English language	215
CINAHL [EBSCO CINAHL Plus with Full Text]		
#	Search Statement	Results
1	(MH "Orthopedic Surgery+") OR TI ((orthop?edic procedure\$ OR orthop?edic surger\$ OR orthop?edic operation\$ OR arthroplast\$ OR hip replacement\$ OR knee replacement\$ OR spine fusion\$ OR carpal tunnel\$ OR spine decompression\$ OR rotator cuff OR meniscectom\$ OR meniscal repair OR anterior cruciate ligament OR ACL OR finger replacement\$ OR joint replacement\$ OR joint implantation\$ OR ankle replacement\$ OR elbow replacement\$ OR shoulder replacement\$ OR spine surgery OR lumbar surgery OR spondylodes\$) OR AB ((orthop?edic procedure\$ OR orthop?edic surger\$ OR orthop?edic operation\$ OR arthroplast\$ OR hip replacement\$ OR knee replacement\$ OR spine fusion\$ OR carpal tunnel\$ OR spine decompression\$ OR rotator cuff OR meniscectom\$ OR meniscal repair OR anterior cruciate ligament OR ACL OR finger replacement\$ OR joint replacement\$ OR joint implantation\$ OR ankle replacement\$ OR elbow replacement\$ OR shoulder replacement\$ OR spine surgery OR lumbar surgery OR spondylodes\$))	157792
2	(MH "Smoking Cessation") OR TI ((smoking cessation OR nicotine patch OR nicotine polacrilex OR nicotine inhalant\$ OR nicotine device\$ OR nicotine nasal spray OR nicotine replacement\$ OR nicotine lozenge\$ OR smoking behavio?r\$ OR (smoking N1 (quit OR quitting OR stop OR stopping or giving up)))) OR AB ((smoking cessation OR nicotine patch OR nicotine polacrilex OR nicotine inhalant\$ OR nicotine device\$ OR nicotine nasal spray OR nicotine replacement\$ OR nicotine lozenge\$ OR smoking behavio?r\$ OR (smoking N1 (quit OR quitting OR stop OR stopping or giving up)))))	30384
3	1 AND 2	138
4	limit 3 to English language	137

APPENDIX B: EXCLUDED STUDIES

Exclude reasons: 1=Ineligible population, 2=Ineligible intervention, 3=Ineligible comparator, 4=Ineligible outcome, 5=Ineligible timing, 6=Ineligible study design, 7=Ineligible publication type, 8=Outdated or ineligible systematic review.

Citation	Exclude Reason
Cut it out sooner than later. <i>Nursing Review</i> (1173-8014). 2014;14(3):16-16.	E7
Akhavan S, Nguyen LC, Chan V, Saleh J, Bozic KJ. Impact of smoking cessation counseling prior to total joint arthroplasty. <i>Orthopedics</i> . 2017;40(2):e323-e328.	E4
Alamanda VK, Springer BD. The prevention of infection: 12 modifiable risk factors. <i>Bone & Joint Journal</i> . 2019;101-B(1_Supple_A):3-9.	E8
Beaupre LA, Hammal F, DeSutter C, Stiegelmar RE, Masson E, Finegan BA. Impact of a standardized referral to a community pharmacist-led smoking cessation program before elective joint replacement surgery. <i>Tobacco Induced Diseases</i> . 2019;17:14.	E4
Bishop JY, Santiago-Torres JE, Rimmke N, Flanigan DC. Smoking predisposes to rotator cuff pathology and shoulder dysfunction: A systematic review. <i>Arthroscopy</i> . 2015;31(8):1598-1605.	E8
Boylan MR, Bosco JA, 3rd, Slover JD. Cost-effectiveness of preoperative smoking cessation interventions in total joint arthroplasty. <i>Journal of Arthroplasty</i> . 2019;34(2):215-220.	E4
Chen J, Cui Y, Li X, et al. Risk factors for deep infection after total knee arthroplasty: A meta-analysis. <i>Arch Orthop Trauma Surg</i> . 2013;133(5):675-687.	E8
Davis EM, Notier AE, Douaihy A, et al. A telemedicine pathway to increase tobacco cessation in patients undergoing total joint replacement surgery. <i>NEJM Catalyst Innovations in Care Delivery</i> . 2021;2(3):1-1.	E4
Deguchi M, Rapoff AJ, Zdeblick TA. Posterolateral fusion for isthmic spondylolisthesis in adults: Analysis of fusion rate and clinical results. <i>Journal of Spinal Disorders</i> . 1998;11(6):459-464.	E2
Glassman SD, Anagnost SC, Parker A, Burke D, Johnson JR, Dimar JR. The effect of cigarette smoking and smoking cessation on spinal fusion. <i>Spine</i> . 2000;25(20):2608-2615.	E3
Grau L, Orozco FR, Duque AF, Post ZD, Ponzio DY, Ong AC. A simple protocol to stratify pulmonary risk reduces complications after total joint arthroplasty. <i>Journal of Arthroplasty</i> . 2019;34(6):1233-1239.	E2
Grønkjær M, Eliassen M, Skov-Ettrup LS, et al. Preoperative smoking status and postoperative complications: A systematic review and meta-analysis. <i>Ann Surg</i> . 2014;259(1):52-71.	E8
Iannotti F, Prati P, Fidanza A, et al. Prevention of periprosthetic joint infection (pji): A clinical practice protocol in high-risk patients. <i>Tropical Medicine & Infectious Disease</i> . 2020;5(4):11.	E7
Jackson KL, 2nd, Devine JG. The effects of smoking and smoking cessation on spine surgery: A systematic review of the literature. <i>Global Spine Journal</i> . 2016;6(7):695-701.	E8

Citation	Exclude Reason
Kainiemi K, Malmivaara A, Sillman-Tetri S, et al. Smoking cessation intervention prior to orthopedic surgery: A study protocol to determine patient outcomes and feasibility. <i>Tobacco Prevention & Cessation</i> . 2022;8:33.	E3
Kang J, Shi C, Gu Y, Yang C, Gao R. Factors that may affect outcome in cervical artificial disc replacement: A systematic review. <i>European Spine Journal</i> . 2015;24(9):2023-2032.	E8
Kanneganti P, Harris JD, Brophy RH, Carey JL, Lattermann C, Flanigan DC. The effect of smoking on ligament and cartilage surgery in the knee: A systematic review. <i>Am J Sports Med</i> . 2012;40(12):2872-2878.	E8
Kim JH, Patel S. Is it worth discriminating against patients who smoke? A systematic literature review on the effects of tobacco use in foot and ankle surgery. <i>Journal of Foot & Ankle Surgery</i> . 2017;56(3):594-599.	E8
Kozak E. A preoperative smoking intervention decreased postoperative complications in elective knee or hip replacement. <i>ACP Journal Club</i> . 2002;137(1):7-7.	E7
Kunutsor SK, Whitehouse MR, Blom AW, Beswick AD. Re-infection outcomes following one- and two-stage surgical revision of infected hip prosthesis: A systematic review and meta-analysis. <i>PLoS One</i> . 2015;10(9):e0139166.	E8
Kwon BK, Hilibrand AS, Malloy K, et al. A critical analysis of the literature regarding surgical approach and outcome for adult low-grade isthmic spondylolisthesis. <i>Journal of Spinal Disorders & Techniques</i> . 2005;18 Suppl:S30-40.	E8
Lambers Heerspink FO, Dorrestijn O, van Raay JJ, Diercks RL. Specific patient-related prognostic factors for rotator cuff repair: A systematic review. <i>J Shoulder Elbow Surg</i> . 2014;23(7):1073-1080.	E8
Lee MS, Jimenez AE, Owens JS, et al. Comparison of outcomes between nonsmokers and patients who discontinued smoking 1 month before primary hip arthroscopy: A propensity-matched study with minimum 2-year follow-up. <i>Orthopaedic Journal of Sports Medicine</i> . 2022;10(6):1-8.	E2
Lindstrom D, Sadr Azodi O, Wladis A, et al. Effects of a perioperative smoking cessation intervention on postoperative complications: A randomized trial. <i>Annals of Surgery</i> . 2008;248(5):739-745.	E1
Liu J, Hai Y, Kang N, Chen X, Zhang Y. Risk factors and preventative measures of early and persistent dysphagia after anterior cervical spine surgery: A systematic review. <i>European Spine Journal</i> . 2018;27(6):1209-1218.	E8
Mak JC, Fransen M, Jennings M, et al. Evidence-based review for patients undergoing elective hip and knee replacement. <i>ANZ Journal of Surgery</i> . 2014;84(1-2):17-24.	E8
Malay DS. Cigarette smoking and foot and ankle surgery. <i>Journal of Foot & Ankle Surgery</i> . 2011;50(5):515-516.	E7
Meng J, Sun T, Zhang F, Qin S, Li Y, Zhao H. Deep surgical site infection after ankle fractures treated by open reduction and internal fixation in adults: A retrospective case-control study. <i>International Wound Journal</i> . 2018;15(6):971-977.	E1
Murray EW. A preoperative smoking intervention decreased postoperative complications in elective knee or hip replacement. <i>Evidence Based Nursing</i> . 2002;5(3):84-84.	E7

Citation	Exclude Reason
Papas PV, Gold CA, Scuderi GR. The effects of smoking on postoperative complications after total joint arthroplasty. <i>Techniques in Orthopaedics</i> . 2019;34(3):183-186.	E7
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? <i>Arthroplasty Today</i> . 2023;19:101087.	E3
Pearson RG, Clement RG, Edwards KL, Scammell BE. Do smokers have greater risk of delayed and non-union after fracture, osteotomy and arthrodesis? A systematic review with meta-analysis. <i>BMJ Open</i> . 2016;6(11):e010303.	E8
Ring J, Shoaib A, Shariff R. Smoking cessation advice in limb reconstruction: An opportunity not to be missed. <i>Injury</i> . 2017;48(2):345-348.	E1
Santiago-Torres J, Flanigan DC, Butler RB, Bishop JY. The effect of smoking on rotator cuff and glenoid labrum surgery: A systematic review. <i>American Journal of Sports Medicine</i> . 2015;43(3):745-751.	E8
Sullivan JP, Huston LJ, Zajichek A, et al. Incidence and predictors of subsequent surgery after anterior cruciate ligament reconstruction: A 6-year follow-up study. <i>American Journal of Sports Medicine</i> . 2020;48(10):2418-2428.	E2
Truntzer J, Comer G, Kendra M, Johnson J, Behal R, Kamal RN. Perioperative smoking cessation and clinical care pathway for orthopaedic surgery. <i>JBJS Reviews</i> . 2017;5(8):e11.	E7
Verweij JP, Houppermans PN, Gooris P, Mensink G, van Merkesteyn JP. Risk factors for common complications associated with bilateral sagittal split osteotomy: A literature review and meta-analysis. <i>Journal of Cranio-Maxillo-Facial Surgery</i> . 2016;44(9):1170-1180.	E8
Zhu Y, Zhang F, Chen W, Liu S, Zhang Q, Zhang Y. Risk factors for periprosthetic joint infection after total joint arthroplasty: A systematic review and meta-analysis. <i>J Hosp Infect</i> . 2015;89(2):82-89.	E8

APPENDIX C: EVIDENCE TABLES

CHARACTERISTICS OF INCLUDED PRIMARY STUDIES

Experimental Studies

Author Year	Study Design Follow-up	Participant Characteristics Duration and Frequency of Smoking	Surgery Type	Intervention	Comparator
Moller 2002 ¹⁶ Moller 2003 ¹⁷ N=120	RCT 4 weeks	Mean age 65 42.59% male Race/ethnicity NR Pack years (smoking years X daily consumption): 35 years for intervention group, 37 years for control group. 15 cigarettes per day for both groups	Primary elective hip or knee alloplasty	Counseling and NRT	Standard care (little or no information about the risk of tobacco smoking or smoking cessation counseling)

Abbreviations. NR=not reported; NRT=nicotine replacement therapy; RCT=randomized controlled trial.

Observational Studies

Author Year	Study Design Follow-up	Participant Characteristics Duration and Frequency of Smoking	Surgery Type	Intervention	Comparator
Herrero 2020 ¹⁸ N=201	Retrospective cohort 90 days	Mean age 57.6 51.74% male 34.83% Black 45.77% White NR	Total joint arthroplasty	Smoking cessation program (assessment, education, counseling, NRT)	Patients who did not enroll in the voluntary smoking cessation program

Author Year N	Study Design Follow-up	Participant Characteristics Duration and Frequency of Smoking	Surgery Type	Intervention	Comparator
Khalid 2022 ¹⁹ N=5,769	Retrospective cohort 90 days	Median age between 50- 54 years 39.26% male Race/ethnicity NR NR	Single-level anterior cervical discectomy and fusion	Nicotine replacement (varenicline and/or nicotine gum, patches, and lozenges)	Patients with active smoking history
Khalid 2022 ²⁰ N=31,935	Retrospective cohort 30 days, 90 days, or 2.5 years	Median age between 45 and 64 years 39.58% male Race/ethnicity NR NR	Single-level lumbar fusion	Nicotine replacement (nicotine products or varenicline along with smoking cessation counseling)	Active smokers

Abbreviations. NR=not reported; NRT=nicotine replacement therapy.

OUTCOME DATA OF INCLUDED PRIMARY STUDIES

Experimental Studies

Author Year	Follow-up	Intervention	Complication Outcomes	Length of Stay Outcomes	Readmission/Revision Surgery Outcomes
Moller 2002 ¹⁶ Moller 2003 ¹⁷	4 weeks	NRT and counseling	Relative risk (95% CI) (below 1 favors intervention): Any complications 0.34 (0.17- 0.58) Wound-related complications 0.16 (0.05-0.52) Overall complication rate 18% for intervention group and 52% for control group ($p = 0.0003$). Wound-related complication rate 5% for intervention group and 31% for control group ($p =$ 0.001). Rates for other complication types were not significantly different between groups.	Median (range) length of stay 11 days (7-55) for intervention group and 13 days (8-65) for control group ($p = 0.41$)	Relative risk (95% CI): Secondary surgery 0.23 (0.05- 1.02) Rate of secondary surgery 4% for intervention group and 15% for control group ($p = 0.07$)

Abbreviations. CI=confidence interval; NRT=nicotine replacement therapy.

Observational Studies

Author Year	Follow-up	Intervention	Complication Outcomes	Length of Stay Outcomes	Readmission/Revision Surgery Outcomes
Herrero 2020 ¹⁸	90 days	Smoking cessation program	<p>Enrolled in SCP vs not enrolled: Infection rates 7.3% for SCP and 12.5% for non-SCP, $p = 0.27$</p> <p>Smoking vs quit (regardless of SCP enrollment): Infection rates 3.7% for quitters and 12.5% for smokers, $p = 0.03$</p>	<p>Enrolled in SCP vs not enrolled: Length of stay 2.47 days for SCP and 2.62 days for non-SCP, $p = 0.52$</p> <p>Smoking vs quit (regardless of SCP enrollment): Length of stay 2.5 days for quitters and 2.6 days for smokers, $p = 0.65$</p>	<p>Enrolled in SCP vs. not enrolled: Readmission rate 5.8% for SCP and 4.7% for non-SCP, $p = 0.73$</p> <p>Smoking vs. quit (regardless of SCP enrollment): Readmissions 4.9% for quitters and 9.2% for smokers, $p = 0.26$</p>
Khalid 2022 ¹⁹	90 days	Nicotine replacement	<p>Odds ratios (95% CI) for matched smoking vs smoking cessation cohort:</p> <p>Composite surgical complications 0.845 (0.705–1.014)</p> <p>Dysphagia 0.559 (0.330–0.947)</p> <p>Hematoma 1.589 (0.769–3.282)</p> <p>Pseudarthrosis 1.034 (0.724–1.479)</p> <p>Instrumentation removal 0.750 (0.495–1.136)</p>	NR	<p>Readmission within 30 days 1.000 (0.691–1.447)</p> <p>Readmission within 90 days 0.932 (0.705–1.231)</p> <p>Revision surgery 0.846 (0.726–0.988)</p>



Author Year	Follow-up	Intervention	Complication Outcomes	Length of Stay Outcomes	Readmission/Revision Surgery Outcomes
Khalid 2022 ²⁰	30 days, 90 days, or 2.5 years	Nicotine replacement	<p>Odds ratios (95% CI) for matched smoking vs smoking cessation cohort:</p> <p>Any complication 0.862 (0.804-0.925)</p> <p>Pseudoarthritis 1.041 (0.929-1.166)</p> <p>1,811 complications ('any complication') in smoking cessation group compared to 2,045 in smoking group ($p < 0.05$). Group differences non-significant for pseudoarthritis.</p>	NR	<p>Readmission within 30 days 1.026 (0.924-1.140)</p> <p>Readmission within 90 days 1.102 (1.005-1.207)</p> <p>Revision surgery 0.835 (0.694-1.001)</p> <p>Group differences non-significant for readmissions and revision surgery</p>

Abbreviations. CI=confidence interval; NR=not reported; SCP=smoking cessation program.

QUALITY ASSESSMENT OF INCLUDED PRIMARY STUDIES

RCTs – RoB 2 Tool

Author Year	Risk of Bias from Randomization Process	Risk of Bias from Deviation from Intended Interventions (Assignment)	Risk of Bias from Deviation from Intended Interventions (Adherence)	Risk of Bias from Missing Outcome Data	Risk of Bias in Measurement of Outcome	Risk of Bias in Selection of Reported Result	Overall Bias (High, Low, Some Concerns)
Moller 2002 ¹⁶ Moller 2003 ¹⁷	Low Participants randomly assigned using stratified block randomization and assignments were concealed using opaque sealed envelopes. Baseline differences between groups do not suggest a problem with the randomization process.	Low Cannot blind participants or providers. Conducted ITT analysis that included all participants randomized except for 12 whose operations were postponed or cancelled.	Unclear Information about adherence to the intervention is not reported.	Unclear ITT analysis was conducted, but extent and handling of missing data is unclear.	Low An assessor masked to the intervention recorded all complications.	Unclear Protocol not identified.	Some concerns

Abbreviations. ITT=intent to treat.

Observational Studies – ROBINS-I Tool for Cohort Studies

Author Year	Selection Bias	Bias in Classification of Interventions	Bias Due to Departures from Intended Intervention	Bias Due to Measurement of Outcomes	Bias Due to Confounding	Bias Due to Missing Data	Bias in the Selection of Reported Results	Overall Bias (Low, Moderate, Serious, Critical, No Information)
Herrero 2020 ¹⁸	Serious Included consecutive patients meeting criteria identified from a database during a specified period. However, referral to the SCP was recommended but not required of attending surgeons and not all patients were offered the intervention.	Low Groups clearly defined and status obtained from medical records.	Moderate All patients who enrolled in SCP were included in SCP group, and a substantial number enrolled did not complete the program.	Low Complication outcomes were assessed and recorded as part of routine care.	Moderate Information was collected on smoking characteristics of sample but was not accounted for in analyses. No significant differences between groups were found for demographic variables collected.	No Information Unclear level and handling of missing data.	Low No pre-study protocol but appears to report outcomes and analyses mentioned in methods section.	Serious

Author Year	Selection Bias	Bias in Classification of Interventions	Bias Due to Departures from Intended Intervention	Bias Due to Measurement of Outcomes	Bias Due to Confounding	Bias Due to Missing Data	Bias in the Selection of Reported Results	Overall Bias (Low, Moderate, Serious, Critical, No Information)
Khalid 2022 ¹⁹	Low Unclear if some characteristics used for matching/final selection were observed before or after start of NRT, but patients were matched exactly on these characteristics, but if bias exists, it seems likely to be non-differential.	Low Information on NRT prescription provided in medical record and documented at start of intervention.	No information Adherence not reported; no information on how frequently patients skipped prescribed medication, were prescribed NRT and then stopped taking it prior to 90 days, or were prescribed NRT within 90 days of surgery.	Low Outcomes reported as ICD codes; unlikely to have been influenced by knowledge of outcomes.	Moderate Exact matching likely reduces bias due to confounding but could be residual confounding for socioeconomic factors.	No Information Unclear level and handling of missing data.	Low No pre-study protocol but appears to report outcomes and analyses mentioned in methods section.	Moderate

Author Year	Selection Bias	Bias in Classification of Interventions	Bias Due to Departures from Intended Intervention	Bias Due to Measurement of Outcomes	Bias Due to Confounding	Bias Due to Missing Data	Bias in the Selection of Reported Results	Overall Bias (Low, Moderate, Serious, Critical, No Information)
Khalid 2022 ²⁰	Low Appear to include all patients meeting criteria identified from health records during a specified period in their initial cohort. Unclear if some characteristics used for matching/final selection were observed before or after start of NRT, but no indication that bias would be differential between groups.	Low Information on NRT use and smoking cessation counseling provided in medical record and documented at start of intervention.	No information No information provided on adherence to NRT or smoking cessation counseling.	Low Outcomes reported as ICD codes; unlikely to have been influenced by knowledge of outcomes.	Moderate Exact matching likely reduces bias due to confounding but could be residual confounding for socioeconomic factors.	No Information Unclear level and handling of missing data.	Low No pre-study protocol but appears to report outcomes and analyses mentioned in methods section.	Moderate

Abbreviations. ICD=International Classification of Diseases; NRT=nicotine replacement therapy; SCP=smoking cessation program.



APPENDIX D: SYSTEMATIC REVIEWS ON ORTHOPEDIC SURGERY COMPLICATION RISKS ASSOCIATED WITH TOBACCO USE

Author, Year Search Timeframe	Surgery Type	Exposure(s) and Comparator(s)	Included Studies and Total Number of Participants (N)	Relevant Outcomes	Main Findings
Hip					
Emara 2021 ³⁵ Jan 1985-Jan 2020	Hip arthroscopy	Smoking vs not smoking	4 prospective and 3 retrospective cohorts; N = 18,585	Complication rates and rates of revision arthroscopy and/or conversion to THA	Increased risk of VTE and infection with smoking. No difference in need for revision arthroscopy and/or conversion to THA.
Teng 2015 ²⁴ Inception through Aug 2014	THA	Smoking vs not smoking	4 retrospective and 2 prospective cohorts; N = 8,181	LOS after THA and prosthesis-related complications	Increased risk of aseptic loosening, deep infection, and all-cause revisions with smoking. No difference LOS after THA or the risk of implant dislocation.
Knee					
He 2022 ²⁵ Inception through Feb 2021	TKA	Smoking (current or former) vs never smoked	9 cohorts; N = 2,109,482	Surgical complications, pneumonia, need for blood transfusion, VTE, UTI, need for revision, total complications, and mortality	Increased risk of surgical complications (superficial and deep wound infections), pneumonia, need for revision, and total complications with smoking. No difference in VTE, UTI, or mortality.
Kong 2016 ²⁶ Inception through Feb 2016	TKA	Risk factors for infection including smoking vs absence of risk factors	4 observational studies (type NR); NR	SSI	Increased risk of infection with smoking.
Novikov 2016 ³⁶ Jan 1975-Feb 2016	ACL reconstruction	Smoking vs not smoking	5 observational studies (type NR); NR	Complications (infection, VTE), ipsilateral graft tear and contralateral ACL tear, need for early revision	Increased risk for infection, VTE, and ipsilateral graft tear with smoking.
Shoulder					
Fan 2022 ³⁷ Inception through Jan 2021	Patients who underwent arthroscopic or open rotator cuff repair	Smoking vs not smoking	6 cohort and 4 case series; N = 505 (retear risk) and N = 72,284 (reoperation risk)	Retears and reoperations	Increased risk for retear and reoperation with smoking.

Author, Year Search Timeframe	Surgery Type	Exposure(s) and Comparator(s)	Included Studies and Total Number of Participants (N)	Relevant Outcomes	Main Findings
Spine					
Kong 2017 ²⁷ <i>Inception through June 2016</i>	Spinal surgery including of the cervical, thoracic, lumbar, and sacral vertebrae	Smoking (current and former) vs never smoking	15 cohort and 11 case-control studies; N = 67,405	SSI	Increased risk of infection with smoking.
Li 2021 ³⁰ <i>Inception through Mar 2021</i>	Spinal fusion surgery including of the cervical, thoracic, lumbar, and sacral vertebrae	Smoking (variable definitions) vs not smoking	22 cohort and 4 case-control studies; N = 4,409	Fusion rate	Lower rates of spinal fusion with smoking.
Xing 2013 ²⁸ <i>Inception through Jun 2012</i>	Spinal surgery	Smoking vs not smoking	2 cohorts, 2 case-control studies; N = 858	SSI	Increased risk of infection with smoking.
Zheng 2022 ²⁹ <i>Inception through Jul 2021</i>	Cervical spine surgery	Smoking (variable definitions) vs not smoking	16 cohorts and 27 case-control studies; N = 10,020	Operating time, LOS, estimated blood loss, complications, fusion, and reoperation	Increased risk of respiratory complications, dysphagia, wound infection, and reoperation with smoking. No difference in operating time, LOS, estimated blood loss, or fusion.
Multiple					
Bedard 2019 ²¹ <i>Inception through Jan 2018</i>	THA or TKA	Current tobacco use (within 30 days before surgery), non-current tobacco use (past use but not in the 30 days before surgery), any history of tobacco use, and no history of tobacco use	14 observational studies (type NR); N = 227,289	Any wound complication and PJI	Increased risk of wound complications and PJI with any tobacco use compared to no use. Increased risk of PJI among current tobacco users compared to former tobacco users.
Kunutsor 2016 ²² <i>Inception through Sep 2015</i>	Primary or revision total joint arthroplasty (THA, TKA, total shoulder arthroplasty, total elbow arthroplasty, total ankle arthroplasty)	Smoking vs not smoking	8 observational studies (type NR); N = 20,689	PJI	Increased risk of PJI with smoking.

Author, Year Search Timeframe	Surgery Type	Exposure(s) and Comparator(s)	Included Studies and Total Number of Participants (N)	Relevant Outcomes	Main Findings
Singh 2011 ²³ <i>Inception through Mar 2010</i>	THA or TKA	Smoking (current or former) vs not smoking	15 cohort, 6 case- control studies; NR	Any postoperative complication, reoperation or revision, implant loosening, deep infections, mortality	Increased risk of complications and death among current and former smokers compared to non-smokers.

Abbreviations. ACL=anterior cruciate ligament; BMI=body mass index; NR=not reported; LOS=length of stay; OA=osteoarthritis; PJI=periprosthetic joint infection; RA=rheumatoid arthritis; SSI=surgical site infection; THA=total hip arthroplasty; TJA=total joint arthroplasty; TKA=total knee arthroplasty; UTI=urinary tract infection; VTE=venous thromboembolism.

APPENDIX E: PEER REVIEW DISPOSITION

Comment #	Reviewer #	Comment	Author Response
<i>Are the objectives, scope, and methods for this review clearly described?</i>			
1	3	Yes	None
2	4	Yes	None
3	5	Yes	None
4	7	Yes	None
5	8	Yes	None
<i>Is there any indication of bias in our synthesis of the evidence?</i>			
6	3	No	None
7	4	Yes - see comments	
8	5	Yes - See comment below. There was one sentence that sounded a little biased.	
9	7	No	None
10	8	No	None
<i>Are there any <u>published</u> or <u>unpublished</u> studies that we may have overlooked?</i>			
11	3	No	None
12	4	No	None
13	5	No	None
14	7	No	None
15	8	<p>Yes - It could be worth searching clinicaltrials.gov to comment on the presence or absence of ongoing clinical trials that could contribute to this literature in the next few years. If no relevant trials are currently being conducted, the absence of current trials would be worth including the report.</p> <p>This protocol paper describing a current trial might be worth briefly describing in the report: Kainiemi K, Malmivaara A, Sillman-Tetri S, Lasander M, Heinonen M, Korhonen T, Sand J, Laatikainen T, Kyrö A. Smoking cessation intervention prior to orthopedic surgery: A study protocol to determine patient outcomes and</p>	<p><i>Thank you for this suggestion. In response, we conducted a search of clinicaltrials.gov for ongoing trials and identified no ongoing trials that meet our criteria. We identified the Kainiemi 2022 protocol during our initial literature search. This study planned to include adults undergoing orthopedic surgery, regardless of smoking status, and all the tobacco users received the smoking cessation intervention. We excluded this study because the comparison group was not tobacco users who did not receive a smoking cessation intervention or alternate type of smoking cessation intervention.</i></p>

Comment #	Reviewer #	Comment	Author Response
		feasibility. Tob Prev Cessat. 2022 Aug 29;8:33. doi: 10.18332/tpc/152608. PMID: 36118614; PMCID: PMC9422999.	
<i>Additional suggestions or comments can be provided below. If applicable, please indicate the page and line numbers from the draft report.</i>			
16	3	This systematic review involves three important research questions: 1) What is the effect of smoking on orthopedic surgical complications? 2) What is the effect of smoking cessation on orthopedic surgical complications? and 3) What is the effect of FDA-approved NRT on orthopedic surgical complications? These questions are highly relevant for the field. The main focus of this ESP review is on the 2nd question and is the focus of Key Question 1. The first question is addressed but not until the end of the review; waiting until the end of the review is puzzling. The third question is implied or embedded in Key Question 1. I think it would be helpful if in the introduction there was an overview these three questions are being addressed in the review and how.	<i>Thank you for this comment. The Key Question of this systematic review was the effect of smoking cessation interventions on orthopedic surgical complications, including NRT. We did not synthesize evidence on the effect of smoking on orthopedic surgical complications in general, but thought that this background provided important context, which is why we included this information in the discussion. We did not discuss this background in depth in the introduction because we did not want to create confusion about the Key Question of the systematic review, which was specifically on the effect of smoking cessation interventions.</i>
17	3	The justification for how and why the vast majority of articles were excluded needs more explanation. When looking at the titles of the articles of those excluded, it seems like some would be appropriate for inclusion in this review. More detailed explanation is needed.	<i>Thank you for this comment regarding the exclusion of studies. Reasons for exclusion are provided in the literature flow diagram of the report (Figure 1) and in the list of excluded studies in the Supplementary Materials (Appendix B). Some studies were excluded because they looked at the effect of smoking on orthopedic surgery complications rather than the effect of smoking cessation interventions. Other studies did examine smoking cessation interventions but did not include a comparison group of tobacco users who received no intervention or an alternate intervention, or only examined outcomes related to smoking behaviors and not complications. We added this detail regarding excluded studies to the Methods section.</i>
18	3	With respect to smoking cessation and orthopedic surgical complications, the bottom line of this review concludes that the evidence is quite limited and more research is needed. On page 14, this ESP review seems to question the benefit of smoking cessation and whether or not smoking cessation	<i>Thank you for this suggestion. We agree that the overall benefits of tobacco cessation should be highlighted and not confused with the questions raised by this report. We have revised the</i>

Comment #	Reviewer #	Comment	Author Response
		<p>should be recommended prior to orthopedic surgery. However, this message is inconsistent with US national clinical practice guidelines and current evidence and I suspect not what the authors intend. A suggestion to address this is to consider this review in the context of the extensive existing literature and evidence (four clinical practice guidelines, multiple Surgeon General Reports) regarding the harmful effects of smoking on health and the beneficial effects of smoking cessation on health. Orthopedic surgical complications are only one set of outcomes and are short-term outcomes. Yes, the evidence regarding orthopedic surgical complications is limited. However, evidence of the beneficial effects of smoking cessation on health outcomes such as cardiovascular outcomes (e.g., reduced heart attack risk at one year), cancer risk, COPD, etc... are well-established. A surgical procedure represents an opportunity to advise and encourage a patient to quit smoking. US Public Health Service Tobacco Use guidelines recommend, at every clinical encounter, patients who smoke should be advised to quit and be offered smoking cessation assistance.</p>	<p><i>Discussion text accordingly and cite the 2020 US Surgeon General report.</i></p>
19	3	<p>For future research: consider recommending a comparative effectiveness trial of NRT versus non-nicotine treatment (e.g., varenicline) in order to assess whether nicotine in NRT is an independent risk factor for worse orthopedic surgical outcomes.</p>	<p><i>Thank you for this suggestion. We have added this suggestion to the future research section of the Discussion.</i></p>
20	4	<p>This is a well done and written manuscript. I agree with the concepts and conclusions.</p>	<p><i>Thank you for this comment.</i></p>
21	4	<p>The author's methodology is somewhat limited. Systematic reviews over broad policy tend to be more adaptable with numerous stakeholders input. For example, patients, endocrinology, pharmacists.</p>	<p><i>Thank you for this comment. We aimed to synthesize the available evidence related to this review's key questions. The process of creating clinical guidelines (which is not this review's purpose) often incorporates input from a variety of stakeholders. While we make a suggestion regarding how to apply the report's findings to clinical practice, we defer to VHA leadership to use this report to formally inform clinical guidance as appropriate.</i></p>

Comment #	Reviewer #	Comment	Author Response
22	4	<p>There is orthopedic surgeon in the author listing -this presents inherent bias in that the review of articles with limited by no clinical expertise on the subject matter</p> <p>Limiting to English language should be considered a limitation in the study design</p> <p>Why not contrast the positive effects of smoking cessation compared to complications for cessation?</p>	<p><i>Thank you for your comments on limitations of the review. While none of the report authors have a background in orthopedic surgery, the scope of this report was developed in consultation with representatives of the VHA National Surgery Office and peer reviewers include those practicing orthopedic surgery. We do not view the authors' backgrounds as a source of bias.</i></p> <p><i>Regarding limiting the search to English-language studies, while we agree that this limitation can be a concern, we think it is unlikely that we missed a study with high relevance to the review question and VHA population. Of note, we searched multiple databases and did not exclude any studies for non-English language.</i></p> <p><i>Regarding your last comment, we focused on surgical complications because whether tobacco cessation mitigates surgical complication risks was the key question of this review. We agree that tobacco cessation has many positive effects and have added text highlighting that point in the Discussion section.</i></p>
23	4	<p>I believe the terms used to define search are restricting the number of papers. Most orthopedic surgery is elective and often in the research papers/abstracts this word is not used (elective). In addition spine surgery is also done through neurologic surgery. Hand surgery with plastic surgeons... SO restricting to word orthopedics limits the articles for orthopedic procedures</p>	<p><i>Thank you for these comments on the search strategy. We did not require the term 'elective' to be present in our literature searches. In addition to search terms for 'orthopedic surgery,' we included search terms for specific procedures (see Appendix A of the Supplemental Materials).</i></p>
24	4	<p>In methodology why did you combine ortho procedures/smoking cessation with 4(systematic reviews....) does this not limit your set to 1 and 2 that are included in a review? (I maybe misunderstanding this)</p>	<p><i>Thank you for this question on the search strategy. Our search procedure involves first searching for systematic reviews ('part 1' of the search strategy in Appendix A) and then conducting a search for all study types. This search is described in 'part 4' of the search strategy.</i></p>

Comment #	Reviewer #	Comment	Author Response
25	5	This is a very well-written and conducted review. Thank you for inviting me to comment.	<i>Thank you for this comment.</i>
26	5	The background section is very well-written and provides excellent information on current recommendations and practices and their rationale. These sentences, in particular, are very helpful: "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."	<i>Thank you for this comment.</i>
27	5	The additional context on the association between tobacco use and surgical complications is helpful as are the findings from the VA's EXTEND QUERI project. On page 15 line 30, should that be "compared with patients not currently smoking or having an unknown smoking status?"	<i>Thank you for this comment. We have corrected the text to indicate that the VA EXTEND QUERI comparison was between current tobacco users and those not currently using tobacco or with an unknown smoking status.</i>
28	5	Page 15, line 37. I'm not following how the first 2 sentences lead to the conclusion "These observations suggest that restrictive policies...". I can see how the data in the review "suggest" this, but not necessarily the observations made between tobacco use (former and current) and complications.	<i>Thank you for this comment. We agree that the text starting "These observations suggest..." was not adequately supported by our summary of the evidence. We have revised the text in this section to be more explicit about what can and cannot be concluded from the available evidence and what questions remain.</i>
29	3	Page 15, lines 40-41: "Instead," Do we know this? Maybe tone down a bit to say: "It is unclear to what extent cessation requests or requirements may unintentionally..." This paragraph sounds a bit biased. The following sentence is great.	<i>Thank you for this comment. We agree that the text you refer to was not adequately supported by our summary of the evidence. We have revised the text in this section to be more explicit about what can and cannot be concluded from the available evidence and what questions remain.</i>
30	7	It appears that the literature search was limited to terms including orthopedic. While it is not known if a search for "orthopaedic" vs. "orthopedic" would result in additional articles for inclusion, this should be assessed. These are often used interchangeably and many societies/academies/associations use orthopaedic (e.g., The American Academy of Orthopaedic Surgeons (AAOS),	<i>Thank you for this comment regarding the search strategy. We agree that the alternate spelling should be included and updated our searches with inclusion of this term. We did not identify additional relevant studies.</i>

Comment #	Reviewer #	Comment	Author Response
		American Orthopaedic Association. If there is a reason it was limited to 'orthopedic', this should be mentioned.	
31	7	This study “Effects of a perioperative smoking cessation intervention on postoperative complications: a randomized trial” (David Lindström, Omid Sadr Azodi, Andreas Wladis, Hanne Tønnesen, Stefan Linder, Hans Näsell, Sari Ponzer, Johanna Adami) was excluded due to Ineligible Population (p 25); however, it does examine whether an intervention with smoking cessation starting 4 weeks before general and orthopedic surgery (hip or knee prosthesis) would reduce the frequency of postoperative complications. Was it not included because it was not solely focused on orthopedic surgery? If so, this should be noted.	<i>Thank you for this comment. You are correct that this study was excluded because it included patients undergoing surgery types other than orthopedic surgery and outcomes were not reported separately for patients who had orthopedic surgery who did and did not receive the smoking cessation intervention. We added further explanation of why we excluded studies to the Methods section (please also see the response to comment #17).</i>
32	7	There are times in the review that statements seem to be generalizing to all surgeries (for example, p 13, lines 46-54 when discussing NRT and surgical complications), not just elective orthopedic surgeries.	<i>Thank you for this comment. We edited text throughout the report to clarify that we are referring to elective orthopedic surgery rather than all surgeries.</i>
33	8	The eligibility table is generally clear, though the inclusion criteria could benefit from some additional context. The table lists a comparator as an eligibility criteria, but that could mean either 1) the study must have a comparator to be included in the review, or 2) the comparator must meet the eligibility criteria, but only if there is a comparator.	<i>Thank you for this comment regarding eligible comparators. We required that studies have a comparison condition, which could have been either a no-treatment comparison or an alternate intervention. We have added text to the criteria specifying that studies without a comparison condition were excluded.</i>
34	8	On page 15, lines 35-37, the statement about people who stopped smoking shortly before surgery could share a similar level of complication risk as people who continue smoking could be balanced by a statement that the lone trial testing this question found that those who stopped smoking had	<i>Although the text of this comment is incomplete, we assume that the comment suggested referring to the trial in Denmark finding a lower risk of wound-related complications among patients who quit smoking 6-8 weeks before elective knee and hip replacement. We agree with this point and have revised this section of the Discussion to highlight the findings of this trial.</i>
35	8	Though the report appropriately has a narrow focus on post-surgical complications, I suggest include some comment on the overall impact of smoking cessation on a Veteran’s health. Since tobacco use is the leading preventable cause of mortality, there is substantial value to the Veterans and to VHA of providing and encouraging	<i>Thank you for this comment. We agree and revised the Discussion text accordingly (please also see the response to comment #18).</i>

Comment #	Reviewer #	Comment	Author Response
		tobacco cessation treatment. In addition, it is noteworthy that major medical events like surgery have the potential to motivate patients to make a smoking cessation attempt that they had been considering.	
36	8	This report does a good job of noting the limitations of the small literature on pre-surgical smoking cessation interventions specifically. It also makes good recommendations about the type of trials that could most effectively inform the types of interventions that work best, and the duration of smoking abstinence typically required to confer benefit for reduced post-surgical complications.	<i>Thank you for this comment.</i>
37	8	Considering the evidence presented, the skepticism about the benefits vs. risks of requiring smoking cessation before surgery seems warranted. The risks of restricting access to surgery have to be weighed against the risks of smoking, especially when people often take many attempts over a long period of time before they are ultimately able to stop smoking. Alternatively, recommending smoking cessation and providing access to evidence-based smoking cessation aids still seems worthwhile from an overall risk vs. benefit perspective. I suggest adding a brief comment to the conclusions stating something about how smoking cessation provides substantial health benefits generally, though the current evidence is insufficient to conclude that smoking cessation shortly before orthopedic surgery results in reduced post-surgical complications. It's possible that clinical decision-makers could read the current conclusion as a recommendation to discou	<i>Thank you for this comment. We agree and have revised the text in this section to be more explicit about what can and cannot be concluded from the available evidence and what questions remain. We also highlight the benefits of tobacco cessation in general and importance of promoting tobacco cessation.</i>