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Smoking and Outcomes after Knee and Hip Arthroplasty: A Systematic Review

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Abstract

Background—Studies have suggested higher rates of peri- and post-operative complications in smokers compared to non-smokers. The objective of this systematic review was to assess the association of smoking and post-operative outcomes following total hip arthroplasty (THA) or total knee arthroplasty (TKA).

Methods—A search of six databases (*The Cochrane Library*, Scopus, Proquest Dissertation abstracts, CINAHL, OVID MEDLINE and EMBASE) was performed by a Cochrane librarian. All titles and abstracts were screened by two independent reviewers, with expertise in performing systematic reviews. Studies were included if they were fully published reports that included smoking and any prior post-operative clinical outcome in patients with either TKA or THA.

Results—21 studies were included for the review, of which six included multivariable-adjusted analyses, 14 univariate analyses and one statistical modeling. For most outcomes, results from 1-2 studies could be pooled. Current smokers were significantly more likely to have any post-operative complication (risk ratio, 1.24 [95% confidence interval, 1.01 to 1.54]) and death (risk ratio, 1.63 [95% confidence interval, 1.06 to 2.51]), compared to non-smokers. Former smokers were significantly more likely to have any post-operative complication (risk ratio, 1.32 [95% confidence interval, 1.05 to 1.66]) and death (risk ratio, 1.69 [95% confidence interval, 1.08 to 2.64]).

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Author Contributions: J.A.S. conceptualized and designed the study, requested search from the Cochrane librarian, reviewed abstracts and titles, abstracted data from all included studies, analyzed data, drafted and submitted the manuscript.

“The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs or the United States government.”

Conclusion—This systematic review finds that smoking is associated with significantly higher risk of post-operative complication and mortality following THA or TKA. Studies examining long-term consequences of smoking on implant survival and complications are needed. Smoking cessation may improve outcomes after THA or TKA.

Keywords

Smoking; arthroplasty; outcomes; Total knee arthroplasty; Total Hip Arthroplasty (THA)

INTRODUCTION

Total Knee and Total Hip Arthroplasty (TKA and THA) are very effective surgical treatment options for patients with refractory joint disease/arthritis that have failed to respond to conservative medical treatment. These procedures are performed mostly as elective procedures and are associated with reduction in pain and improvement in quality of life and lower extremity function¹⁻². Several patient-related factors such as age, gender and socioeconomic status impact the outcome of TKA/THA³⁻⁵. In addition, modifiable factors such as smoking, medical comorbidity and obesity may also impact these outcomes⁵⁻⁹. Identification of modifiable risk factors such as smoking is important, since pre-surgical smoking cessation interventions can improve outcomes of TKA/THA. Smoking has been shown to be as risk factor for non-union after spinal surgery¹⁰ and delayed bone healing after hemicallotasis, an orthopedic procedure to correct knee deformity¹¹. However, the association of smoking with risk of complications after THA/TKA has not been quantified.

The purpose of this study was to perform a systematic review of studies of smoking status and outcomes following TKA or THA to assess whether smoking is significantly associated with any complications following arthroplasty, and if so, which complications and to provide estimates for this risk. We also aimed to identify knowledge gaps.

METHODS

An experienced Cochrane librarian (L.F.) searched six databases in March 2010 using the key terms “knee hip arthroplasty/replacement”, “hip arthroplasty/replacement” AND “smoking” or “tobacco” (detailed search strategy in Appendix 1). All databases were searched from inception to March 2010 and included: (1) *The Cochrane Library*, Wiley InterScience (www.thecochranelibrary.com), to include the Cochrane Central Register of Controlled Trials (CENTRAL), Health Technology Assessment Database (HTA) and, Database of Abstracts of Reviews of Effects (DARE); (2) Scopus; (3) Proquest Dissertation abstracts; (4) CINAHL (via EBSCOHost); (5) OVID MEDLINE and; (6) EMBASE. Inclusion of these standard databases is recommended by the Cochrane Handbook of Systematic Reviews¹² and is similar to previously published Cochrane Systematic Reviews¹³⁻¹⁴; these relevant databases were chosen by an experienced Cochrane librarian (L.F.).

All titles and abstracts were screened by two independent reviewers (A.B., J.S.) with expertise in performing systematic reviews¹⁵⁻¹⁷. Studies were included if they were fully published reports that included smoking and any peri- or post-operative clinical outcome in

patients with either TKA or THA. Studies were excluded if they were abstracts, reviews or editorials, did not provide clinical outcomes data. Since this study aimed at assessing smoking as a risk factor for poor post-surgical outcomes, studies of smoking interventions were not included. A Cochrane systematic review of efficacy of smoking cessation interventions has been published¹⁸. Therefore we did not include these randomized studies, since the Cochrane review had combined multiple studies across several surgeries including but not limited to arthroplasty and had provided good estimates for smoking cessation interventions.

Each study was reviewed and pertinent data were extracted using a standardized data collection form. Study characteristics including the author, year of publication, number of patients, number of joints, patient demographics (age, race, gender, body mass index), follow-up duration, type of arthroplasty (hip versus knee versus both), type of study (cross-sectional, cohort), setting (single versus multi-center), population, definition of smoking exposure (duration; pack-years, defined as number of packs per day times number of years smoked) were extracted. .

Each included study was assessed for quality using the Newcastle-Ottawa scale for assessment of observational studies¹⁹. This scale is designed for quality assessment of observational studies with separate scales for case-control and cohort studies. Four points could be assigned for selection of appropriate cases/controls, two points for comparability of cases and controls and three points for adequacy of exposure assessment. The score can range from 0-9, with 9 representing the best quality score.

We planned to examine the studies for TKA and THA combined, since there was no reason to believe that post-operative complication risk would differ by the type of joint undergoing replacement. We had planned to analyze THA and TKA separately in subgroup analyses, in case significant heterogeneity was evident; however, due to lack of obvious heterogeneity and small number of studies available for quantitative analyses, we analyzed the groups together. We compared the number of patients with complications in each group and calculated the relative risk and 95% confidence interval (CI) using the Mantel- Haenszel method. A p-value <0.05 was considered statistically significant, which is similar to relative risk excluding unity.

We also calculated the number needed to harm (NNH) related to smoking as a risk factor. This represents the number of patients exposed to the risk (current smoking, former smoking) that leads to one extra patient with an unfavorable outcome (for example, death). This was calculated by obtaining the inverse of the absolute risk difference between current smokers and non-smokers and between former smokers and non-smokers, using the Cates calculator Visual Rx²⁰. Absolute risk difference was defined as the difference between risk in the treatment group and risk in the control group. The 95% CI for NNH was calculated by taking the inverse of the 95% CI of the absolute risk difference, where the lower 95% CI for absolute risk reduction becomes the higher 95% CI for NNH and vice versa.

RESULTS

Of these 516 titles and abstracts, 45 qualified for the full text review after duplicate independent review (Figure 1). Of these, 24 studies were excluded: 7 were reviews, commentaries or editorials ^{21-26,27}; 8 did not contain outcomes of interest or did not have smoking as a predictor ^{28-33,34,35}; 1 was related to economic outcome ³⁶; 1 was a qualitative study related to patient survey ³⁷; 1 thesis was not available for review ³⁸; 4 were related to smoking cessation ^{39-41,42}; 1 was a duplicate article ⁴³; and 1 was related to arthroscopy ⁴⁴. 21 studies from the original search met the inclusion and exclusion criteria and data were extracted from these. Of the 21 included studies 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65, 13 included patients with THA ^{45,49-54,56,59-63}, 4 with TKA ^{47,55,58,64}, 3 with patients THA or THA ^{46,48,57} and 1 was a statistical modeling exercise ⁶⁵. No additional studies were identified from the reference lists of included studies.

Overview of Epidemiology Studies

Table 1 summarizes demographic characteristics of patient populations in the included 21 observational studies 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65, of which one was a statistical modeling study ⁶⁵ (which provided no usable data). Most studies compared smokers to non-smokers, with few studies categorizing patients into former, current and non-smokers. Association of pack years (cumulative smoking exposure) with outcomes was reported in a few studies.

Table 2 provides a summary of the main findings from the study. We present data from studies that provided multivariable analyses ^{45,46,47,48,49,50,51} followed by those that performed univariate analyses ^{52,53,54,55,56,57,58,59,60,61,62,63,64}. The quality score for each study is based on the Newcastle-Ottawa scale (range, 0-9) provided in Table 2. In general, most studies with multivariable-adjusted analyses scores higher than those with only univariate analyses, although a wide range in scores was noted. This is followed by pooled estimates from these studies with calculation of number needed to harm (Table 3).

Observational Studies assessing Smoking as a risk factor- Multivariable-adjusted Analyses

This section summarizes studies that provided multivariable-adjusted analyses. Sadr Azodi et al. studied 3,309 patients with primary THA using the Swedish Inpatient register ⁴⁵. 373 of the 3309 patients (11%) developed one or more post-operative complications. Smoking was significantly associated with increase in risk of systemic complications. In multivariable-adjusted analyses, former and current smokers had significantly higher multivariable-adjusted odds of systemic complications compared to non-smokers, with odds ratios of 1.32 (1.04, 1.97) and 1.56 (1.14, 2.14), respectively. Higher number of pack years was significantly associated with systemic complications. Patients who smoked >40 pack years were significantly more likely than non-smokers to have systemic complications with Odds ratio of 2.21 (1.28, 3.82). Those smoking 0-19.9 pack years were not significantly associated with systemic complications compared to non-smokers with odds of 1.35 (0.99, 1.84).

Lavernia et al. compared hospital charges following primary or revision THA or TKA between former, current and non-smokers ⁴⁶. Smoking was a significant predictor for charges ($p=0.03$), operative time ($p=0.01$) and anesthesia time ($p=0.003$). Fisher et al. found that smoking was protective and associated with lower risk of painful/stiff knee in 71 patients who underwent TKA ⁴⁷. Moller et al. performed an observational study of 811 patients with THAs or TKAs ⁴⁸. Analyses were adjusted for age, gender, BMI, ASA class, comorbidity, surgery type, anesthesia duration, surgery duration and alcohol use. Smoking was significantly associated with higher risk of any complication, OR, 3.2 (95% CI, 1.8 to 6.0); wound complication OR, 8.5 (95% CI, 1.6 to 47); and ICU admission, OR, 2.4 (95% CI, 1.4 to 3.8).

Espehaug studied 536 patients who had undergone a primary and revision THA (cases) and 1,092 patients who had undergone primary THA only (controls) ⁴⁹. Smoking was categorized as current, former and non-smokers and pack years were collected. Overall, neither former nor current smoking was associated with increased with revision. Former heavy smokers (≥ 12 pack years) had significantly higher risk of revision with odds ratio of 2.6 (95% confidence interval, 1.5 to 4.4). These associations did not change after adjustment for alcohol intake, occupation, weight and height. Sadr Azodi et al. studied 2,106 patients who underwent THA using Swedish Inpatient Register ⁵⁰. In multivariable analyses that adjusted for age, calendar period, BMI and fixation, there was no significant association of smoking status or pack years of smoking and risk of implant dislocation up to 3 years after the primary THA. Meldrum et al. compared outcomes in 147 patients undergoing THA ⁵¹. In multivariable models adjusted for age, gender, BMI, diagnosis, stem fixation and alcohol use, smoking had a non-significant borderline association with higher revision rates with a hazard rate of 4.5 ($p=0.006$).

Observational Studies assessing Smoking as a risk factor- Univariate Analyses

All remaining studies used univariate analyses, i.e., the association of smoking with the outcomes were not adjusted for important confounders. Bischoff-Ferrari et al. studied the predictors of poor functional status defined as WOMAC score <50 a sample of Medicare recipients 3-years after THA ⁵². In univariate analyses, current smoking was not associated with poor functional status with odds ratio for being 0.8 (0.3-2.0) ⁵². Anderson et al. examined the predictors of post-operative complications including venous thromboembolism (VTE) in patients undergoing THA ⁵³. Smoking was not associated with risk of VTE. Beksac et al. studied the risk of venous thromboembolism in 1947 patients undergoing elective THA at a single medical center ⁵⁴. Smoking was not a significant risk factor for loosening in uni- or multi-variable models ($p=0.1$ and 0.3 , respectively). Sharrock et al. found no association of smoking and deep venous thrombosis in 458 patients who underwent cemented TKA ⁵⁵. Horne et al. found that smoking was not associated with risk of infection after TKAs in their study of 40 patients ⁵⁶. Malinzack examined the infection rate in 17,561 total joint replacements ⁵⁷. Smoking was not a significant correlate of postoperative wound infections.

Cates et al. examined the factors predictive of results of closed manipulation following TKA ⁵⁸. Smoking was not associated with any improvement in 1-year flexion or 1-year

extension following closed manipulation. Grosflam et al. found that smoking status was not a significant predictor of intra-operative blood loss in 295 patients undergoing primary elective THA ⁵⁹. Inoue et al. examined 151 THAs in 130 patients ⁶⁰. There was no significant association of smoking and implant loosening OR, 0.30 (0.06 to 1.52). In a study, 127 patients with cemented THA were surveyed regarding smoking status by Nixon et al. ⁶¹. Active smoking was not associated with loosening with odds ratio of 5.5 (0.8, 38) ⁶¹. Khan et al. studied 1767 patients undergoing THA followed up to 5 years ⁶². Smoking was not associated with deep infection, OR, 3.4 (0.7 to 17.2); superficial infection, OR, 1.0 (0.5 to 1.8) and revision, OR, 0.8 (0.1 to 2.6). Malik et al. found no association of smoking and aseptic loosening in 224 patients who underwent cemented THA ⁶³.

In a retrospective single-center study by Peersman et al., 113 infections were identified in 6489 TKA ⁶⁴. Smoking was reported to be significantly associated with the risk of infection following TKA ($p=0.01$). .

Pooled Estimates of Risk and Number needed to harm (NNH)

Table 3 provides the overall risk ratios for five main post-operative outcomes comparing current and former smokers to non-smokers. Compared to non-smokers, the current smokers had a 24% higher risk of any postoperative complication and former smokers a 32% higher risk. Similarly, the risk of death at 3-year follow up was 63% higher in current smokers and 69% higher in former smokers, with data from one study. The NNH for various complications are shown in Table 3.

Knowledge Gap analysis

We found that several studies of small sample size have assessed the association of smoking with complications after THA/TKA. Most studies performed univariate analyses and therefore residual confounding due to other important factors is an important limitation of these studies. Very few studies had long-term follow-up beyond 5-10 years to assess risk of revision surgery after THA/TKA. A majority of studies did not explicitly define the complication. We noted that very few studies investigated the association of duration of smoking exposure and the current amount of smoking with various postoperative complications. Several complications such as gastrointestinal complications, admission to the intensive care unit, reintubation, poor function and pain and quality of life outcomes after arthroplasty have not been studied well. Health care costs and resource utilization outcomes were also rarely studied as related to smoking.

DISCUSSION

In summary, we found that compared to non-smokers, current smokers and former smokers had 24% and 32% higher risk of any post-operative complication after THA/TKA. Similarly, the risk of death was 62% higher in current smokers and 69% higher in former smokers 3-years after THA/TKA, compared to non-smokers. These estimates are helpful guides to the providers in their discussions with patients undergoing THA or TKA regarding smoking related risks. In conjunction with findings from a recent Cochrane systematic review of efficacy of intensive preoperative smoking cessation interventions in reducing any

complication and surgical site infections¹⁸, this observation has significant implications. Patients can be informed that their risk of post-operative complications is significantly increased by smoking and that quitting smoking can significantly reduce risk of these preventable complications. This can provide patients with a convincing argument to consider quitting smoking. The benefits of smoking cessation are particularly greater in those with an intensive program (starting 4-8 weeks preoperative with at least one face-to-face interaction weekly), compared to shorted, less intensive programs¹⁸. Clinicians have viewed peri-operative period as a “teachable moment” and “window of opportunity” to motivate patients to quit smoking⁶⁶. Since >95% of joint arthroplasty surgeries are elective, this also provides for meaningful discussion with the patient and enough time in most cases to implement an intensive tobacco cessation program. Of course, the short- and long-term benefits of smoking cessation on cardiac, pulmonary and overall health will then be realized, if patients can stay quit after their joint replacement surgery.

Implications for Clinical Practice

The increased risk for mortality among current and former smokers is particularly impressive and concerning, considering that the post-operative mortality in all-comers for THA/TKA is extremely low, <1% at 90-days⁶⁷. Since smokers have a significantly increased risk of mortality, this risk merits a discussion with all smokers planning to undergo elective knee or hip arthroplasty. There are no data to-date that have shown difference in peri-operative mortality in patients quitting smoking pre-operatively, however, such a study may require tens of thousands of patients to detect differences in mortality, since the baseline risk of mortality is low in all-comers. Even in absence of such data, with the current knowledge of increased risk of mortality with smoking and all other negative health effects of smoking, it seems prudent to discuss smoking cessation interventions prior to joint arthroplasty with the patients. The NNH of 34-50 for current and former smokers for immediate postoperative complication and 34 for death at 3-years can be interpreted by comparing to NNH from other studies. For example, using the data from the Women’s Health Initiative (WHI)⁶⁸⁻⁶⁹, the NNH with hormone replacement therapy was 1,250 for stroke and 1,250 for pulmonary embolism after 1 year of treatment and 238 for breast cancer after 5.2 years of treatment. Thus smoking in the perioperative period is a significant risk factor for poor outcomes and offers a potential target for intervention.

In our review of observational studies in patients with THA or TKA, a higher complication rate was noted in smokers. Current smokers and former smokers were both at higher risk than never smokers. We did not observe a linear trend of risk from never smokers, former smokers to current smokers; however most of the pooled data for any postoperative complication and death for these categories are based on 1-2 studies. Thus, more data are needed to examine differences in risk between former and current smokers, since current smokers tend to be a younger cohort than never smokers and former smokers due to survival disadvantage and confounding bias can lead to falsely lower unadjusted rates in current smokers. Although, there is some suggestion, further studies should examine whether there is a clear dose relationship with amount of smoking (pack-years) and outcomes.

The evidence for the association of smoking with post-operative outcomes were derived from several studies that were multivariable-adjusted⁴⁵⁻⁵⁰ with few univariate analyses^{43,51-63}. Multivariable adjusted analyses also showed association of smoking with higher resource utilization among former smokers and current smokers compared to non-smokers and were mostly of higher quality compared to univariate analyses. Therefore the evidence must be interpreted considering the study quality, with more confidence in evidence emerging from higher-quality studies.

Implications for Research

Our study highlights that several knowledge gaps exist in this area. The evidence from included studies is suggestive but not conclusive that smoking is associated with poor post-surgical outcomes in patients undergoing THA or TKA. Most studies performed to date had small sample size and smoking exposure as a risk factor was measured differently (current, former and never smoker is some and smoker versus non-smoker in others). Few studies examined pack years to examine the dose relationships. Due to lack of data, it is unknown, whether smoking is associated with long-term implant-related complications. Future studies needed to address these knowledge gaps.

Conclusions

In conclusion, we performed a systematic review of the literature regarding smoking and postoperative complications following elective THA or TKA. We found that smoking is a risk factor for higher post-operative complications and post-operative mortality. The number of pack years also seems to be related to risk of these complications. More research is needed to further examine the association of smoking with other post-operative complications, including cardiac and pulmonary complications, prosthetic loosening and infection in patients undergoing THA or TKA. Research is also needed to study the most optimal time for quitting smoking pre-operatively and assess its impact on these immediate post-operative and late outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Flow chart of included studies

Table 1

Patient characteristics of included studies

Study	#patients/ #joints	Single- vs. multi- center	Age (yrs)	%female	% Caucasian	BMI (kg/m ²)	Follow-up duration	Comments
Sadr Azodi 2006 ⁴⁵	3,309 pts, THA	Swedish Inpatient register	66	0% (all men)	--	26	During post- op hospitalization period	
Lavemia 1999 ⁴⁶	203 pts/203 THAs or TKAs (primary or revision)	Single	66	62%	--	--	Hospital stay	
Fisher 2006 ⁴⁷	71 pts/71 TKAs (148 controls)	Single	64	--	--	34	1-year	
Moller 2003 ⁴⁸	811 pts/811 THAs or TKAs	Multicenter	71	--				
Espehaug 1997 ⁴⁹	674 primary THAs; 1,343 controls	Norwegian register- based	67	57%	--	--	Unclear	
Sadr Azodi 2008 ⁵⁰	2,106 THA patients	Swedish Inpatient register	55% 65 years	0% (all men)	--	30% 30 kg/m ²	Up to 8 years or 2004	
Meldrum 2005 ⁵¹	147 pts/165 THAs	Single	61	54%	--	28	Unclear	
Bischoff- Ferrari 2003 ⁵²	THA; 933 pts.,	Medicare, multiple centers	73	60%	97%	25% >30 kg/m ²	Unclear	
Anderson 1979 ⁵³	101 pts/101 THAs	Single	85% >50 years	58%	--	--	Unclear	
Beksac 2006 ⁵⁴	1947 pts /2032 THAs	Single	--	--	--	--	3 months	
Sharrock 1993 ⁵⁵	448 pts/448 TKAs	Single	68	--	--	--	Hospital stay	
Horne 2008 ⁵⁶	40 pts/40 TKAs (352 controls)	Single	--	--	--	--	Unclear, 76- months	

Study	#patients/ #joints	Single- vs. multi- center	Age (yrs)	%female	%Caucasian	BMI (kg/m ²)	Follow-up duration	Comments
Malinzack 2006 ⁵⁷	17,561 pts/ 17,561 THAs or TKAs	Single	--	--	--	--	Unclear	
Cates 2009 ⁵⁸	37 pts/ 37 TKAs	Single	--	--	--	--	1-year	
Grosflam 1995 ⁵⁹	295 pts/295 THAs	Single	64	63%	97%	--	Hospital stay	
Inoue 1999 ⁶⁰	130 pts/ 151 THAs	Single	62	85%	--	--	2 years	
Nixon 2007 ⁶¹	127 pts/ 127 THAs	Single	69	64%	99%	--	8 years	78 cases, 49 controls
Khan 1999 ⁶²	1767 pts/ 1767 THAs	Single	69	64%	--	--	5-years	
Malik 2004 ⁶³	224 pts/ 224 THAs	Single	69	58%	--	--	6 years	143 controls
Peersman 2001 ⁶⁴	6120 pts/ 6489 TKAs-	Single	--	--	--	--	Unclear, ? 3 months	113 pts with 113 infected TKAs/ 226 controls

Table 2

Summary of Findings from included Observational studies

Study, year	# patients, THA or TKA or both	Type of study/ Quality score	Population/ setting	Smoking definition	Covariates included	Finding
Multivariable-adjusted analyses						
Sadr Azodi 2006 ⁴⁵	3,309 pts, THA	Observational, cohort study Score: 7	Swedish Arthroplasty Register	Former, current and non-smoker; pack years of smoking	Age, calendar period, region, diabetes, heart failure, lung disease, stroke, BMI, tobacco-related	Multivariable: Compared to non-smokers, significantly higher risk of systemic complications in: Former smokers, OR, 1.32 (95% CI, 1.04 to 1.97); Current smokers OR, 1.56 (95% CI, 1.14 to 2.14). >40 pack years OR, 2.21 (95% CI, 1.28 to 3.82).
Lavernia 1999 ⁴⁶	203 pts/203 THAs or TKAs (primary or revision)	Observational cohort Score: 9	Single center	Former, current and non-smoker; pack years of smoking	Age, gender, BMI, diagnosis, surgeon, procedure, comorbidities	Multivariable: Smoking was a significant predictor for charges (p=0.03), operative time (p=0.01) and anesthesia time (p=0.003).
Fisher 2006 ⁴⁷	71 pts/71 TKAs (148 controls)	Observational case-control study Score: 4	Single center	Smoking: yes/no	Gender, arthrotoomy, disabled, diabetes, chronic lung disease, retired	Multivariable: Smoking associated with LOWER risk of painful/stiff knee- OR, 0.26 (p-value = 0.049)
Moller 2003 ⁴⁸	811 pts/811 THAs or TKAs	Observational cohort study Score: 9	Single center	Smoking: Current smoker vs non-smoker (included prior surgery smokers)	Age, gender, BMI, ASA class, comorbidity, surgery type, anesthesia duration, surgery duration, alcohol use	Multivariable: Smoking was significantly associated with higher risk of any complication, OR, 3.2 (95% CI, 1.8 to 6.0); wound complication OR, 8.5 (95% CI, 1.6 to 47); and ICU admission, OR, 2.4 (95% CI, 1.4 to 3.8)
Espehaug 1997 ⁴⁹	674 primary THAs; 1,343 controls	Observational, matched case-control Score: 8	Norwegian Arthroplasty Register	Smoking: never, former, current	Antibiotic, cement, prosthesis brand; matched for age, operation date, bilaterality	Multivariable: Neither former nor current smoking associated with increased with revision; Former heavy smokers (12 pack years) significantly increased risk of revision: OR, 2.6 (95% CI: 1.5 to 4.4).

Study, year	# patients, THA or TKA or both	Type of study/ Quality score	Population/ n/setting	Smoking definition	Covariates included	Finding
Sadr-Azodi 2008 ⁵⁰	2,106 THA patients	Observational, cohort study Score: 7	Swedish Inpatient Register	Former, current and non-smoker; pack years of smoking	Age, calendar period, BMI, fixation	Multivariable: No significant association of smoking status or pack years of smoking and risk of implant dislocation up to 3 years after the primary THA
Meldrum 2005 ⁵¹	147 pts/165 THAs	Observational, cohort study Score: 8	Single center	Smoking: yes/no	Age, gender, BMI, diagnosis, stem fixation, alcohol use	Multivariable: Smokers with nonsignificantly higher hazard rate of revision than non-smokers, 4.5 (p=0.066)
Univariate Analyses						
Bischoff-Ferrari 2003 ⁵²	922 pts/922 primary THAs	Observational, Cohort study Score: 8	Stratified random Medicare sample	Current smoking: yes/no	N/A	Univariate: poor functional status in Smokers vs. non-smokers: OR, 0.8 (95% CI: 0.3 to 2.0)
Anderson 1979 ⁵³	101 pts/101 THAs	Observational cohort study Score: 6	Multicenter	Smoking: yes/no	Univariate	Univariate: Smoking not associated with risk of venous thromboembolism
Beksac 2006 ⁵⁴	1947 pts, 2,032 THAs	Observational, cohort study Score: 4	Hospital for Special Surgery database	Smoking: yes/no	N/A	Univariate: No significant association of smoking and venous thromboembolism up to 3-months post-THA
Sharrock 1993 ⁵⁵	448 pts/448 TKAs	Observational cohort study Score: 5	Single center	Smoking: yes/no	Univariate	Univariate: Smoking not associated with risk of deep vein thrombosis
Horne 2008 ⁵⁶	392 pts/392 TKAs	Observational case-control study Score: 4	Single center	Smoking: yes/no	N/A	Univariate: Smoking was not associated with risk of infection following TKA: OR, 1.6 (95% CI, 0.3 to 6.3; p-value=0.46)
Malinzack 2006 ⁵⁷	17,561 pts/17,561 THAs or TKAs	Observational cohort study Score: 5	Single center	Smoking: yes/no	Univariate	Univariate: Smoking not associated with risk of infection
Cates 2009 ⁵⁸	37 pts/37 TKAs	Observational cohort study Score: 6	Single center	Smoking: yes/no	Univariate	Univariate: Smoking not associated with flexion or extension gain at 1-year post-manipulation
Grofflam 1995 ⁵⁹	295 pts/295 THAs	Observational cohort study Score: 7	Single center	Smoking: yes/no	Univariate	Univariate: Smoking not associated with total blood loss intra-operatively
Inoue 1999 ⁶⁰	130 pts/151 THAs	Observational cohort study Score: 5	Single center	Smoking: yes/no	Univariate	Univariate: Smoking not associated with early implant loosening, OR 0.30 (95% CI, 0.06 to 1.52; p=0.15)

Study, year	# patients, THA or TKA or both	Type of study/ Quality score	Population n/setting	Smoking definition	Covariates included	Finding
Nixon 2007 ⁶¹	127 pts, 127 THAs	Observational, case-control study Score: 5	Single center, UK hospital-based cohort	Active smokers: yes/no	Univariate	Univariate: Among those with loosening of implant, more active smokers (8/59) than that among those with stable implants (1/26) (OR, 5.5 (95% CI, 0.8 to 38); p=0.08)
Khan 1999 ⁶²	1767 pts/ 1767 THAs	Observational cohort study Score: 7	Single center	Smoking: yes/no	Univariate	Univariate: Smoking not associated with risk of superficial infection, OR, 1.0 (0.5 to 1.8), deep infection, OR, 3.4 (0.7 to 17.2) or revision, OR, 0.8 (0.1, 2.6)
Malik 2004 ⁶³	224 pts/ 224 THAs	Case-control study Score: 7	Single center	Former, current and non-smokers	Univariate	Univariate: Smoking not associated with implant loosening at 6-year follow-up
Peersman 2001 ⁶⁴	6120 pts, 6489 TKAs- 113 infected TKAs in 113 pts	Observational, case control study Score: 4	Single center	Smoking: yes/no	N/A	Univariate: Smoking associated with risk of infection following TKA (p=0.01)

^a Quality scores were calculated using the Ottawa-Newcastle score system designed for observational studies with separate scales for case-control and cohort studies; Studies can be awarded four points for selection of cases/controls, two points for comparability of cases and controls and three points for exposure assessment. The score ranges from 0-9, with 9 representing the best quality score.

OR, Odds ratio; 95% CI, 95% confidence interval; N/A, not applicable

THA, Total Hip Arthroplasty; TKA, Total Knee Arthroplasty; O.A, osteoarthritis, F, female; M, male; Prim, primary; Rev, revision

Table 3
Postoperative outcomes following Total Hip Arthroplasty comparing current and former smokers to non-smokers

	Current smoker			Prior smoker		
	#studies/ #patients	Relative Risk (95% CI)	Number needed to harm (95% CI)	#studies/ #patients	Relative Risk (95% CI)	Number needed to harm (95% CI)
Reoperation or revision	4 studies ^a / 4,000 patients	1.14 [0.62, 2.10]	∞ (NE)	3 studies ^f / 4,180 patients	1.17 [0.84, 1.63]	100 (NE)
Implant loosening	2 studies ^b / 238 patients	1.25 [0.97, 1.62]	34 (NE)	1 study ^g /200 patients	1.16 [0.83, 1.63]	50 (NE)
Any post-operative complication	2 studies ^c / 2,512 patients	1.24 [1.01, 1.54]	50 (20, ∞)	1 study ^h /2,221 patients	1.32 [1.05, 1.66]	34 (17, 100)
Deep Infections	1 study ^d / 1,185 patients	3.42 [0.69, 16.85]	100 (NE)	1 study ⁱ /1,499 patients	3.68 [0.95, 14.16]	100 (NE)
Death	1 study ^e / 1,539 patients	1.63 [1.06, 2.51]	34 (20, 100)	1 study ^j /1,400 patients	1.69 [1.08, 2.64]	34 (20, 100)

RR, relative risk; 95% CI, 95% confidence interval; Number needed to harm, calculated as = 1/absolute risk reduction; NE, confidence interval not estimable since 95% confidence interval includes both positive and negative numbers

^aData from 4 studies: Espehaug 1997 [42], Sadr Azodi 2008 [43], Khan 1995 [54], Meldrum 2005 [56]; Espehaug 1997 [42] and Sadr Azodi 2008 [43] were multivariable-adjusted; Khan 1995 [54] and Meldrum 2005 [56] were univariate analyses

^bData from 2 studies: Malik 2004 [55] and Nixon 2007 [53], both univariate studies

^cData from 2 studies: Sadr Azodi 2008 [43] (multivariable-adjusted), Meldrum 2005 [56] (univariate)

^dData from 1 study: Khan 1995 [54] (univariate)

^eData from 1 study: Sadr Azodi 2008 [43] (multivariable-adjusted)

^fData from 3 studies for re-operation: Espehaug 1997 [42], Sadr Azodi 2008 [43], Khan 1995 [54]; Espehaug 1997 [42] and Sadr Azodi 2008 [43] were multivariable-adjusted; Khan 1995 [54] included univariate analysis

^gData from 1 study: Malik 2004 [55] (univariate)

^hData from 1 study: Sadr Azodi 2008 [43] (multivariable-adjusted)

ⁱData from 1 study: Khan 1995 [54] (univariate)

^jData from 1 study: Sadr Azodi 2008 [43] (multivariable-adjusted)