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Venous thromboembolism following 672,495 primary total shoulder and elbow replacements: meta-analyses of incidence, temporal trends and potential risk factors

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Abstract

Background: There is wide variability in reported venous thromboembolism (VTE) incidence following total shoulder replacement (TSR) or total elbow replacement (TER). It is uncertain which risk factors influence the risk of VTE following TSR or TER. We conducted a PRISMA compliant meta-analysis to evaluate the incidence, temporal trends and potential risk factors for VTE following primary TSR and TER.

Methods: MEDLINE, Embase, Web of Science, and Cochrane Library were searched through September 2019 for longitudinal studies reporting VTE outcomes after TSR or TER. Incidence and relative risks (RR) (95% confidence intervals) were estimated.

Results: We identified 43 articles with data on 672,495 TSRs and TERs (668,699 TSRs and 3,796 TERs). The overall pooled 3-month VTE incidence following TSR was 0.85% (0.39-1.46). For TER, the 3-month incidence of VTE was 0.23% (0.08-0.44). Older age, body mass index (BMI) ≥25 kg/m^2, and alcohol abuse were each associated with increased VTE risk following TSR. Comorbidities associated with increased VTE risk following TSR were chronic pulmonary disease, previous VTE, heart failure, anaemia, coagulopathy, arrhythmia, epilepsy, urinary tract infection, sleep apnoea, and fluid & electrolyte imbalance. Anatomic and outpatient TSR were each associated with decreased VTE risk.

Conclusions: The average 3-month incidence of VTE following TSR or TER is less than 1%. High risk groups such as older patients, those with a previous VTE history and those undergoing reverse or inpatient TSR may need close monitoring. Modifiable factors such as high BMI, alcohol abuse, and comorbidities could be identified and addressed prior to surgery.

Systematic review registration: PROSPERO 2019: CRD42019134096

Keywords: incidence; risk factor; venous thromboembolism; deep vein thrombosis; pulmonary embolism; total shoulder replacement; total elbow replacement; meta-analysis

1. Introduction

Venous thromboembolism (VTE), which comprises pulmonary embolism (PE) and deep vein thrombosis (DVT), is a frequent complication of total joint replacement (TJR).[1] VTE carries a substantial public health burden, being an important cause of morbidity, high costs to healthcare systems and a preventable cause of death.[2] VTE has long been established as a major complication of lower extremity joint replacements (i.e., hip and knee) and there is a minefield of literature on the its incidence, risk factors, diagnosis, prevention, and treatment. In the absence of pharmacological thromboprophylaxis, VTE incidence has been reported to be as high as 40-85% following lower limb joint replacement;[1, 2] with routine anticoagulant therapy, VTE rates of 1-10% have been reported.[1, 2] Compared to lower extremity joint replacements, relatively few upper extremity replacements (total shoulder and elbow replacement, TSR and TER) are performed. In 2018, as recorded in the National Joint Registry for England, Wales and Northern Ireland and the Isle of Man, 99,093 and 92,874 primary joint replacements were performed in knees and hips respectively; whereas only approximately 7,000 shoulder and 600 elbow replacements were performed.[3] Given the few numbers of TSRs and TERs done every year, the literature is very sparse on the incidence of VTE and potential risk factors that influence VTE incidence. Whereas there are established guidelines on the use of thromboprophylaxis in patients undergoing hip and knee replacements, those for shoulder and elbow replacements are not clearly defined.[4] VTE has typically been considered an uncommon complication after shoulder or elbow replacement. However, limited published literature suggest that VTE incidence following shoulder and elbow replacements range widely from 0.1% to 13%.[5-7]

Total joint replacement has gained acceptance as one of the most successful orthopaedic procedures for end stage joint disease. Amongst all orthopaedic joint replacements, shoulder replacements are the most rapidly growing and it is expected there will be a seven-fold increase over the next 15 years.[8] Hence, there is a need for robust data on the actual incidence of VTE and identification of patients who are at the greatest risk of developing VTE following TSR or TER. This information will be of value for policy makers and clinicians to aid in planning and implementing more efficacious

preventative strategies. Furthermore, though there is established evidence that several host-related factors are associated with the risk of VTE following total hip and knee replacement,[9] it is uncertain if these potential risk factors also influence VTE risk following TSR or TER in a similar way. In this context, using a systematic meta-analytic approach, we sought to (i) assess and pool incidence of VTE (including DVT and PE) following primary TSR and TER and characterise their temporal trends; and (ii) quantify the nature, magnitude and specificity of potential associations of several patient-, surgery-, and hospital-related factors with the risk of VTE following primary TSR and TER.

Methods and methods

2.1. Data sources and search strategy

This review was based on a pre-defined protocol which was registered with the prospective register of systematic reviews, PROSPERO (CRD42019134096) and was conducted using PRISMA and MOOSE guidelines (**Appendices A-B**). We performed an electronic search of MEDLINE, Embase, Web of Science and Cochrane databases from inception to 26 September 2019 for studies reporting on VTE outcomes (DVT and/or PE) following TSR or TER. The computer-based searches combined free and MeSH search terms and combination of key words related to the population (e.g., "total shoulder replacement", "total elbow replacement") and outcome (e.g., "venous thromboembolism", "deep vein thrombosis", "pulmonary embolism"). There were no restrictions on language. Full details of the search strategy are reported in **Appendix C.** The titles and abstracts of retrieved studies were initially screened to assess their suitability for inclusion, after which we acquired full texts of potentially relevant articles for detailed evaluation. Two reviewers independently conducted full text evaluation and any disagreements regarding eligibility of an article was discussed, and consensus reached with a third author. Reference lists of identified studies and relevant review articles were scanned manually and the "Cited Reference Search" function in Web of Science was used to check for additional eligible studies.

2.2. Eligibility criteria

Longitudinal studies (prospective or retrospective cohort, case-cohort, nested-case control, or clinical trials) were eligible for inclusion if they recruited patients who had undergone primary TSR (anatomic (ATSR) or reverse (RTSR)) or TER, reported on cases of VTE (DVT and/or PE) following the surgery and/or reported on the associations of VTE with patient-related factors (such as sociodemographic characteristics, anthropometric measures, or past medical and/or surgical history), surgery-related factors (such as surgical approach, procedure type, or use of bone cement), or hospital-related factors (such as hospital volume or surgeon experience). The primary outcome was VTE, including either DVT or PE. We excluded the following studies: (i) those restricted to patients with prevalent disease conditions (e.g. diabetes, epilepsy etc) or selected populations with no

comparison or control groups; (ii) those that assessed exposures (potential risk factors) after the joint replacement; and (iii) of any other surgical approach apart from total elbow or shoulder replacement such as in the setting of only infection, fracture, arthroscopy or hemiarthroplasty. Our population setting included mainly patients undergoing elective joint replacement, hence joint replacements solely in the setting of traumatic indications were not included due to the differing risk profile. Disagreements on inclusion or exclusion were discussed by two reviewers (SKK and MCB), with involvement of a third reviewer (MRW) when necessary.

2.3. Data extraction and quality assessment

One author initially extracted data from eligible studies using a standardized predesigned data collection form. A second reviewer independently checked these data with that in original articles. Any disagreements were discussed, and consensus reached with involvement of a third author. We extracted data on study characteristics, sample size, number of VTE outcomes, risk estimates of VTE (relative risks (RRs), hazard ratios (HRs), or odds ratios (ORs)) and degree of adjustment for potential confounders (univariate or multivariate). To avoid double counting of a cohort, study selection was limited to a single set of most comprehensive results when there were multiple publications involving the same cohort. The priority for selection was the most up-to-date comprehensive study (longest follow-up or analysis covering the largest number of participants). The methodological quality of each study was assessed using the nine-star Newcastle-Ottawa Scale (NOS), [10] which uses three pre-defined domains including: (i) selection of participants; (ii) comparability; and (iii) ascertainment of outcomes of interest. The Cochrane Collaboration's risk of bias tool was used to assess the quality of RCTs.[11]

2.4. Data synthesis and analyses

For the meta-analysis of VTE incidence, the summary measure was incidence (estimated from the number of VTE outcomes within follow-up period/total number of participants or procedures as reported) with 95% confidence intervals (CIs). Given the nature of the data, the Freeman-Tukey variance stabilising double arcsine transformation [12] was used in calculating incidence, because the

use of the inverse variance weight in fixed-effects meta-analysis is suboptimal when dealing with binary data with low rates. Temporal trends in incidence were evaluated using the median year of data collection/surgery reported by studies, as previously reported.[13] Summary measures of associations (risk factors for VTE) were presented as RRs with 95% CIs. Following Cornfield's rare disease assumption[14], HRs and ORs were assumed to approximate the same measure of RR. Fully-adjusted risk estimates were used when reported, otherwise crude RRs were calculated from studies that provided raw counts. Due to the different cut-offs used for BMI by the included studies, we employed the following risk comparisons based on the data available: ≥25 vs. <25; ≥30 vs. <30; ≥35 vs. <35; ≥40 vs. <40; ≥50 vs. <50 kg/m^2 and per unit increase in BMI, to ensure consistency in the pooling approach and enhance comparability and interpretation of findings.[9]. Random-effects models using the inverse variance weighted method (DerSimonian and Laird) were used to combine RRs to minimize the effect of heterogeneity. In the absence of substantial heterogeneity, fixed-effect models were employed. Heterogeneity was assessed and quantified using the Cochrane χ^2 statistic and the I^2 statistic.[15] We also estimated 95% prediction intervals to determine the degree of heterogeneity, as they provide a region in which about 95% of the true effects of a new study are expected to be found.[16, 17] Several pre-defined study-level characteristics which may explain heterogeneity were explored using stratified analysis and random effects meta-regression. To assess the potential for small study effects or publication bias, we conducted Egger's regression symmetry test.[18] All statistical analyses were conducted using STATA release 15 (Stata Corp, College Station, Texas, USA).

3. Results

3.1. Study identification and selection

The review progress is summarised in **Figure 1**. The literature search and manual screening of references identified 79 potentially relevant articles, of which 60 were potentially relevant to the review question after screening of titles and abstracts. Following detailed evaluation, 17 articles were excluded because (i) they were duplicates of another study included in review (n=8); (ii) population was not relevant (n=5); (iii) the outcome was not relevant (n=3); and (iv) study design was not

relevant (n=1). The remaining 43 articles corresponding to 24 non-overlapping studies were eligible for the review (**Figure 1; Appendix D**).

3.2. Study characteristics and study quality

Table 1 provides an overall summary of relevant characteristics of studies included in the review. **Table 2** provides details of the key characteristics and quality assessment scores of the 43 individual articles. Publication years of included articles ranged from 2003-2019. Of the 24 non-overlapping studies, only five studies of TER were included in the review. Overall, the studies comprised of 672,495 total shoulder and elbow replacements or procedures (668,699 TSRs and 3,796 TERs) and 3,888 VTE cases (3,876 for TSR and 12 for TER). Twenty studies were conducted in North America (USA) and four in Europe (Italy and UK). The average baseline age of participants in the eligible studies ranged from 51.3 to 72.5 years, with a weighted mean age of 68.9 years; the weighted mean age was 69.0 and 57.4 years for TSR and TER respectively. Except for three studies,[5, 19, 20] none of the studies provided specific information on type of thromboprophylaxis administered to patients. For one study, DVT prophylaxis was initiated after surgery and consisted of enteric coated aspirin (325 mg twice a day); pneumatic compression foot pumps; and early ambulation.[5] In the other study, low-molecular heparin was used in the majority of cases, with use of unfractionated heparin, antiplatelet therapy, or other anticoagulants in a few cases.[19] The third study utilized sequential compression devices as DVT prophylaxis.[20] The average follow-up for studies ranged from 30 days to 8 years, with a weighted mean follow-up of 0.19 years (approximately 3 months). Methodological quality of included studies ranged from 6-9. Using the Cochrane risk of bias tool for the only RCT included, this trial demonstrated a low risk of bias for all areas of study quality except for random sequence generation and other bias, which were of unclear risk of bias.

3.3. Incidence of VTE

Across 19 studies comprising of 668,699 TSRs over a weighted mean follow-up duration of 3 months, the pooled random effects incidence (95% CI) of VTE following TSR was 0.85% (0.39-1.46) (**Figure 2**). The 95% prediction interval for the summary incidence was 0.00 to 4.80%, suggesting that the true

VTE incidence for any single new study will usually fall within this range. There was substantial heterogeneity between contributing studies (I^2>70%; $p < 0.01$), which was not explained by any of the study-characteristics evaluated (**Figure 3**). There was no significant evidence of publication bias using the Egger test (p=0.326), which was consistent with the absence of selective reporting when studies were grouped by size (**Figure 3**). On exclusion of the study with the highest VTE incidence at 16.00%,[5] the pooled VTE incidence was 0.66% (0.26-1.22). Furthermore, on single exclusion of the study with the second highest VTE incidence at 4.40%,[21] the pooled VTE incidence was 0.64% (0.30-1.09). The incidence of DVT and PE following TSR was 0.37% (0.16-0.65) and 0.31% (0.16-0.49) respectively over a weighted mean follow-up duration ranging from 15 to 26 days (**Appendix E**). The pooled incidence rate of VTE at specific average follow-up periods reported by studies was 0.10% (0.09-0.11) at <30 days, 0.36% (0.15-0.65) at 30 days, 1.72% (1.54-1.92) at 60 days, 1.17% (0.53-2.03) at 90 days, 1.22% (0.99-1.52) at 1 year, 0.96% (0.72-1.25) at 2 years, and 0.44% (0.29-0.65) at 5 years (**Appendix F**). Based on the median year of data collection/surgery, the pooled incidence rate of VTE was 0.51% (0.39-0.66) in the 1990s, 1.53% (0.57-2.91) in 2000-2009 and 0.25% (0.05-0.54) in 2010 and beyond (**Appendix G1**). In meta-regression analysis, there was no significant association between VTE incidence rates and median year of data collection/surgery (p=0.99) (**Appendix G2**).

Across 5 studies comprising of 3,796 TERs over a weighted mean follow-up duration of approximately 3 months, the incidence of VTE following TER ranged from 0.25% to 9.09%, with a pooled incidence (95% CI) of 0.00% (0.00-0.08) (**Appendix H**). On exclusion of the study with a sample size of only 11 joints,[22] the pooled VTE incidence (95% CI) was 0.23% (0.08-0.44).

3.4. Associations of patient-related factors with VTE risk

Sociodemographic characteristics and BMI The associations of several sociodemographic characteristics and BMI categories with risk of VTE following TSR are reported in **Figure 4**. Older age was associated with an increased risk of VTE when age was evaluated as a categorical or continuous variable: RRs (95% CIs) of 1.15 (1.08-1.22) and 1.01 (1.00-1.02) comparing age ≥70

years vs <70 years and per one-year increase respectively. Comparing males to females in 4 studies, the pooled adjusted RR (95% CI) for VTE was 0.98 (0.86-1.12) (**Figure 4; Appendix I**). Race was not associated with VTE risk in any of the comparisons evaluated. On the role of lifestyle factors, alcohol abuse was associated with an increased risk of VTE RR (95% CI) 2.50 (1.82-3.44), with no significant association for drug abuse and VTE RR (95% CI) 0.57 (0.08-4.12). Comparing BMIs ≥50 vs. <50; ≥30 vs. <30; and ≥25 vs. <25 kg/m^2, the pooled RRs (95% CIs) were 1.97 (1.63-2.37); 1.28 (1.09-1.50); and 3.56 (1.21-10.49) respectively.

No studies conducted in patients undergoing primary TER were identified to have formally assessed the associations of potential risk factors with risk of VTE. However, one study evaluated the influence of obesity on several complications following TER and no significant association could be demonstrated between obesity and VTE risk given the zero-event rate.[23]

Medical and surgical history Associations between several medical and surgical history characteristics with risk of VTE following TSR are reported in **Figure 5**. A Deyo-Charlson Index ≥ 1 was associated with an increase in risk of VTE. In pooled analysis of contributing studies, the following comorbidities were each associated with an increased risk of VTE following TSR: chronic pulmonary disease, history of VTE, congestive heart failure, anaemia, and coagulopathy. In pooled analysis of 3 studies, a history of coronary heart disease was associated with reduced risk of VTE RR (95% CI) 0.77 (0.62-0.97). In results of single reports, there was evidence of statistically significant associations of VTE with histories of arrhythmia, epilepsy, urinary tract infection, sleep apnoea, and fluid & electrolyte imbalance. In evaluation of surgical indications for TSR, neither osteoarthritis, avascular necrosis, nor rheumatoid arthritis was associated with VTE risk (**Figure 5**).

3.5. Associations of surgery- and hospital-related factors with VTE risk

Comparing anatomic vs. reverse TSR and outpatient TSR vs inpatient TSR, RRs (95% CIs) for VTE were 0.59 (0.40-0.87) and 0.43 (0.24-0.76) respectively. Other factors such as implant fixation (cemented vs. uncemented), type of anaesthesia (general vs. regional), period or seasonality of

surgery, and surgeon experience were not associated with VTE risk following TSR **(Appendix J**). A single study evaluated the association between the altitude of the hospital and the risk of VTE following TSR and demonstrated an increased risk of VTE comparing a high altitude (>4000 feet above sea level) with a low altitude hospital (<100 feet above sea level) RR (95% CI) of 1.67 (1.02-2.72).

4. Discussion

Given the variable incidence of VTE following TSR and TER reported in the literature and the lack of robust data on the role of potential risk factors that influence VTE risk, we have conducted a literature-based meta-analysis that comprehensively summarises the incidence and temporal trends of VTE as well as potential associations of patient-, surgery-, and hospital-related factors with the risk of VTE following TSR and TER. Based on individual study findings, VTE incidence following TSR averaged approximately 0.85% in pooled analysis over an average period of 3 months. The incidence of VTE following TSR is not constant in the post-operative period but appears to sharply increase from the immediate postoperative period and peaks at 60 days, with a gradual decline afterwards. For elbow joints, the 3-month VTE incidence following TER was approximately 0.23%. With regard to temporal trends, there appeared to be a decline in the incidence of VTE following TSR from the period 2000-2009 to 2010 and beyond, but findings were not robust given the limited data used in the analysis. In shoulder replacement patients, several relevant associations were demonstrated. At the patient level, older age, alcohol abuse, and high BMI were each associated with an increased risk of VTE. Comorbidities associated with an increased risk of VTE were chronic pulmonary disease, history of VTE, congestive heart failure, anaemia, coagulopathy, arrhythmia, epilepsy, urinary tract infection, sleep apnoea, and fluid & electrolyte imbalance. A history of coronary heart disease was associated with a reduced VTE risk. Compared to reverse TSR, anatomic TSR was associated with a lower incidence of VTE, which may reflect the observation that reverse TSR is associated with an increased risk of complications which include fracture, haematoma, infection, instability, mechanical baseplate failure, and scapular notching.[24] Compared to inpatient TSR, outpatient TSR was associated with reduced VTE risk, which may reflect a patient selection effect. At the hospital level, a high-altitude hospital increased VTE risk compared to a low-altitude hospital.

There have been a number of previous attempts to assess VTE incidence following TSR and TER and the role of potential risk factors in VTE development, but these previous reviews have either been based on a limited number of reports; focussed on few selected potential risk factors; were conducted in the setting of fracture, arthroscopy or hemiarthroplasty; included a mixture of primary and revision

joint replacements; or findings were not based on meta-analytic approaches.[4, 25-27] Dattani and colleagues, mostly using a narrative approach, reported a VTE incidence of 0.52% and 0.26% for shoulder and elbow replacement respectively and identified diabetes, rheumatoid arthritis, and ischaemic heart disease to be associated with an increased risk of VTE following shoulder surgery.[25] Saleh and colleagues in a narrative synthesis of 14 articles, reported the incidence of VTE after shoulder replacement to range from 0.2% to 16.0% and identified factors such as history of VTE, thrombophilia, major surgery, advanced age, current malignant disease, immobility, and bed confinement to increase the risk of VTE. Though these previous reports provide relevant findings, a major limitation in their approach was the use of simple proportions and narrative text to synthesize the data; hence, such findings are not robust. By employing relevant statistical approaches which take into account the weighted average follow-up period, our review represents the first attempt at evaluating and synthesising VTE incidence, temporal trends and the associations of several factors with VTE risk in more detail than ever before.

Whether these identified potential risk factors are just risk markers for VTE risk or have causal relevance are yet to be ascertained. However, a number of plausible mechanistic pathways may explain some of the associations demonstrated. We confirmed the evidence that older age is well established to be an independent risk factor for VTE following joint replacement, which has been demonstrated in a previous review restricted to hip and knee replacements.[9] It has recently been shown in hip and knee replacement patients that females have an increased risk of VTE.[9] In the current study, we were unable to show a significant association between gender and VTE risk in TSR. Though this finding was based on pooled analysis of only four studies; based on the pooled sample size, event rate and confidence intervals, there seemed to be adequate power to demonstrate an association if it existed. However, the role of gender in VTE is a contentious topic and inconsistent results have always been reported. The relationship between high BMI and increased VTE risk is not new and attributed to factors which increase the risk of VTE such as limited mobilisation post-surgery, increased underlying inflammation, and mechanical restriction to venous return.[28] A history of sleep apnoea was associated with an increased risk of VTE, which might reflect the fact that

sleep apnoea may be a surrogate measure for obesity, smoking, or cardiopulmonary complications;[29, 30] factors which have been consistently shown to increase the risk of VTE.[31] Unlike moderate and regular alcohol consumption which has been shown to exert a variety of health benefits including decreasing the risk of VTE,[32] alcohol abuse may be associated with an increased risk of VTE[33, 34] as demonstrated in our study findings; this has been attributed to an unfavourable effect on the coagulation system by increasing levels of factor VII and plasminogen activator inhibitor-1.[35] Heavy drinkers are likely to have sleep apnoea and at risk of prolonged immobilisation, which are risk factors for VTE. The increased risk of VTE associated with a high altitude hospital likely reflects that exposure to high altitude either during air travel, ascent of a mountain, or while engaging in sports activities, results in a hypercoagulable state, which predisposes to thromboembolic events.[36]

Though only few TSRs and TERs are performed compared to hip and knee replacements,[3] recent data suggests that the demand for these upper extremity joint replacements is increasing rapidly and it is expected there will be a seven-fold increase in the number of TSRs over the next 15 years.[8] Though our limited data suggests that VTE incidence following TSR may be on a temporal decline, VTE incidence is expected to rise with the increase in demand for TSRs and TERs and especially given that guidelines for thromboprophylaxis in patients undergoing these joint replacements are not clearly defined.[4] The social, health and economic costs associated with VTE and its treatment are substantial and potentially devastating.[37] Our findings are clinically relevant as we have identified several potentially modifiable factors that can be identified and optimised prior to joint surgery. Recognition of unmodifiable factors such as older age should aid in careful planning before and after surgery such as administering enhanced thromboprophylaxis to these patient groups and ensuring early mobilisation.

In addition to several strengths mentioned above, our analyses employed appropriate meta-analytic approaches previously not utilised which included taking into account the heterogeneity between contributing studies and ensuring that studies with zero rates were not excluded from the pooled

analysis; employment of comprehensive data checks to ensure the uniqueness of each study in contributing data given that some of the articles were based on the same data; quantification and exploration of heterogeneity; subgroup analyses; and exploring for publication bias. We also conducted a detailed quality assessment of all studies using a validated tool and none of the studies was reported to be of poor quality. The limitations deserve consideration, though these were inherent to the included studies and not our approach: (i) the majority of studies included were retrospective cohort designs and case series, hence not of high methodological quality; (ii) majority of studies did not distinguish between anatomic TSR and reverse TSR; (iii) due to inconsistent or lack of reporting of the definition and/or diagnosis of specific VTE endpoints (e.g., symptomatic or asymptomatic DVT and PE) and the relatively limited number of studies available for pooling, incidence data could not be estimated separately for these endpoints; (iv) furthermore, the wide variability in the incidence estimates may suggest that asymptomatic VTE events were included and hence there may be biases in the estimates; however, we have no way of knowing this as none of the included studies specifically reported asymptomatic VTE events; (v) the majority of studies did not adjust for confounding and hence pooling was based on variably adjusted data, therefore the possibility of residual confounding; (vi) some of our findings were based on single or few reports, hence require replication in further studies; (vii) given that most of the studies were conducted in the USA and UK, the generalizability of the findings to other populations is limited; (viii) the majority of studies did not provide specific information on type of thromboprophylaxis administered to patients; and (ix) the cutoffs of certain risk factors such as alcohol and drug abuse were not provided by the individual studies, hence the inability to draw conclusions for clinical application. Given the several limitations, the findings should be interpreted with caution and further large-scale studies are warranted to confirm or refute these findings.

5. Conclusions

Though the incidence of VTE following primary TSR or TER is variable and ranges from 0.04 to 16%, the average incidence within the first 3 months is less than 1%. The risk of VTE following primary TSR may be driven by patient-related factors such as age, BMI, lifestyle factors, and the

presence of comorbidities and surgery- and hospital-related factors such as reverse TSR and inpatient TSR. High risk groups such as older patients, those with a previous VTE history and those undergoing reverse or inpatient TSR may need close monitoring. Modifiable factors such as high BMI, alcohol abuse, and comorbidities could be identified and addressed prior to surgery.

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Declarations of interest

MRW undertakes teaching on basic sciences for Orthopaedic trainees preparing for the FRCS, his institution receives market rate payment for this teaching from Heraeus. MRW and AWB are co-applicants on a grant from Stryker investigating the outcome of the Triathlon total knee replacement. MRW and AWB are members of the National Joint Registry lot 2 contract (statistical analysis) team.

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Beulens, R. Dankner, C. Cooper, S. Giampaoli, J.F. Deen, A. Gomez de la Camara, L.H. Kuller, A. Rosengren, P.J. Svensson, D. Nagel, C.J. Crespo, H. Brenner, J.R. Albertorio-Diaz, R. Atkins, E.J. Brunner, M. Shipley, I. Njolstad, D.A. Lawlor, Y.T. van der Schouw, R.M. Selmer, M. Trevisan, W.M.M. Verschuren, P. Greenland, S. Wassertheil-Smoller, G.D.O. Lowe, A.M. Wood, A.S. Butterworth, S.G. Thompson, J. Danesh, E. Di Angelantonio, T. Meade, C. Emerging Risk Factors, Cardiovascular Risk Factors Associated With Venous Thromboembolism, JAMA Cardiol 4(2) (2019) 163-173.

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Figure legends

Figure 1 PRISMA flow diagram

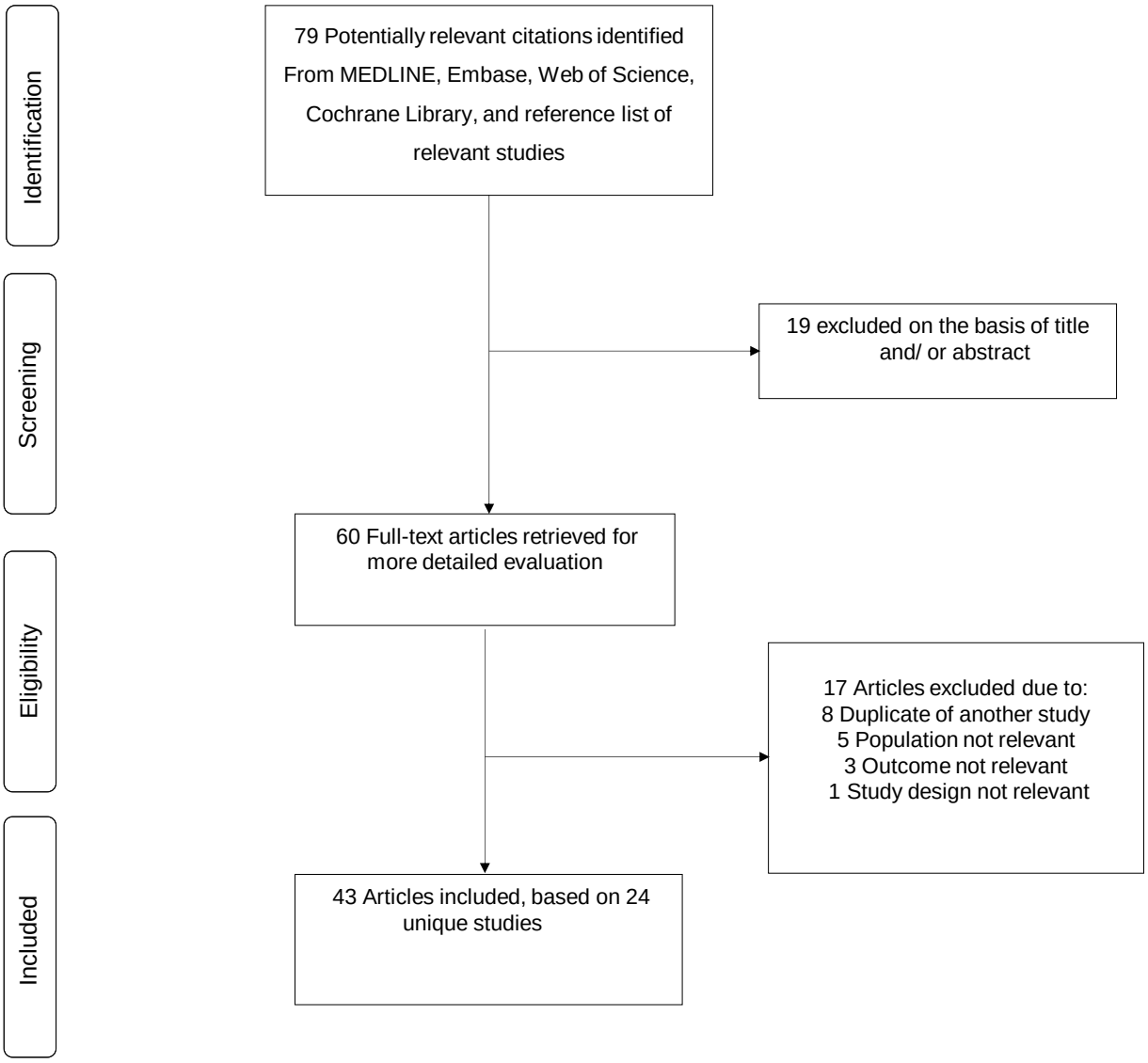
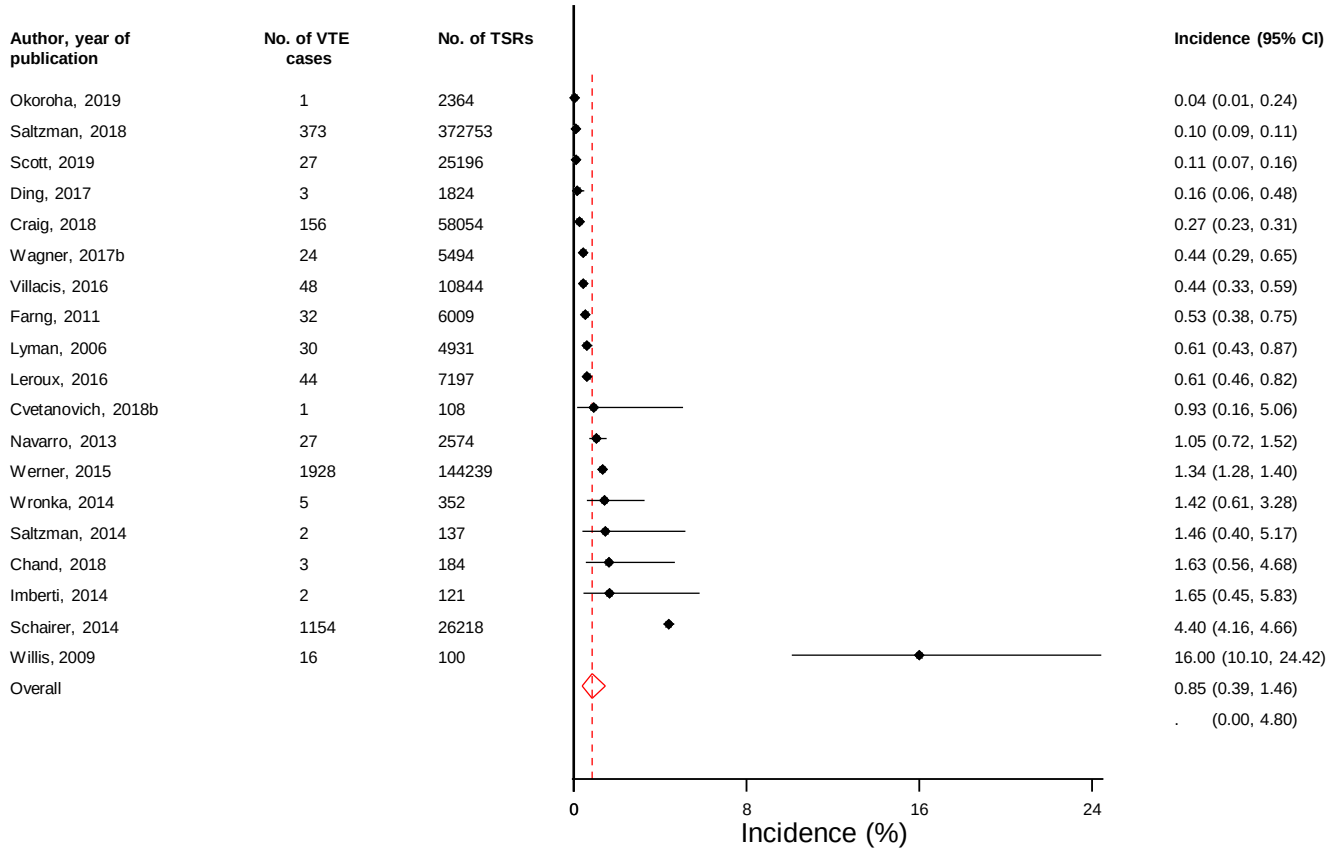
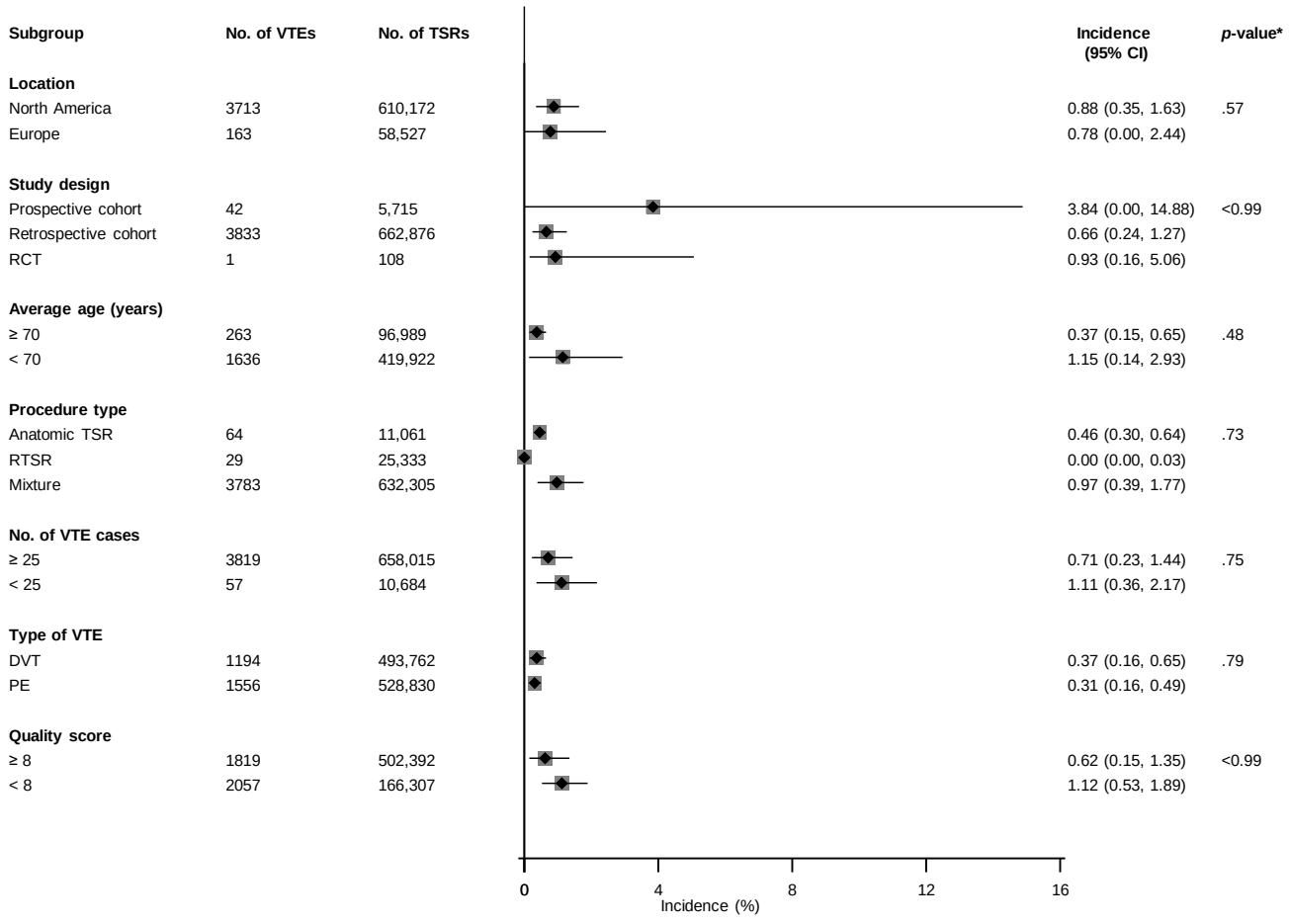


Figure 2 Incidence of venous thromboembolism following TSR across eligible studies



CI, confidence interval (bars); TSR, total shoulder replacement; VTE, venous thromboembolism

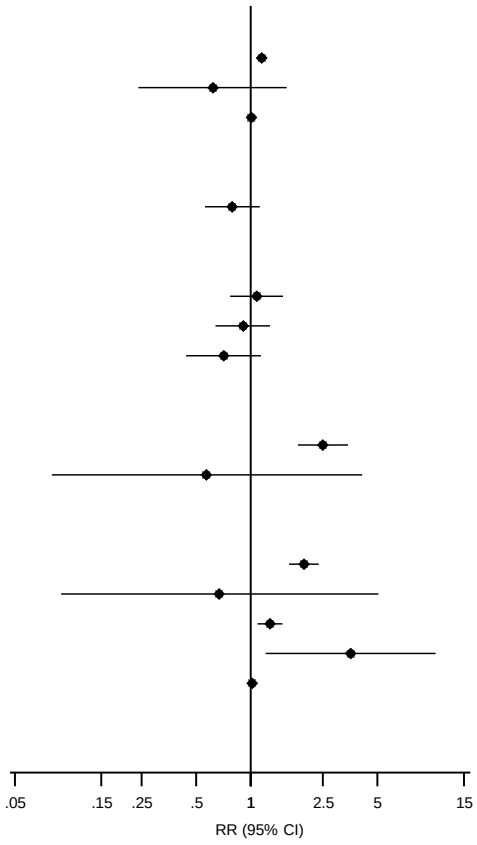
Figure 3 Incidence of venous thromboembolism following TSR, grouped according to several study level characteristics



DVT, deep vein thrombosis; PE, pulmonary embolism; RCT, randomised controlled trial; RTSR, reverse total shoulder replacement; TSR, total shoulder replacement; VTE, venous thromboembolism

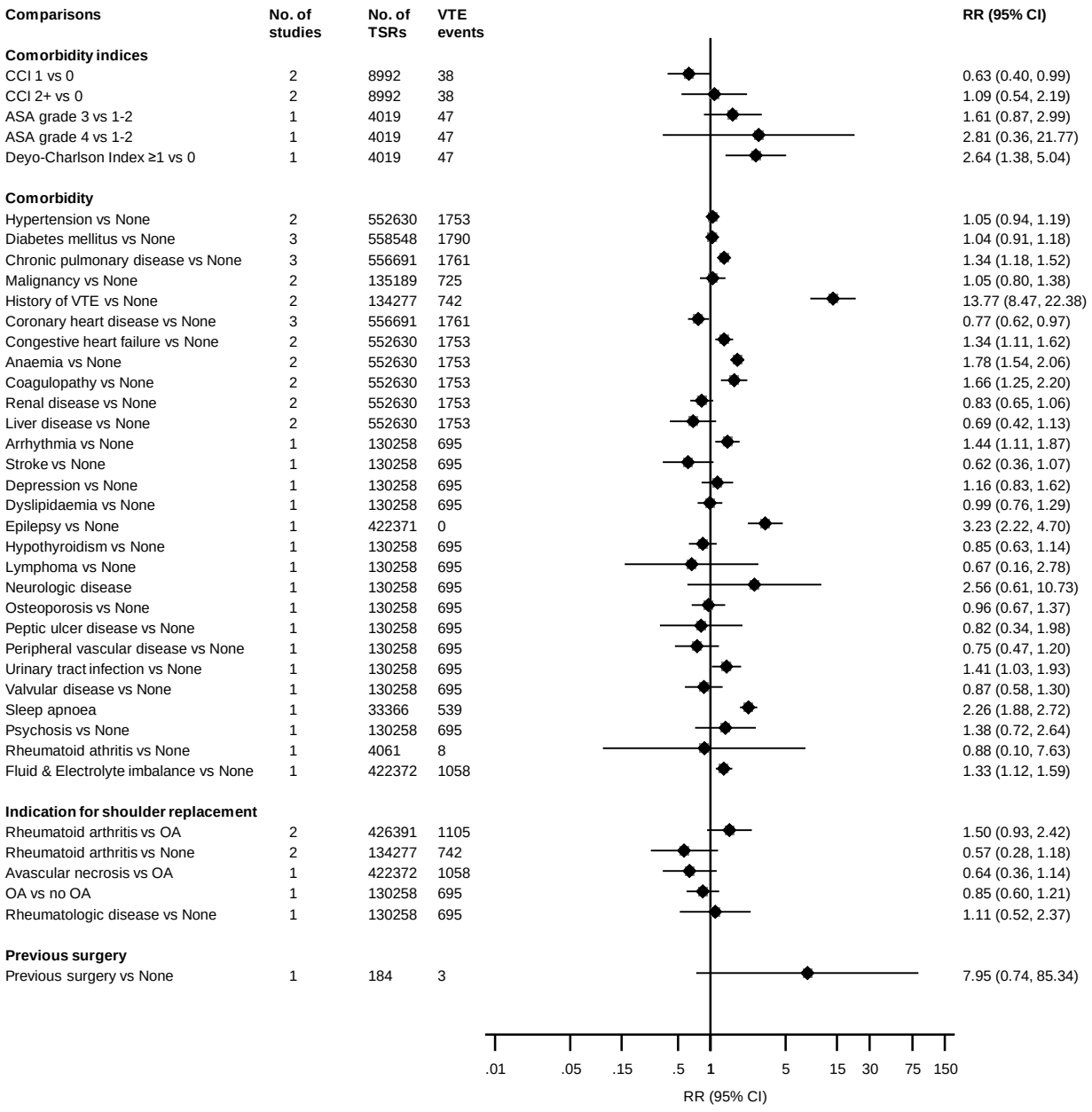
Figure 4 Sociodemographic characteristics and body mass index comparisons and risk of venous thromboembolism following TSR

Comparisons	No. of studies	No. of TSRs	No. of VTE events	RR (95% CI)
Age				
Age ≥70 years vs <70 years	2	9,555	32	1.15 (1.08, 1.22)
Age ≥60 years vs <60 years	3	15,049	56	0.62 (0.24, 1.58)
Per 1-year increase in age	2	427,303	1,088	1.01 (1.00, 1.02)
Gender				
Males vs Females	4	384,277	477	0.79 (0.56, 1.12)
Race				
Black vs White	2	425,157	1,067	1.08 (0.77, 1.51)
Hispanic vs White	1	422,372	1,058	0.91 (0.64, 1.28)
Other vs White	1	422,372	1,058	0.71 (0.44, 1.14)
Lifestyle				
Alcohol abuse vs None	2	552,629	1,539	2.50 (1.82, 3.44)
Drug abuse vs None	1	130,258	695	0.57 (0.08, 4.12)
BMI				
≥50 vs <50	4	576,956	7,712	1.97 (1.63, 2.37)
≥40 vs <40	1	4,567	23	0.67 (0.09, 5.06)
≥30 vs <30	4	589,121	1,840	1.28 (1.09, 1.50)
≥25 vs <25	1	4,019	47	3.56 (1.21, 10.49)
Per unit BMI increase	1	4,567	23	1.02 (0.97, 1.08)



BMI, body mass index; CI, confidence interval (bars); RR, relative risk

Figure 5 Medical and surgical history comparisons and risk of venous thromboembolism following TSR



ASA, American Society of Anesthesiologists; CCI, Charlson Comorbidity Index; CHD, coronary heart disease; FHx, family history; HRT, hormone replacement therapy; OA, osteoarthritis; VTE, venous thromboembolism

Table 1. Summary characteristics of included studies (2003-2019)

Characteristics	
Participants	**N**
Total number of participants or joint replacements	672,495
Total number of VTE cases	3,888
Study characteristics	
Location	N studies (N participants or joint replacements)
North America	20 (613,957)
Europe	4 (58,538)
Study design	N studies (N participants or joint replacements)
Retrospective cohorts	20 (666,672)
Prospective cohorts	3 (5,715)
RCT	1 (108)
Median (min-max) study quality score	8 (6-9)
Study level participant characteristics	
Weighted mean (min-max) age, years	68.9 (51.3-72.5)
Median (IQR) % males	43.7 (36.7-46.7)
Weighted mean (min-max) follow-up, years	0.19 (0.01-8.00)
Joint type	N studies (N participants or joint replacements)
Shoulder	19 (668,699)
Elbow	5 (3,796)

IQR, interquartile range; N, number; RCT, randomised controlled trial; VTE, venous thromboembolism

Table 2. Characteristics of studies included in review (2003-2019)

Author, year of publication	Year of study	Country	Average age (Years)	Joint replacement	Study Design	% Male	Mean/median follow-up duration	No. of participants / procedures	No. of VTEs	VTE diagnostic method	Type of adjustment	Study quality
Espag, 2003	1991-2000	UK	NR	TER	Retrospective cohort	NR	5.7 years	11	1	NR	NA	7
Lyman, 2006	1985-2003	USA	66.4	TSR	Retrospective cohort	39.7	NR	4931	30	NR	Multivariable	7
Duncan, 2007	1981-2001	USA	NR	TER	Retrospective cohort	NR	3 days	816	2	PE: CT scan or autopsy	NA	8
Willis, 2009	2003-2004	USA	67.0	TSR	Prospective cohort	44.0	12 weeks	100	13	DVT: Doppler ultrasound	NA	7
Jameson, 2011	2005-2008	UK	70.0	TSR	Retrospective cohort	NR	90 days	4061	8	NR	Univariable	7
Krenek, 2011	1995-2005	USA	56.0	TER	Retrospective cohort	36.0	90 days	1625	4	NR	NA	9
Farng, 2011	1995-2005	USA	68.3	TSR	Retrospective cohort	46.9	90 days	6009	32	NR	NA	6
Gay, 2012	1997-2006	USA	58.3	TER	Retrospective cohort	28.8	90 days	1155	3	NR	NA	7
Singh, 2012	1976-2008	USA	65.0	TSR	Prospective cohort	44.0	90 days	4019	47	NR	Univariable	9
Navarro, 2013	2005-2009	USA	72.3	TSR	Retrospective cohort	43.7	90 days	2574	14	Doppler ultrasound	Univariable	8
Baghdadi, 2014	1987-2006	USA	62.3	TER	Retrospective cohort	24.0	5.8 years	723	1	NR	Univariable	8
Griffin, 2014	200-2008	USA	68.8	TSR	Retrospective cohort	38.0	3 days	58790	176	NR	NA	8
Griffin, 2014b	1998-2008	USA	68.8	TSR	Retrospective cohort	44.0	3 days	31924	64	NR	Univariable	8
Schairer, 2014	2005-2010	USA	67.5	TSR	Retrospective cohort	48.2	90 days	26218	1154	NR	NA	8
Wronka, 2014	NR	UK	NR	TSR	Retrospective cohort	NR	6 weeks	352	5	USS Doppler study, VQ scan or CT scan of the chest / CTPA	NA	8
Jiang, 2014	2010-2011	USA	69.5	TSR	Retrospective cohort	43.0	NR	19497	52	NR	Multivariable	9
Imberti, 2014	2009-2011	Italy	51.3	TSR	Prospective cohort	54.4	90 days	121	2	DVT: Compressive ultrasonography, echocolordoppler, CT scan, venography; for PE: perfusion lung scan matched with chest X-ray, VQ scan, CTPA	NA	9
Saltzman, 2014	2007-2011	USA	72.5	TSR	Retrospective cohort	34.0	90 days	137	3	NR	NA	8
Werner, 2015	2005-2012	USA	NR	TSR	Retrospective cohort	38.6	90 days	144239	1928	NR	Univariable	6
Day, 2015	2004-2009	USA	73.0	TSR	Retrospective cohort	73-76	90 days	130258	695	NR	Multivariable	9
Young, 2015	2002-2011	USA	69.0	TSR	Retrospective cohort	39.7	NR	422372	1058	NR	Multivariable	8
Ponce, 2015	2002-2011	USA	69.0	TSR	Retrospective cohort	40.0	NR	422371	844	NR	Multivariable	7
Leroux, 2016	2005-2014	USA	18-85+*	TSR	Retrospective cohort	51.3	30 days	7197	44	NR	Univariable	8
Villacis, 2016	2011-2013	USA	70.1	TSR	Retrospective cohort	45.0	90 days	10844	48	NR	Univariable	6
Churchill, 2016	2002-2011	USA	68.8	TSR	Retrospective cohort	40.0	NR	422371	NR	NR	Multivariable	7
Fu, 2017	2011-2014	USA	NR	TSR	Retrospective cohort	NR	30 days	5918	37	NR	Univariable	7
Basques, 2017	2005-2012	USA	NR	TSR	Retrospective cohort	38.4	90 days	123347	1063	NR	Multivariable	8
Lovy, 2017	2007-2013	USA	63.3	TSR	Retrospective cohort	25.0	30 days	189	2	NR	NA	7
Rao, 2017	2005-2012	USA	NR	TSR	Retrospective cohort	NR	30 days	1591	8	NR	Univariable	8
Wagner, 2017	1970-2013	USA	68.0	TSR	Retrospective cohort	45.0	20.0 years	4567	23	NR	Multivariable	8

Author, year of publication	Year of study	Country	Average age (Years)	Joint replacement	Study Design	% Male	Mean/median follow-up duration	No. of participants / procedures	No. of VTEs	VTE diagnostic method	Type of adjustment	Study quality
Wagner, 2017b	1970-2012	USA	67.0	TSR	Prospective cohort	45.0	8.0 years**	5494	24	NR	Multivariable	8
Belmont, 2017	2011-2013	USA	70.1	TSR	Retrospective cohort	43.4	30 days	3547	13	NR	NA	8
Ding, 2017	2011-2014	USA	68.4	TSR	Retrospective cohort	45.4	90 days	1824	0	NR	Univariable	8
Arshi, 2018	2007-2016	USA	70-74*	TSR	Retrospective cohort	40.3	60 days	17542	302	NR	NA	8
Chand, 2018	2010-2016	USA	71.7	TSR	Retrospective cohort	46.7	90 days	184	3	NR	Univariable	6
Saltzman, 2018	2002-2011	USA	66.0-70.8*	TSR	Retrospective cohort	40.3	2.8 days	372753	373	NR	Multivariable	8
Damodar, 2018	2005-2014	USA	NR	TSR	Retrospective cohort	43.7	90 days	13964	42	NR	Multivariable	9
Cvetanovich, 2018	2015-2016	USA	66.4	TSR	RCT	47.2	90 days	108	1	NR	NA	NA
Craig, 2018	1998-2017	UK	72.2	TSR	Retrospective cohort	28.0	90 days	58,054	156	NR	NA	9
Wang, 2019	2005-2014	USA	NR	TSR	Retrospective cohort	48.9	90 days	33366	539	NR	Univariable	7
Yin, 2019	2006-2015	USA	63.9	TSR	Retrospective cohort	39.0	30 days	2785	9	NR	Multivariable	8
Okoroha, 2019	2007-2015	USA	69.0	TSR	Retrospective cohort	42.3	3.8 years	2364	1	NR	NA	8
Scott, 2019	2014	USA	72.3	TSR	Retrospective cohort	36.7	90 days	25196	27	NR	NA	8

*, age range of participants; **, for participants who did not undergo revision surgery; CT, computed tomography; CTPA, chest tomography pulmonary angiogram; DVT, deep vein thrombosis; NA, not applicable; NR, not reported; PE, pulmonary embolism; RCT, randomised controlled trial; TSR, total shoulder replacement; TER, total elbow replacement; VQ, ventilation-perfusion

Supplementary Material

Appendix A	PRISMA checklist
Appendix B	MOOSE checklist
Appendix C	Literature search strategy
Appendix D	Reference list of 43 included articles (2003-2019)
Appendix E	Incidence of deep vein thrombosis and pulmonary embolism following primary TSR
Appendix F	Incidence of VTE following primary TSR at specific follow-up periods
Appendix G	Temporal trends in VTE incidence following primary TSR
Appendix H	Incidence of VTE following primary TER
Appendix I	Risk of venous thromboembolism comparing males to females following primary TSR
Appendix J	Associations of surgery- and hospital-related factors with risk of venous thromboembolism following primary TSR

Appendix A. PRISMA checklist

Section/topic	Item No	Checklist item	Reported on page No
Title			
Title	1	Identify the report as a systematic review, meta-analysis, or both	1
Abstract			
Structured summary	2	Provide a structured summary including, as applicable, background, objectives, data sources, study eligibility criteria, participants, interventions, study appraisal and synthesis methods, results, limitations, conclusions and implications of key findings, systematic review registration number	2
Introduction			
Rationale	3	Describe the rationale for the review in the context of what is already known	4-5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS)	5
Methods			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (such as web address), and, if available, provide registration information including registration number	2
Eligibility criteria	6	Specify study characteristics (such as PICOS, length of follow-up) and report characteristics (such as years considered, language, publication status) used as criteria for eligibility, giving rationale	6
Information sources	7	Describe all information sources (such as databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated	Appendix C
Study selection	9	State the process for selecting studies (that is, screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis)	6-7
Data collection process	10	Describe method of data extraction from reports (such as piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators	6-7
Data items	11	List and define all variables for which data were sought (such as PICOS, funding sources) and any assumptions and simplifications made	6-7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis	7-8
Summary measures	13	State the principal summary measures (such as risk ratio, difference in means).	7-8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (such as I^2 statistic) for each meta-analysis	7-8
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (such as publication bias, selective reporting within studies)	7-8
Additional analyses	16	Describe methods of additional analyses (such as sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified	7-8
Results			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram	8 and Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (such as study size, PICOS, follow-up period) and provide the citations	8-9, Table 1, Appendix E
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome-level assessment (see item 12).	9-10, Appendix E
Results of individual studies	20	For all outcomes considered (benefits or harms), present for each study (a) simple summary data for each intervention group and (b) effect estimates and confidence intervals, ideally with a forest plot	9-10, Figures 2-5
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency	9-10, Figures 2-5; Appendices F, 9,10,11
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see item 15)	Appendix E
Additional analysis	23	Give results of additional analyses, if done (such as sensitivity or subgroup analyses, meta-regression) (see item 16)	9-10; Figure 4
Discussion			
Summary of evidence	24	Summarise the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (such as health care providers, users, and policy makers)	10-11
Limitations	25	Discuss limitations at study and outcome level (such as risk of bias), and at review level (such as incomplete retrieval of identified research, reporting bias)	11-12
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research	12
Funding			
Funding	27	Describe sources of funding for the systematic review and other support (such as supply of data) and role of funders for the systematic review	13

Appendix B. MOOSE checklist

Venous thromboembolism following 672,495 primary total shoulder and elbow replacements: meta-analyses of incidence, temporal trends and potential risk factors

Criteria		Brief description of how the criteria were handled in the review
Reporting of background		
√	Problem definition	There is uncertainty regarding the exact incidence of venous thromboembolism (VTE) following upper extremity joint replacement. Whether risk factors for VTE following hip and knee joint replacements influence the risk for VTE following upper extremity joint replacement in a similar manner is unknown. We conducted a systematic meta-analysis to evaluate the incidence of and potential risk factors for VTE following total shoulder and elbow replacement.
√	Hypothesis statement	Several patient-, surgery-, and hospital-related related factors after upper extremity joint replacement.
√	Description of study outcomes	Venous thromboembolism
√	Type of exposure	Patient-, surgery-, and hospital-related factors
√	Type of study designs used	Longitudinal studies (prospective or retrospective case control, prospective cohort, retrospective cohort, case-cohort, nested-case control, or clinical trials)
√	Study population	Patients followed for VTE outcomes following total shoulder or elbow replacement
Reporting of search strategy should include		
√	Qualifications of searchers	
√	Search strategy, including time period included in the synthesis and keywords	Time period: from inception to 26 September 2019 The detailed search strategy can be found in Appendix C
√	Databases and registries searched	MEDLINE, EMBASE, Web of Science, and Cochrane databases
√	Search software used, name and version, including special features	OvidSP was used to search EMBASE and MEDLINE EndNote used to manage references
√	Use of hand searching	We searched bibliographies of retrieved papers
√	List of citations located and those excluded, including justifications	Details of the literature search process are outlined in the flow chart. The citation list for excluded studies are available on request.
√	Method of addressing articles published in languages other than English	Not applicable
√	Method of handling abstracts and unpublished studies	Abstracts with no full text publications were not included.
√	Description of any contact with authors	We contacted authors of studies that did not provide adequate data in their studies
Reporting of methods should include		
√	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	Detailed inclusion and exclusion criteria are described in the Methods section.
√	Rationale for the selection and coding of data	Data extracted from each of the studies were relevant to the population characteristics, study design, exposure, and outcome.
√	Assessment of confounding	We assessed confounding by ranking individual studies on the basis of different adjustment levels and performed sub-group analyses to evaluate differences in the overall estimates according to levels of adjustment.
√	Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results	Study quality was assessed based on the nine-star Newcastle–Ottawa Scale using pre-defined criteria namely: population representativeness, comparability (adjustment of confounders), ascertainment of outcome. Sensitivity analyses by several quality indicators such as study size, duration of follow-up, and adjustment factors.
√	Assessment of heterogeneity	Heterogeneity of the studies was quantified with I^2 statistic that provides the relative amount of variance of the summary effect due to the between-study heterogeneity and explored using meta-regression and stratified analyses
√	Description of statistical methods in sufficient detail to be replicated	Description of methods of meta-analyses, sensitivity analyses, meta-regression and assessment of publication bias are detailed in the methods. We performed random or fixed effects meta-analysis where appropriate using STATA 15.

√	Provision of appropriate tables and graphics	Table 1; Figures 1-5; Appendices E, F, G, H, I, J, K
Reporting of results should include		
√	Graph summarizing individual study estimates and overall estimate	Figures 2-5; Appendices G, I, J, K
√	Table giving descriptive information for each study included	Appendix E
√	Results of sensitivity testing	Not applicable
√	Indication of statistical uncertainty of findings	95% confidence intervals were presented with all summary estimates, I^2 values and results of sensitivity analyses
Reporting of discussion should include		
√	Quantitative assessment of bias	Sensitivity analyses indicate heterogeneity in strengths of the association due to most common biases in observational studies. The systematic review is limited in scope, as it involves published data. Individual participant data is needed. Limitations have been discussed.
√	Justification for exclusion	All studies were excluded based on the pre-defined inclusion criteria in methods section.
√	Assessment of quality of included studies	Brief discussion included in 'Methods' section
Reporting of conclusions should include		
√	Consideration of alternative explanations for observed results	Discussion
√	Generalization of the conclusions	Discussed in the context of the results.
√	Guidelines for future research	We recommend analyses of individual participant data
√	Disclosure of funding source	In "Acknowledgement" section

Appendix C. Literature search strategy

Relevant studies, published from inception to 26 September 2019 (date last searched), were identified through electronic searches limited to the English language using MEDLINE, Embase, Web of Science, and Cochrane databases. Electronic searches were supplemented by scanning reference lists of articles identified for all relevant studies (including review articles) and by hand searching of relevant journals.

1 exp Arthroplasty, Replacement, Shoulder/ (736)
2 exp Arthroplasty, Replacement, Elbow/ (345)
3 exp Venous Thromboembolism/ (9326)
4 exp Venous Thrombosis/ (53028)
5 deep vein thrombosis.mp. (15554)
6 exp Pulmonary Embolism/ (37391)
7 exp Thromboembolism/ (53489)
8 1 or 2 (1079)
9 3 or 4 or 5 or 6 or 7 (132255)
10 8 and 9 (15)
11 limit 10 to humans (15)

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Each part was specifically translated for searching the other databases (EMBASE, Web of Science, and Cochrane databases)

Appendix D. Reference list of 43 included articles

1. Arshi A, Leong NL, Wang C, Buser Z, Wang JC, Vezeridis PS, McAllister DR, Petrigliano FA. Relative Complications and Trends of Outpatient Total Shoulder Arthroplasty. Orthopedics 2018;**41**(3):e400-e409.

2. Baghdadi YM, Veillette CJ, Malone AA, Morrey BF, Sanchez-Sotelo J. Total elbow arthroplasty in obese patients. J Bone Joint Surg Am 2014;**96**(9):e70.

3. Basques BA, Erickson BJ, Leroux T, Griffin JW, Frank RM, Verma NN, Romeo AA. Comparative outcomes of outpatient and inpatient total shoulder arthroplasty: an analysis of the Medicare dataset. Bone Joint J 2017;**99-B**(7):934-938.

4. Belmont PJ, Jr., Kusnezov NA, Dunn JC, Bader JO, Kilcoyne K, Waterman BR. Predictors of Hospital Readmission After Total Shoulder Arthroplasty. Orthopedics 2017;**40**(1):e1-e10.

5. Chand MR, Meiyappan A, Villa JM, Kanwar S, Sabesan VJ, Gilot G. Ninety-Day Readmission Following Shoulder Arthroplasty. Journal of Shoulder and Elbow Arthroplasty 2018;**2**:2471549218810016.

6. Churchill J, Menendez ME, Ponce BA. Early Postoperative Complications After Shoulder Arthroplasty in Patients With Epilepsy. Orthopedics 2016;**39**(6):e1075-e1079.

7. Craig RS, Lane JCE, Carr AJ, Furniss D, Collins GS, Rees JL. Serious adverse events and lifetime risk of reoperation after elective shoulder replacement: population based cohort study using hospital episode statistics for England. BMJ 2019;**364**:l298.

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10. Day JS, Ramsey ML, Lau E, Williams GR. Risk of venous thromboembolism after shoulder arthroplasty in the Medicare population. J Shoulder Elbow Surg 2015;**24**(1):98-105.

11. Ding DY, Mahure SA, Mollon B, Shamah SD, Zuckerman JD, Kwon YW. Comparison of general versus isolated regional anesthesia in total shoulder arthroplasty: A retrospective propensity-matched cohort analysis. J Orthop 2017;**14**(4):417-424.

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14. Farng E, Zingmond D, Krenek L, Soohoo NF. Factors predicting complication rates after primary shoulder arthroplasty. J Shoulder Elbow Surg 2011;**20**(4):557-63.

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16. Gay DM, Lyman S, Do H, Hotchkiss RN, Marx RG, Daluiski A. Indications and reoperation rates for total elbow arthroplasty: an analysis of trends in New York State. J Bone Joint Surg Am 2012;**94**(2):110-7.

17. Griffin JW, Hadeed MM, Novicoff WM, Browne JA, Brockmeier SF. Patient age is a factor in early outcomes after shoulder arthroplasty. J Shoulder Elbow Surg 2014;**23**(12):1867-1871.

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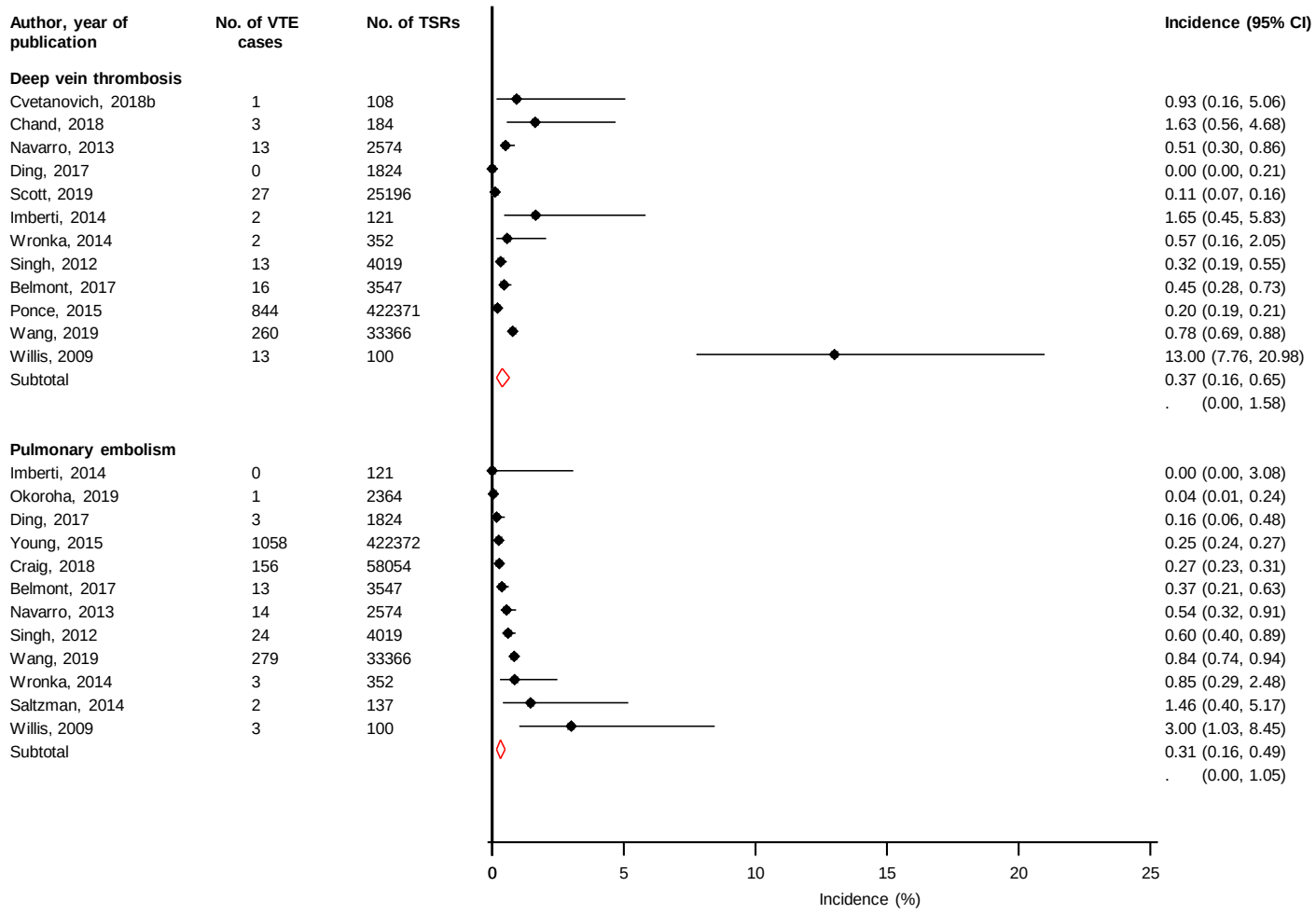
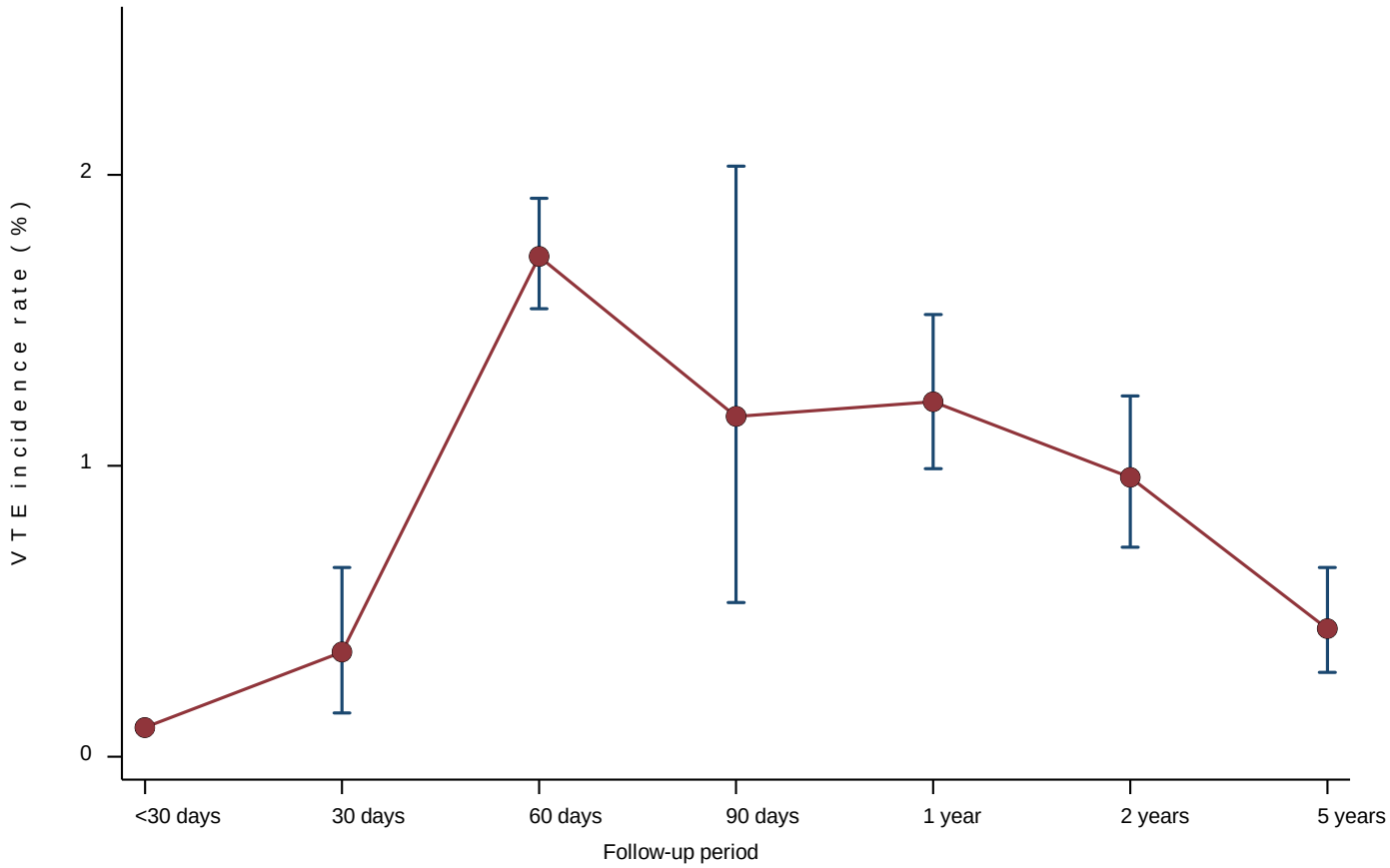
Appendix E. Incidence of deep vein thrombosis and pulmonary embolism following primary TSR



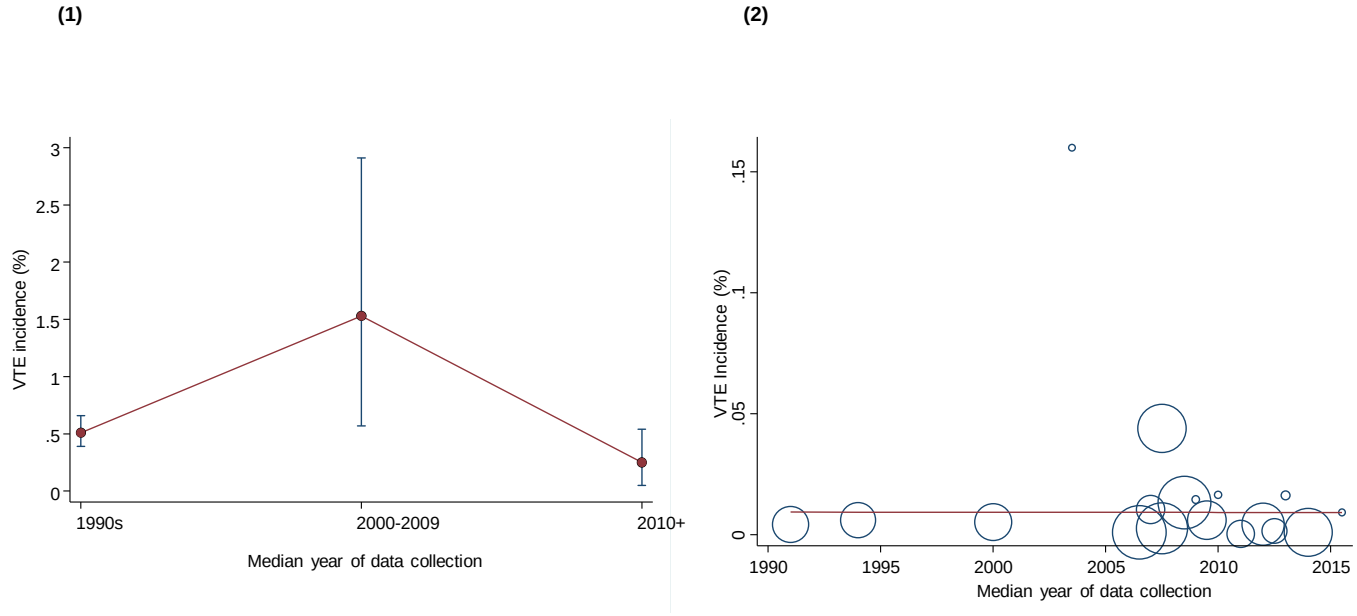
CI, confidence interval (bars); TSR, total shoulder replacement; VTE, venous thromboembolism

Appendix F. Incidence of VTE following primary TSR at specific follow-up periods



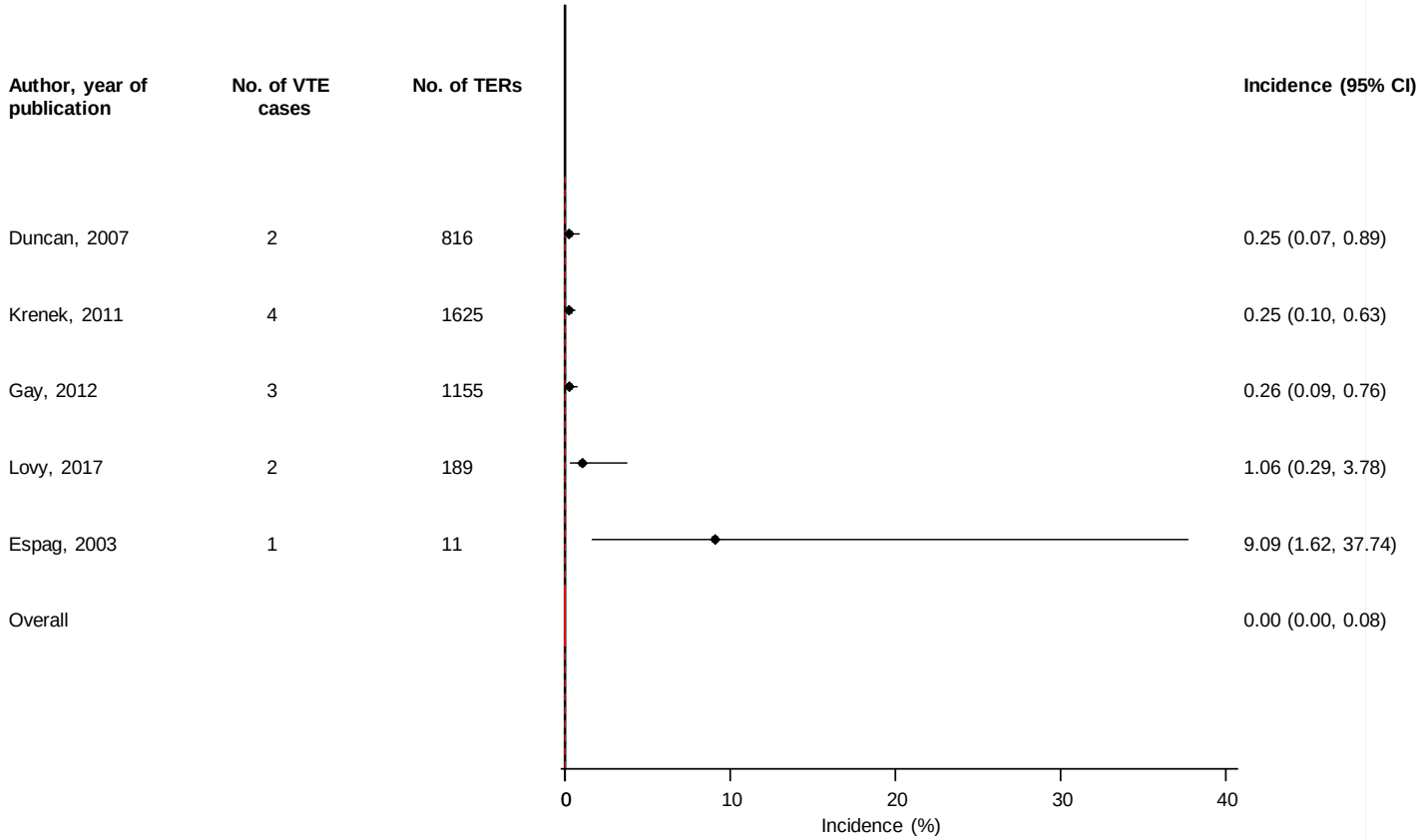
TSR, total shoulder replacement; VTE, venous thromboembolism

Appendix G. Temporal trends in VTE incidence following primary TSR



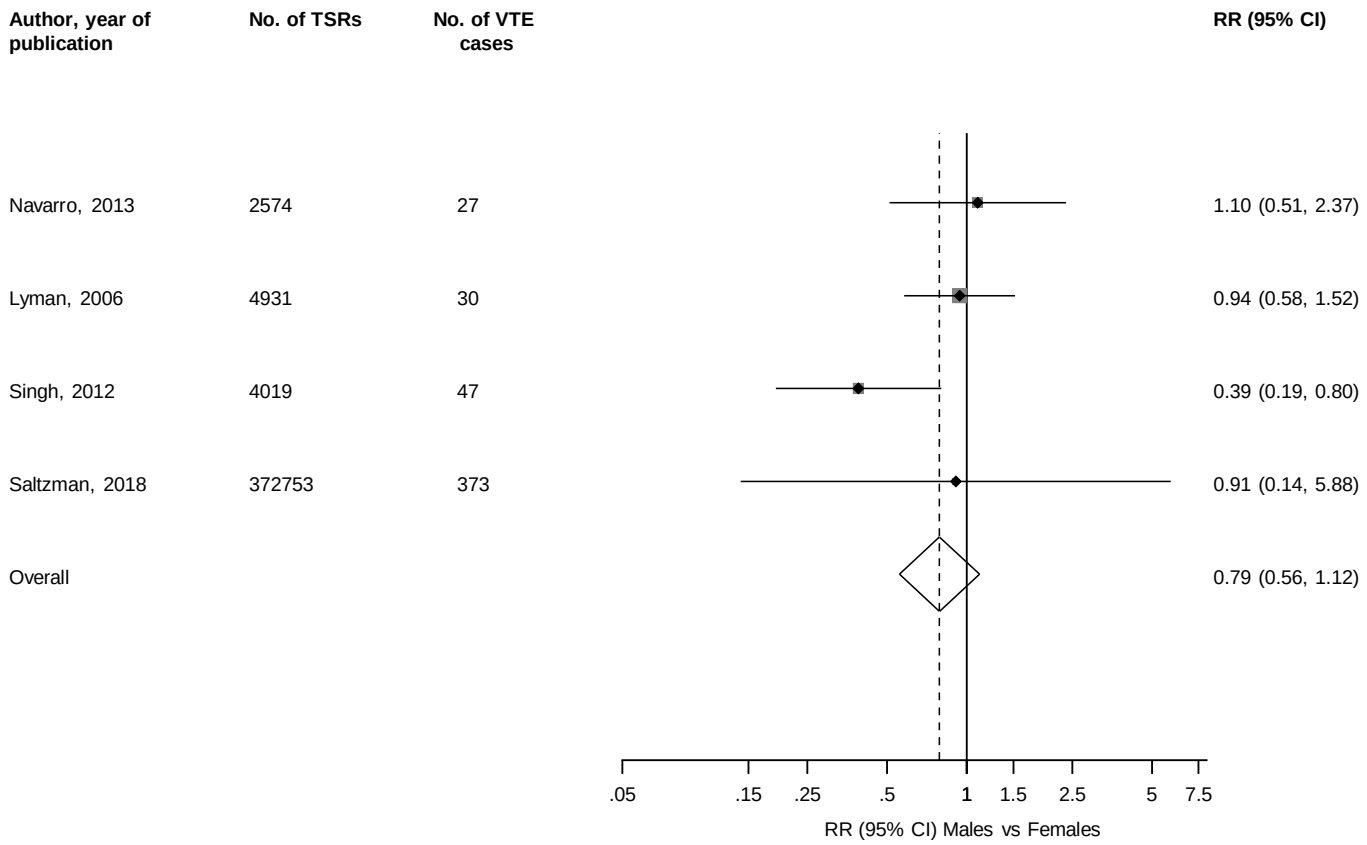
A, Incidence of TSR VTE by median year of data collection; B, Meta-regression bubble plot of incidence of TSR VTE against median year of study data collection; TSR, total shoulder replacement; VTE, venous thromboembolism

Appendix H. Incidence of VTE following primary TER



CI, confidence interval (bars); TER, total elbow replacement; VTE, venous thromboembolism

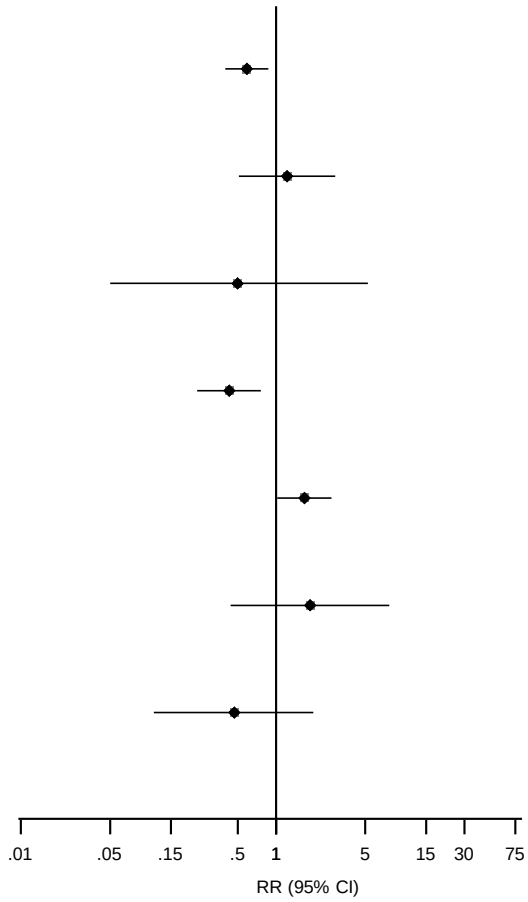
Appendix I. Risk of venous thromboembolism comparing males to females following primary TSR



CI, confidence interval (bars); RR, relative risk; TSR, total shoulder replacement

Appendix J. Associations of surgery- and hospital-related factors with risk of venous thromboembolism following primary TSR

Comparison	No. of studies	No. of participants	No. of VTE events	RR (95% CI)
Procedure type				
ATSR vs RTSR	3	32,915	127	0.59 (0.40, 0.87)
Implant fixation				
Cemented vs Uncemented	1	4,019	47	1.22 (0.51, 2.91)
Type of anaesthesia				
General vs Regional	1	1,824	3	0.50 (0.05, 5.24)
Length of stay				
Outpatient vs Inpatient TSR	2	130,544	1,107	0.43 (0.24, 0.76)
Altitude of hospital				
High vs Low altitude hospital	1	13,964	69	1.67 (1.02, 2.72)
Seasonality				
July effect vs None	1	1,591	8	1.85 (0.44, 7.70)
Surgeon experience				
Residents/Fellows vs None	1	1,591	8	0.47 (0.11, 1.96)



CI, confidence interval (bars); RR, relative risk; RTSR; reverse total shoulder replacement; ATSR, anatomic total shoulder replacement; VTE, venous thromboembolism