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

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ABSTRACT. Objective. Studies have suggested higher rates of perioperative and postoperative complications in smokers compared to nonsmokers. The objective of this systematic review was to assess the association of smoking and postoperative outcomes following total hip arthroplasty (THA) or total knee arthroplasty (TKA).

Methods. A search of 6 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 2 independent reviewers with expertise in performing systematic reviews. Studies were included if they were fully published reports that included smoking and any perioperative or postoperative clinical outcome in patients with TKA or THA.

Results. A total of 21 studies were included for the review, of which 6 provided 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 postoperative complication (risk ratio 1.24, 95% CI 1.01 to 1.54) and death (risk ratio 1.63, 95% CI 1.06 to 2.51) compared to nonsmokers. Former smokers were significantly more likely to have any post-operative complication (risk ratio 1.32, 95% CI 1.05 to 1.66) and death (risk ratio 1.69, 95% CI 1.08 to 2.64) compared to nonsmokers.

Conclusion. This systematic review found that smoking is associated with significantly higher risk of postoperative complication and mortality following TKA or THA. Studies examining longterm consequences of smoking on implant survival and complications are needed. Smoking cessation may improve outcomes after THA or TKA. (First Release June 1 2011; J Rheumatol 2011;38:1824–34; doi:10.3899/jrheum.101221)

Key Indexing Terms:
SMOKING ARTHROPLASTY OUTCOMES
TOTAL KNEE ARTHROPLASTY TOTAL HIP ARTHROPLASTY

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 function. Several patient-related factors such as age, sex, and socioeconomic status influence the outcome of TKA and THA. In addition, modifiable factors such as smoking, medical comorbidity, and obesity may also affect these outcomes. Identification of modifiable risk factors such as smoking is important, since presurgical smoking cessation interventions can improve outcomes of TKA and THA. Smoking has been shown to be a risk factor for non-union after spinal surgery and delayed bone healing after hemicallotasis, an orthopedic procedure to correct knee deformity. However, the association of smoking with risk of complications after TKA or THA has been investigated in a few studies.

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 was significantly associated with any complications following arthroplasty, and if so, which complications.

MATERIALS AND METHODS
An experienced Cochrane librarian (L. Falzon) searched 6 databases in March 2010 using the key terms “knee hip arthroplasty/replacement,” “hip arthroplasty/replacement,” and “smoking” or “tobacco” (Appendix). All
databases were searched from inception to March 2010 and included 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), Scopus, Proquest Dissertation abstracts, CINAHL (via EBSCOHost), Ovid Medline, and Embase. Inclusion of these standard databases is recommended by the Cochrane Handbook of Systematic Reviews12 and is similar to previous Cochrane systematic reviews13,14; these databases were chosen by an experienced Cochrane librarian (LF).

All titles and abstracts were screened by 2 independent trained reviewers (J. Singh, A. Bharat) with expertise in performing systematic reviews15,16,17. Studies were included if they were fully published reports that included smoking and any perioperative or postoperative clinical outcome in patients with either TKA or THA. Studies were excluded if they were abstracts, reviews, or editorials, or did not provide clinical outcomes data. Since the study aimed at assessing smoking as a risk factor for poor postsurgical outcomes, studies of interventions targeting smoking were not included. A Cochrane systematic review of efficacy of smoking cessation interventions has been published18 that included randomized studies of smoking cessation. The Cochrane review combined multiple studies across several surgeries including arthroplasty and provided estimates of benefit for preoperative smoking cessation programs.

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

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, 2 points for comparability of cases and controls, and 3 points for adequacy of exposure assessment. The score can range from 0 to 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 postoperative complication risk would differ by the type of joint undergoing replacement. We had planned to analyze TKA and THA 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 nonsmokers, 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 the 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 editorials21,22,23,24,25,26,27; 8 did not contain outcomes of interest or did not have smoking as a predictor28,29,30,31,32,33,34,35; 1 was related to economic outcome36; 1 was a qualitative study related to a patient survey37; 1 thesis was not available for review38; 4 were related to smoking cessation39,40,41,42; 1 was a duplicate article43; and 1 was related to arthroscopy44. A total of 21 studies from the original search met the inclusion and exclusion criteria and data were extracted from these. Of the 21 included studies45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,13 included patients with THA45,49,50,51,52,53,54,56,59,60,61,62,63, 4 included studies TKA47,55,58,64, 3 included patients with THA or TKA46,48,57, and 1 was a statistical modeling exercise65. 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 21 observational studies45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65, of which one was a statistical modeling study65 (which provided no usable data). Most studies compared smokers to nonsmokers, with few studies categorizing patients into former, current, and nonsmokers. 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 analyses45,46,47,48,49,50,51 followed by those that performed univariable analyses52,53,54,55,56,57,58,59,60,61,62,63,64. 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 scored 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 3309 patients with primary THA using the Swedish Inpatient Register45. It was found that 373 of the 3309 patients (11%) developed one or more postoperative 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 nonsmokers, with odds ratios of 1.32 (95% CI 1.04, 1.97) and 1.56 (95% CI 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 nonsmokers to have systemic complications (OR 2.21, 95% CI 1.28, 3.82). Those smoking 0–19.9 pack-years were not significantly associated with systemic complications compared to nonsmokers (OR 1.35, 95% CI 0.99, 1.84).
Lavernia, et al compared hospital charges following primary or revision THA or TKA between former, current, and nonsmokers. 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. Moller, et al performed an observational study of 811 patients with THA or TKA. Analyses were adjusted for age, sex, body mass index (BMI), ASA class, comorbidity, surgery type, duration of anesthesia, duration of surgery, 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 admission to intensive care unit (OR 2.4, 95% CI 1.4 to 3.8).

Espehaug, et al studied 536 patients who had undergone a primary and revision THA (cases) and 1092 patients who had undergone primary THA only (controls). Smoking was categorized as current, former, and nonsmoker and pack-years were recorded. Overall, neither former nor current smoking was associated with increased risk of revision surgery. Former heavy smokers (≥ 12 pack-years) had significantly higher risk of revision (OR 2.6, 95% CI 1.5 to 4.4). These associations did not change after adjustment for alcohol intake, occupation, weight, and height. Sadr Azodi, et al studied 2106 patients who underwent THA using the Swedish Inpatient Register. 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. In multivariable models adjusted for age, sex, BMI, diagnosis, stem fixation, and alcohol use, smoking had a nonsignificant borderline association with higher revision rates (hazard rate 4.5; p = 0.006).

Observational studies assessing smoking as a risk factor; univariate analyses. All remaining studies used univariate analyses, i.e., associations 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 (Western Ontario and McMaster Universities Osteoarthritis Index) score < 50, in a sample of Medicare recipients 3 years after THA. In univariate analyses, current smoking was not associated with poor functional status (OR 0.8, 95% CI 0.3–2.0). Anderson, et al examined the predictors of postoperative complications including venous thromboembolism (VTE) in patients undergoing THA. Smoking was not associated with risk of VTE. Bekas, et al studied the risk of VTE in...
1947 patients undergoing elective THA at a single medical center, smoking was not a significant risk factor for loosening in univariable or multivariable models (p = 0.1 p = 0.3, respectively). Sharrock, et al found no association of smoking and deep venous thrombosis in 458 patients who underwent cemented TKA. Horne, et al found that smoking was not associated with risk of infection after TKA in their study of 40 patients. Malinzak and Ritter examined the infection rate in 17,561 total joint replacements; smoking was not a significant correlate of postoperative wound infections.

Cates, et al examined the factors predictive of results of closed manipulation following TKA. 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 intraoperative blood loss in 295 patients undergoing primary elective THA. Inoue, et al examined 151 THA in 130 patients. There was no significant association of smoking and implant loosening (OR 0.30, 95% CI 0.06 to 1.52). Nixon, et al surveyed 127 patients with cemented THA regarding smoking status; active smoking was not associated with loosening (OR 5.5, 95% CI 0.8, 38). Khan, et al studied 1767 patients undergoing THA followed up to 5 years; smoking was not associated with deep infection (OR 3.4, 95% CI 0.7 to 17.2), superficial infection (OR 1.0, 95% CI 0.5 to 2.0), and revision (OR 0.8, 95% CI 0.1 to 2.6). Malik, et al found no association of smoking and aseptic loosening in 224 patients who underwent cemented THA.

In a retrospective single-center study by Peersman, et al, 113 infections were identified in 6489 TKA. Smoking was reported to be significantly associated with the risk of infection following TKA (p = 0.01). Nixon, et al surveyed 127 patients with cemented THA regarding smoking status; active smoking was not associated with loosening (OR 5.5, 95% CI 0.8, 38). Khan, et al studied 1767 patients undergoing THA followed up to 5 years; smoking was not associated with deep infection (OR 3.4, 95% CI 0.7 to 17.2), superficial infection (OR 1.0, 95% CI 0.5 to 2.0), and revision (OR 0.8, 95% CI 0.1 to 2.6). Malik, et al found no association of smoking and aseptic loosening in 224 patients who underwent cemented THA.

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Table 2. Findings from observational studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>No. Patients, Type of Study/Population</th>
<th>Smoking</th>
<th>Covariates</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sadr Azodi</td>
<td>3309 pts, THA, Observational cohort study</td>
<td>Former, current, and nonsmoker; pack-yrs smoking</td>
<td>Age, calendar period, region, diabetes, heart failure, lung disease, stroke, BMI, tobacco-related</td>
<td>Multivariable: compared to nonsmokers, 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) &gt; 40 pack-yrs (OR 2.21, 95% CI 1.28 to 3.82) Multivariable: smoking was significant predictor for charges (p = 0.03), operative time (p = 0.01), and anesthesia time (p = 0.003) Multivariable: Smoking associated with lower risk of painful/stiff knee (OR 0.26, p = 0.049)</td>
</tr>
<tr>
<td>Lavernia</td>
<td>203 pts: 203 THA or TKA (primary or revision), Observational cohort study</td>
<td>Former current, and non-smoker; pack-yrs smoking</td>
<td>Age, sex, BMI, diagnosis, surgeon, procedure, comorbidities</td>
<td>Multivariable: smoking 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)</td>
</tr>
<tr>
<td>Fisher</td>
<td>71 pts: 71 TKA (148 controls), Observational case-control study</td>
<td>Smoking: yes/no</td>
<td>Sex, arthroscopy, disabled, diabetes, chronic lung disease, retired</td>
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<tr>
<td>Moller</td>
<td>811 pts: 811 THA or TKA, Observational cohort study</td>
<td>Current smoker vs nonsmoker (included prior smokers)</td>
<td>Age, sex, BMI, ASA class, comorbidity, surgery type, anesthesia duration, surgery duration, alcohol use</td>
<td>Multivariable: smoking significantly associated with higher risk of any complication (OR 1.9, 95% CI 1.2 to 2.9) Multivariable: no significant association of smoking status or pack-yrs of smoking and risk of implant dislocation up to 3 yrs after primary THA</td>
</tr>
<tr>
<td>Espehaug</td>
<td>674 primary THA; 1343 controls, Observational matched case-control study</td>
<td>Smoking: never, former, current</td>
<td>Antibiotic, cement, prosthetic brand; matched for age, operation date, bilateralility</td>
<td>Multivariable: neither former nor current smoking associated with increased revision; former heavy smokers (≥ 12 pack-yrs) significantly increased risk of revision (OR 2.6, 95% CI 1.5 to 4.4)</td>
</tr>
<tr>
<td>Meldrum</td>
<td>147 pts: 165 THA, Observational cohort study</td>
<td>Smoking: yes/no</td>
<td>Age, sex, BMI, diagnosis, stem fixation, alcohol use</td>
<td>Multivariable: smokers with nonsignificantly higher hazard rate of revision than nonsmokers, 4.5 (p = 0.066)</td>
</tr>
<tr>
<td>Bischoff-Ferrari</td>
<td>922 pts: 922 primary THA, Observational cohort study</td>
<td>Current smoking yes/no</td>
<td>Univariate: poor functional status in smokers vs nonsmokers (OR 0.8, 95% CI 0.3 to 2.0)</td>
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<tr>
<td>Anderson</td>
<td>101 pts: 101 THA, Observational cohort study</td>
<td>Smoking yes/no</td>
<td>Univariate: smoking not associated with risk of venous thromboembolism</td>
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<tr>
<td>Beksač</td>
<td>1947 pts: 2032 THA, Observational cohort study</td>
<td>Smoking yes/no</td>
<td>Univariate: no significant association of smoking and venous thromboembolism up to 3 mo post-THA</td>
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<td>Sharrock</td>
<td>448 pts: 448 TKA, Observational cohort study</td>
<td>Smoking yes/no</td>
<td>Univariate: smoking not associated with risk of deep vein thrombosis</td>
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<tr>
<td>Horm</td>
<td>392 pts: 392 TKA, Observational case-control study</td>
<td>Smoking yes/no</td>
<td>Univariate: smoking not associated with risk of infection following TKA (OR 1.6, 95% CI 0.3 to 6.3; p = 0.46) Univariate: smoking not associated with risk of infection</td>
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<tr>
<td>Malinzak</td>
<td>17,561 pts: 17,561 THA or TKA, Observational cohort study</td>
<td>Smoking yes/no</td>
<td>Univariate: smoking not associated with risk of deep vein thrombosis</td>
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<tr>
<td>Cates</td>
<td>37 pts: 37 TKA, Observational cohort study</td>
<td>Smoking yes/no</td>
<td>Univariate: smoking not associated with flexion or extension gain at 1 year post-manipulation</td>
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<td>Groslamb</td>
<td>295 pts: 295 THA, Observational cohort study</td>
<td>Smoking yes/no</td>
<td>Univariate: smoking not associated with total blood loss intraoperatively</td>
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</table>
operative complication and former smokers a 32% higher risk. Similarly, the risk of death at 3-year followup was 63% higher in current smokers and 69% higher in former smokers, with data from one study. The NNH for various complications is 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 TKA or THA. 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 longterm followup beyond 5–10 years to assess risk of revision surgery after TKA/THA. 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.

Table 2. Continued.  

<table>
<thead>
<tr>
<th>Study</th>
<th>No. Patients, THA or TKA</th>
<th>Type of Study/ Quality Score*</th>
<th>Population</th>
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<th>Findings</th>
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<tr>
<td>Inoue60</td>
<td>130 pts: 151 THA</td>
<td>Observational cohort study Score 5</td>
<td>Single center</td>
<td>Smoking yes/no</td>
<td>Univariate</td>
<td>Univariate: smoking not associated with early implant loosening (OR 0.30, 95% CI 0.06 to 1.52; p = 0.15)</td>
</tr>
<tr>
<td>Nixon61</td>
<td>127 pts: 127 THA</td>
<td>Observational case-control study Score 5</td>
<td>Single center, Active smokers: yes/no</td>
<td>Univariate</td>
<td>Univariate: among those with loosening of implant, more active smokers (8/59) than among those with stable implants (1/26) (OR 5.5, 95% CI 0.8 to 38; p = 0.08)</td>
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<tr>
<td>Khan62</td>
<td>1767 pts: 1767 THA</td>
<td>Observational cohort study Score 7</td>
<td>Single center</td>
<td>Smoking yes/no</td>
<td>Univariate</td>
<td>Univariate: smoking not associated with the 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)</td>
</tr>
<tr>
<td>Malik63</td>
<td>224 pts: 224 THA</td>
<td>Case-control study Score 7</td>
<td>Single center</td>
<td>Former, current, and nonsmokers</td>
<td>Univariate</td>
<td>Univariate: smoking not associated with implant loosening at 6-yr followup</td>
</tr>
<tr>
<td>Peersman64</td>
<td>6120 pts: 6489 TKA; Observational, case-control study Score 4</td>
<td>Single center</td>
<td>Smoking yes/no</td>
<td>Univariate</td>
<td>Univariate: smoking associated with risk of infection following TKA (p = 0.01)</td>
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</tbody>
</table>

* Quality scores calculated using the Ottawa-Newcastle system designed for observational studies with separate scales for case-control and cohort studies; studies can be awarded 4 points for selection of case/controls, 2 points for comparability of cases and controls, 3 points for exposure assessment. Score range = 0-9, 9 = best quality score. NA: not applicable; THA: total hip arthroplasty; TKA: total knee arthroplasty; OA: osteoarthritis; Prim: primary; Rev: revision; BMI: body mass index; ASA: America Society of Anesthesiologists.

Table 3. Unadjusted postoperative outcomes following total hip arthroplasty comparing current and former smokers to nonsmokers (reference category for both groups).

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No. Studies, No. Patients</th>
<th>Current Smoker</th>
<th>Prior Smoker</th>
<th>NNH (95% CI)</th>
<th>NNH (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reoperation or revision</td>
<td>4 studies4, 4000 pts</td>
<td>1.4 [0.62, 2.10]</td>
<td>(NE)</td>
<td>1.17 [0.84, 1.63]</td>
<td>100 (NE)</td>
</tr>
<tr>
<td>Implant loosening</td>
<td>2 studies6, 238 pts</td>
<td>1.25 [0.97, 1.62]</td>
<td>34 (NE)</td>
<td>1.16 [0.83, 1.63]</td>
<td>50 (NE)</td>
</tr>
<tr>
<td>Any postoperative complication</td>
<td>2 studies6, 2512 pts</td>
<td>1.24 [1.01, 1.54]</td>
<td>50 (20, ∞)</td>
<td>1.32 [1.05, 1.66]</td>
<td>34 (17, 100)</td>
</tr>
<tr>
<td>Deep infections</td>
<td>1 study6, 1185 pts</td>
<td>3.42[0.69, 16.85]</td>
<td>100 (NE)</td>
<td>3.68 [0.95, 14.16]</td>
<td>100 (NE)</td>
</tr>
<tr>
<td>Death</td>
<td>1 study6, 1539 pts</td>
<td>1.63[1.06, 2.51]</td>
<td>34 (20, 100)</td>
<td>1.69 [1.08, 2.64]</td>
<td>34 (20, 100)</td>
</tr>
</tbody>
</table>

NNH: number needed to harm, calculated as 1/absolute risk reduction; NE: confidence interval not estimable since 95% CI includes both positive and negative numbers. * Data from 4 studies: Espehaug49, Sadr Azodi50, Khan62, Meldrum51; Espehaug49 and Sadr Azodi50 were multivariable-adjusted; Khan62, and Meldrum50 were univariate analyses. b Data from 2 studies: Malik63 and Nixon61 both univariate studies. c Data from 2 studies: Sadr Azodi50 (multivariable-adjusted), Meldrum50 (univariate). d Data from 1 study: Khan62 (univariate). e Data from 1 study: Sadr Azodi50 (multivariable-adjusted). f Data from 3 studies for reoperation: Espehaug49, Sadr Azodi50, Khan62, Espehaug49 and Sadr Azodi50 were multivariable-adjusted; Khan62 included univariate analysis. g Data from 1 study: Malik63 (univariate). h Data from 1 study: Sadr Azodi50 (multivariable-adjusted). i Data from 1 study: Khan62 (univariate). j Data from 1 study: Sadr Azodi50 (multivariable-adjusted).
DISCUSSION

We found that, compared to nonsmokers, current smokers and former smokers had 24% and 32% higher risk, respectively, of any postoperative complication after TKA or THA. Similarly, the risk of death was 62% higher in current smokers and 69% higher in former smokers 3 years after TKA/THA, compared to nonsmokers. These (unadjusted) estimates should serve as guides to healthcare providers in their discussions with patients undergoing TKA 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 postoperative complications is significantly increased by smoking and that quitting smoking can significantly reduce risk of these preventable complications. 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 shorter less intensive programs18. Clinicians have viewed the perioperative period as a “window of opportunity” to motivate patients to quit smoking66. Since > 95% of joint arthroplasty surgeries are elective, the preoperative period provides an opportunity for discussion with the patient and enough time in most cases to implement an intensive tobacco cessation program. Of course, the short- and longterm benefits of smoking cessation on cardiac, pulmonary, and overall health will then be realized, if patients can remain off tobacco after their joint replacement surgery.

Implications for clinical practice. The increased risk for mortality among current and former smokers is particularly impressive, considering the elective aspect of TKA/THA. For all candidates for TKA/THA, the postoperative mortality 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 currently no data that have shown differences in perioperative mortality in patients quitting smoking preoperatively; however, such a study may require a high number of patients to detect differences in mortality, since the baseline risk of mortality is low in all candidates. Even in the 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 with patients prior to joint arthroplasty. 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 Initiative68,69, the NNH with hormone replacement therapy was 1250 for stroke and 1250 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 is 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 nonsmokers. We did not observe a linear trend of increased risk of postoperative complications from former smokers to current smokers in pooled unadjusted analyses, which may be more likely related to limited data (from 1 or 2 studies) and residual confounding, rather than lack of such a trend. Current smokers tend to be a younger cohort than nonsmokers and former smokers due to survival disadvantage, and confounding bias can lead to falsely lower unadjusted rates in current smokers. This is further evident by an example from one of the studies by Sadr Azodi, et al65. Compared to nonsmokers, unadjusted odds ratios for systemic complications in current and former smokers were 1.39 and 1.50, respectively (numerically higher for former smokers), whereas respective adjusted odds ratios were 1.56 and 1.32 (numerically higher for current smokers). Therefore, the unadjusted pooled risk ratios shown in Table 3 must be interpreted with some caution and with consideration of this confounding bias.

A recent Cochrane systematic review of randomized controlled trials of preoperative smoking cessation that included various surgical populations provides convincing data regarding risk reduction with smoking cessation18. An intensive 4–8 week preoperative smoking cessation program was associated with 58% risk reduction for any complication (RR 0.42, 95% CI 0.27–0.65) and with 69% risk reduction for wound complications (RR 0.31, 95% CI 0.16–0.62) compared to a control group. Based on this evidence and the fact that most knee and hip arthroplasties are elective, discussing preoperative smoking cessation with patients undergoing TKA and THA seems prudent. Although there is some evidence for it, 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 postoperative outcomes was derived from several multivariable-adjusted studies45,46,47,48,48.50, with few univariate analyses43,51,52,53,54,55,56,57,58,59,60,61,62,63. Multivariable-adjusted analyses also showed association of smoking with higher resource utilization among former smokers and current smokers compared to nonsmokers, 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 smok-
APPENDIX 1. Details of the search strategy.

Ovid MEDLINE(R) 1950 to March Week 2 2010
Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations March 17, 2010
257 to 252 (after de-duplication)
1 exp Arthroplasty/
2 exp Joint Prosthesis/
3 exp "Prostheses and Implants"
4 Knee/
5 exp Knee Joint/
6 or 1-3
7 or 4-5
8 or 6 and 7
9 Arthroplasty, Replacement, Knee/
10 Knee Prosthesis/
11 (knee or knt).tw.
12 (knee$ adj (replace$ or arthroplast$ or prosthe$ or endoprosth$ or implant$)).tw.
13 or 8-12
14 Hip/
15 Hip Joint/
16 or 14 or 15
17 or 6 and 16
18 Arthroplasty, Replacement, Hip/
19 (tha or thr).tw.
20 (hip$ adj (replace$ or arthroplast$ or prosthe$ or endoprosth$ or implant$)).tw.
21 or 17-20
22 or 13 or 21
23 exp Smoking/
24 exp Tobacco/
25 exp "Tobacco Use Cessation"
26 "Tobacco Use Disorder"
27 (smok$ or tobacco or pipe$ or cigar$ or cigarette$).tw.
28 or 23-27
29 or 22 and 28

Ovid EMBASE 1980 to 2010 Week 10
216 to 82 (after de-duplication)
1. exp arthroplasty/
2. exp joint prosthesis/
3. prosthesis/
4. exp implant/
5. or 1-4
6. exp knee/
7. or 5 and 6
8. exp knee arthroplasty/
9. (tka or tkr).tw.
10. (knee$ adj (replace$ or arthroplast$ or prosthe$ or endoprosth$ or implant$)).tw.
11. or 7-10
12. hip/
13. or 5 and 12
14. exp hip arthroplasty/
15. (tha or thr).tw.
16. (hip$ adj (replace$ or arthroplast$ or prosthe$ or endoprosth$ or implant$)).tw.
17. or 13-16
18. or 11 or 17
19. exp smoking/
20. tobacco/
21. tobacco dependence/
22. smoking cessation/
23. (smok$ or tobacco or pipe or cigar$ or cigarette$).tw.
24. or 19-23
25. or 18 and 24

CINAHL via EBSCOHost
34 to 11 (after de-duplication)
30 S23 and S29
S29 S24 or S25 or S26 or S27 or S28
S28 ab smok* or ab tobacco or ab pipe* or ab cigar* or ab cigarette*
S27 ti smok* or ti tobacco or ti pipe* or ti cigar* or ti cigarette*
S26 (MH "Smoking Cessation")
S25 (MH "Tobacco-")
S24 (MH "Smoking"*)
S23 S13 or S22
S22 S17 or S18 or S19 or S20 or S21
S21 S6 and S16
S20 ab hip* replace* or ab hip* arthroplast* or ab hip* prosthe* or ab hip* endoprosth* or ab hip* implant*
S19 ti hip* replace* or ti hip* arthroplast* or ti hip* prosthe* or ti hip* endoprosth* or ti hip* implant*
ing is associated with poor postsurgical outcomes in patients undergoing THA or TKA. Most studies to date had small sample sizes, and smoking exposure as a risk factor was measured differently (current, former, and never-smoker in some, and smoker vs nonsmoker in others). Few studies examined pack-years to determine dose relationships, but more data are needed. Due to lack of data, it is unknown whether smoking is associated with longer-term implant-related complications. Future studies needed to address these knowledge gaps.

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 postoperative complications and postoperative mortality. The number of pack-years also seems to be related to risk of these complications. More research is needed to determine the association of smoking with other postoperative complications, including cardiac and pulmonary complications, prosthetic loosening, and infection in patients undergoing THA or TKA. Evidence from other randomized trials shows the benefit of intensive preoperative quitting smoking preoperatively and assess its influence on randomization.

ACKNOWLEDGMENT

I thank Louise Falzon from the Cochrane Library for performing the search and Assem Bharat for reviewing abstracts and titles for inclusion in the study.

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