Risk of complications and poorer postoperative outcomes in obese and diabetic patients following upper limb arthroplasty: A systematic review and meta-analysis

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Abstract

The impact of obesity and diabetes mellitus on patient outcomes following upper limb arthroplasty is contentious. With increasing demand for joint arthroplasty, risk factors that predispose patients to greater complications and poorer outcomes must be thoroughly investigated. The objective of this review was to synthesise the best available evidence investigating the influence of obesity or diabetes mellitus on complications and/or poorer postoperative outcomes following total shoulder (TSA), reverse total shoulder (RTSA) and total elbow arthroplasty (TEA).

Electronic databases (PubMed, CINAHL, and Embase) and grey literature were searched for studies that evaluated the influence of obesity (Body Mass Index [BMI] ≥ 30 kg/m^2) or diabetes mellitus on arthroplasty outcomes. Two independent reviewers assessed the methodological validity of eligible studies and data was pooled in statistical meta-analysis where appropriate (RevMan 5.3; Cochrane Collaboration). The review was prospectively registered on PROSPERO (CRD42016053299).

Twenty-one studies (20 cohort studies and one case-control) were included. The majority of studies considered TSA and/or RTSA populations, while four studies evaluated TEA patients. Obesity was found to significantly increase operative duration, with obese TSA/RTSA patients experiencing operations 10.00 minutes longer (95% CI [6.31, 13.69]) than patients with a BMI in the normal range, which increased to 12.48 minutes (95% CI [8.40, 16.55]) in patients with a BMI ≥ 35.0. Furthermore, obese and morbidly obese patients had 3.92 (95% CI 3.59, 4.28) to 5.46 (95% [CI 4.91, 6.07]) times greater odds of venous thromboembolism compared to their non-obese counterparts. Similarly, odds of infection increased with increasing BMI, from 2.37 (95% CI [1.65, 3.41]) times in obese, to greater than five times (95% CI [4.70, 5.39]) in morbidly obese. Obesity also increased the odds of revision (OR 1.52; 95% CI [1.43, 1.61]), dislocation (OR = 2.51; 95% CI [2.35, 2.69]) and fracture (OR = 1.94; 95% CI [1.79, 2.10]) in TSA, RTSA and TEA patients, however had no influence on the odds of urinary tract infection (OR = 0.88; 95% CI [0.48, 1.61], length of stay (MD = 0.15; 95% CI [-0.28, 0.58]), unscheduled return to theatre (OR = 0.74; 95% CI [0.44, 1.24]) or mortality (OR = 1.79; 95% CI [0.79, 4.03]). Nonetheless, morbid obesity made a small, yet significant, difference on mean length of stay (MD = 0.28; 95% CI [0.14, 0.43]). Evidence

examining the effect of obesity on blood transfusion was inconclusive, while minimal evidence was available on pneumonia and quality of life.

Diabetic TSA, RTSA and TEA patients had 2.93 (95% CI [1.97, 4.35]) times greater odds of mortality as an inpatient. Furthermore, diabetes mellitus was found to significantly affect odds of blood transfusion (OR = 1.49; 95% CI [1.41, 1.57]) and pneumonia (OR = 1.38; 95% CI [1.14, 1.67]), however had no effect on the odds of pulmonary embolism (OR = 1.17; 95% CI [0.94, 1.44]). The evidence for greater risk of blood transfusion in diabetic patients is a concern given the higher odds of further complications observed in transfused patients. There was also limited evidence on unscheduled return to theatre and urinary tract infection. No evidence was found examining the impact of diabetes mellitus on operative duration, dislocation, fracture, pain, function, quality of life, and revision.

Inferences are limited for a number of the outcomes due to methodological shortcomings and confounders. Operative duration was inconsistently defined, and prophylactic regimes for infection and venous thromboembolism were not standardised and varied, across the included studies. The literature suggests that patient factors such as age and gender influence outcomes including revision, infection and fracture, and that surgical factors may impact the incidence of dislocation. A major limitation of studies investigating diabetes mellitus was that they reported data grouped by diabetes mellitus diagnosis without reporting the criteria used for diagnosis, or the level of glycaemic control at time of surgery. A further inherent limitation is the low level of evidence of observational study designs commonly used in orthopaedic research.

Surgeons are advised to consider the additional risks associated with obesity and diabetes mellitus when determining optimal treatment options for upper limb arthroplasty patients.

Declaration

I, Annika Theodoulou, certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name, in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint-award of this degree.

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Chapter 1: Introduction

The impact of obesity and diabetes mellitus on patient outcomes following upper limb arthroplasty is contentious. Chapter 1 introduces the nature, evolution and context of total shoulder and total elbow arthroplasty, in addition to the incidence of expected outcomes and complications of these procedures. Patient demographics have been explored with a focus on the burden of obesity and diabetes mellitus in this population.

1.1 Upper limb arthroplasty

Arthroplasty is the partial or total artificial replacement of the joint surfaces, used to alleviate pain and physical dysfunction associated with end-stage degenerative disease or injury from trauma. It is a procedure commonly performed across various joints including the hip, knee, shoulder and elbow. This section considers primary, total joint arthroplasty of the shoulder and elbow, that is, the initial procedure involving complete replacement of the articular surface of these joints.[1]

1.1.1 Total shoulder arthroplasty and reverse total shoulder arthroplasty

Artificial replacement of the shoulder joint was first performed in 1893, by French surgeon, JE Péan for the treatment of tuberculous arthritis.[2, 3] Significant advances in this treatment approach were then not made again until 1955, by Dr Charles Neer.[4, 5] Neer developed the first humeral prosthesis for the treatment of humeral head fracture, and in 1974, introduced the first modern-day total shoulder prosthesis with a glenoid component.[6, 7] Today, total shoulder replacement is an increasingly common procedure with 23 252 surgeries reported in Australia between September 1999 and December 2015, with 4193 performed in 2015 alone.[1] Primary diagnoses leading to total shoulder replacement include glenohumeral osteoarthritis, rheumatoid arthritis, rotator cuff arthropathy, osteonecrosis and fracture.[1]

Primary total shoulder replacement is sub-classed into total resurfacing, total mid-head, total conventional and total reverse, however both conventional and reverse total shoulder arthroplasty (RTSA) procedures are most commonly used.[1] Conventional total shoulder arthroplasty (TSA) attempts to reproduce the natural anatomical positioning of the shoulder joint. This procedure

involves prosthetic replacement of the glenoid combined with resection (removal) of the humeral head, and replacement with a stemmed humeral prosthesis and humeral head prosthesis.[1] Despite the success of TSA, poorer outcomes and higher failure rates have been noted in patients with 'cuff tear arthropathy',[2] a term defined by Neer to describe extensive deficiency of the rotator cuff due to chronic tears and cuff tendon retraction, with associated secondary glenohumeral joint degenerative changes.[8, 9] This led to the development of alternate prosthetic designs, which reversed the natural anatomical ball-and-socket arrangement of the shoulder joint.[2, 9] In 1985, Paul Grammont, introduced the first promising RTSA design for treatment of cuff tear arthropathy, which evolved over the following decades.[2, 10] In RTSA, the glenoid socket is replaced with a glenoid head component, or 'glenosphere', which is attached to the glenoid surface via a base plate.[1, 11] This is combined with a humeral cup prosthesis attached to a humeral stem, following resection of the humeral head.[1]

In Australia, RTSA is now the most widely performed total shoulder replacement procedure, composing 53.2% of all procedures.[1] It is most commonly performed in females (65.9%), and in patients 75 years of age or older (51.9%).[1] Failure of this prosthesis is most frequently attributed to instability or dislocation (38.5%), and infection (18%).[1] Similarly, TSA contributes to a large percentage (44.0%) of total shoulder replacement procedures performed in Australia.[1] Fifty-eight per cent of TSA patients are female, and the procedure is most frequently performed in patients between 65 to 74 years of age (44.8%).[1] Like RTSA, the most common cause of prosthetic TSA failure is instability and dislocation (25.2%), closely followed by rotator cuff insufficiency (21.0%).[1]

1.1.2 Total elbow arthroplasty

Early 'arthroplasty' treatment for severe elbow diseases was originally performed as a salvage procedure, involving resection or removal, of the articular surfaces of the ulna and humerus.[12, 13] By the early 1900s, resection was accompanied with soft tissue replacement in which a soft tissue graft is inserted between the articular surfaces of the joint.[12, 14] In 1925, the first elbow replacement with prosthetic materials was documented,[13] an approach that continued to evolve over the following 45 years, with surgeons experimenting with innovative prosthetic designs.[12, 13] Unfortunately, early designs had limited success due to poor patient outcomes including implant loosening, instability and poor function.[12] In 1972, the first 'modern' prosthesis was proposed by R. Dee, with the ground-breaking introduction of methacrylate bone cement.[12, 15]

In comparison to arthroplasty of the hip, knee or shoulder, total elbow arthroplasty (TEA) is relatively infrequent. Between May 2005 and December 2015, 876 TEA procedures were performed in Australia.[1] TEA involves the removal of the olecranon and distal humerus, which is then replaced with stemmed prostheses of the ulna and humerus.[1] This is combined with prosthetic replacement of the radial head when necessary.[1] The procedure is most commonly undertaken in females (73.4%) and in patients 70 to 79 years of age.[1] Primary diagnoses leading to TEA include osteoarthritis, fracture/dislocation, rheumatoid arthritis and other inflammatory arthritis, and less commonly instability, tumour or osteonecrosis.[1] Frequent causes of primary TEA failure in Australia include loosening/lysis (33.7%) and infection (24.8%), followed by fracture (13.4%) and instability (6.8%).[1]

TSA and TEA are effective treatments commonly used in the medical care of the elderly population. However, with advancing age comes a greater risk of further chronic conditions such as obesity and diabetes mellitus, increasing the possibility of comorbid patients presenting for elective arthroplasty.

1.2 Obesity

Obesity is common in Australian adults and the elderly. The Australian Institute of Health and Welfare (AIHW) recently reported increasing rates of overweight and obesity with age, from 39% of those aged 18-24, to 74% of people aged 65-74 years.[16]

1.2.1 Evolutionary progression and measurement of obesity

Food shortages throughout history contributed to former views that an individual with excess adipose tissue symbolised health and prosperity.[17] With technological advances in agriculture, famine has abated in developed countries. This, coupled with changes in lifestyle and a surplus of easily accessible energy-dense foods contribute to the present-day obesity crisis.[17]

Excess subcutaneous and visceral fat deposition is the cumulative product of an imbalance between caloric intake and energy expenditure.[17] However, there are well acknowledged factors, from genetic through to contextual, that influence adiposity.[18] Revelations regarding the negative

effects of a corpulent state were first recognised in the mid-nineteenth century,[17] although some argue the initial observation was made by Hippocrates more than 2000 years prior.[19] Nonetheless, in the early twentieth century, excess fat disposition was identified as a risk factor for morbidity and mortality,[17] and by the new millennium, obesity was progressively accepted as a chronic disease, health burden and escalating global epidemic.[20] Growing concern regarding obesity stirred interest and further investigation into its measurement.

The relationship between height and weight was first proposed in 1832, by Belgian statistician, Adolphe Quételet.[21] Quételet's study of human development led to the creation of the Quételet index, which is based on his concept that weight increased by height squared, excluding periods of growth spurt.[21] Subsequent researchers confirmed the validity of the Quételet index,[21] and in 1972, a pivotal study by Ancel Keys re-coined the measure, the Body Mass Index (BMI).[21, 22] In this study, Keys compared indices of relative weight and concluded that weight divided by height squared (i.e. the newly termed BMI), provided the best estimate.[22]

Despite the widespread use of BMI as an anthropometric measure of obesity, it is heavily criticised due to a number of well-acknowledged shortcomings. A major limitation of the BMI is its inability to distinguish between body fat and lean mass,[23] which results in the potential for misdiagnosis of overweight or obesity,[24] such as in athletic populations with greater muscle mass.[25] Conversely, this may also result in underdiagnoses in individuals with high adiposity and low lean mass.[23] Furthermore, BMI does not distinguish between, or account for, body fat type and distribution.[26] Research suggests that although total body fat is a significant factor, central adipose tissue, or visceral fat, is associated with greater risk of metabolic disorders, such as cardiovascular disease.[26, 27] Nevertheless, BMI continues to be used as a criterion for the diagnosis of obesity.

1.2.2 Obesity and arthroplasty

Obesity is a significant comorbidity in the Australian arthroplasty population, with recent figures demonstrating that the majority (62.3%) of Australian TSA patients are categorised as either pre-obese (BMI: 25.00 – 34.99) or Class 1 obese (BMI: 30.00 – 34.99).[1] In addition, research indicates that obesity plays a role in osteoarthritis and the subsequent need for joint replacement.

The leading diagnosis for total joint arthroplasty of the knee, hip and shoulder is osteoarthritis.[1] Osteoarthritis progression results in chronic pain and dysfunction through a multitude of factors including articular cartilage breakdown, osteophyte formation, subchondral sclerosis and synovium changes.[28] Research has linked osteoarthritis with obesity through a number of mechanical and metabolic mechanisms.

1.2.2.1 Biomechanical factors

Obesity increases joint-loading in weight-bearing joints such as the knee,[29] which has been suggested to exacerbate cartilage degradation.[30] Furthermore, evidence has proposed that varus malalignment of the knee increases the impact of obesity on osteoarthritis development.[31] However, higher BMI has also been associated with osteoarthritis of non-weighting bearing joints, such as the hand,[32-34] suggesting alternative metabolic mechanisms may too impact upon osteoarthritis progression.[30]

1.2.2.2 Metabolic factors

Much research has investigated the influence of obesity, and more specifically, adipokines on the pathophysiology of osteoarthritis.[35-38] Adipokines are molecules such as leptin, adiponectin, resistin and visfatin, which are secreted from white adipose tissue.

Leptin is a peptide hormone encoded by the obese (ob) gene which largely acts on the hypothalamus to regulate appetite.[38-40] Leptin induces anorexigenic factors and suppresses orexigenic neuropeptides resulting in reduced food consumption and increased energy consumption.[38, 39] Circulating levels of leptin have been demonstrated to directly correlate with adipose tissue mass.[41]

Leptin and the leptin receptor (Ob-R) have been found in chondrocytes, the cells responsible for the cartilaginous matrix.[38, 42] In 2003, Dumond and others[36] identified an upregulation in leptin expression in osteoarthritic chondrocytes and osteophytes in comparison to non-arthritic tissue. Consequently, links between cartilage degradation and leptin were investigated. Dumond et al.[36] reported that the level of leptin expression correlated with the grade of cartilage destruction in osteoarthritic knees. However, growth factors involved in simulating chondrocyte cartilage repair, specifically insulin-like growth factor 1 (IGF – 1) or transforming growth factor B (TGFB), were

present proportional to the severity of cartilage damage (i.e. levels of TGFB and IGF – 1 were higher the greater the cartilage damage), suggesting a beneficial effect of leptin on cartilage.[36] These findings also supported the notion of TGFB role in osteophyte formation, with high levels of TGFB found in osteophytes from osteoarthritic knee specimens.[36] Given such findings, authors concluded that leptin was a key hormone involved in the regulation of chondrocyte metabolism and may influence the pathophysiology of osteoarthritis.[36] More recently, King et al.[37] investigated the effect of weight loss on adipokines and cartilage biomarkers in obese patients with or without knee osteoarthritis. The authors found that weight loss was associated with reduced leptin levels, a decrease that was then associated with reduced loss of medial and lateral femoral cartilage volume.[37] Conversely, the adipokine adiponectin has demonstrated both a protective and exacerbating role on osteoarthritis progression with no conclusive evidence.[35, 37] Adiponectin levels have been shown to increase with weight loss and subsequently associated with reduced loss of cartilage volume and thickness.[37] Conversely, adiponectin has been positively associated with an inflammatory cytokine, synovial inter-leukin 1β, suggesting a link between this adipokine and the inflammatory features of osteoarthritis.[35]

Overall, evidence suggests a relationship between obesity and osteoarthritis, a leading cause of joint replacement. Obesity is also identified as a strong risk factor for type 2 diabetes mellitus, with obese Australians having 5.8 times greater odds (95% CI [4.5, 7.4]; $P < 0.0001$) of developing the chronic condition.[43]

1.3 Diabetes mellitus

Diabetes mellitus is one of the leading contributors to the burden of disease in older Australians.[16] Globally, the prevalence of diabetes mellitus in people 20 to 79 years of age has been estimated at 8.8% in 2015, peaking in those 65 years of age and above.[44] This estimate was predicted to increase to 10.4% by the year 2040,[44] highlighting the necessity for further research into the consequences of this rising chronic disease.

Diabetes mellitus was formally defined by the World Health Organization (WHO) as ‘a metabolic disorder of multiple aetiology characterised by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action,

or both'.[45(p540)] Studies have investigated the relationship between hyperglycaemia and outcomes in the perioperative and postoperative periods, discussed in the following section.

1.3.1 Metabolic response to surgery

Glucose homeostasis is affected by a number of neurophysiological changes that occur in response to surgery and anaesthesia.[46, 47] The production of stress hormones such as cortisol and catecholamines including adrenaline and noradrenaline increase, reducing insulin sensitivity.[47] Furthermore, insulin secretion is reduced by the sympathetic nervous system, while growth hormone and glucagon secretions rise, resulting in an overall elevation of blood glucose.[47]

The link between hyperglycaemia and surgery outcomes has been investigated, irrespective of diabetes status. Stress hyperglycaemia following myocardial infarction has been associated with increased risk of mortality in diabetic and non-diabetic patients.[48] Furthermore, Mraovic et al.[49] identified that preoperative blood glucose levels of 200 mg/dL independently increased the risk of pulmonary embolism (PE) by 3.19 times compared to patients with levels less than 110 mg/dL undergoing lower limb arthroplasty. Most interestingly, the authors indicated that hyperglycaemia, rather than the diagnosis of diabetes mellitus, was an independent risk factor for PE.[49] Consequently, the present review aimed to collect data on levels of glycaemic control, where possible.

1.4 Arthroplasty complications and postoperative outcomes

Complications and poor outcomes following arthroplasty can lead to increased morbidity in patients. Additionally, in-hospital complications result in increased costs,[50] imposing further burden on the healthcare system. Here we discuss the incidence of complications and expected outcomes following arthroplasty.

1.4.1 Operative duration and length of stay

Operative duration varies for each upper limb arthroplasty procedure, and is impacted by patient and surgeon specific factors.[51] For surgeons performing more than 15 surgeries per year, the

average operative duration from incision to closure is reportedly 114.4 minutes for TSA and 115.5 minutes RTSA.[52] Mean operative duration for TEA has been reported at 151 minutes (SD = 64.9).[53] Longer operative duration has been linked with increased incidence of postoperative complications such as surgical site infection (SSI)[54] and urinary tract infection (UTI),[55] and imposes practical implications such as on theatre scheduling.[56] Consequently, factors that contribute to longer operative duration have been investigated, with obesity recurrently identified as a risk factor for longer arthroplasty operative time, across various joints.[56-61]

Length of hospital stay has been reported between, 2.0 to 2.4 days following TSA,[62-64] and 3.7 to 4.2 days following TEA.[64, 65] Prolonged length of stay (LoS) creates additional expenses and greater demand on hospital resources.[66] With the increasing rate of upper limb arthroplasty procedures,[1] further considerations must be given to risk factors that increase LoS.

1.4.2 Blood transfusion

Orthopaedics is a medical specialty with an acknowledged high need for red blood cells.[67-69] This is especially so in joint arthroplasty procedures, which can result in significant perioperative blood loss, and the need for blood transfusion.[68, 70] Extensive research over the past 20 years has highlighted large transfusion rates for lower limb joint replacement surgeries,[67, 68, 70] however recent evidence has demonstrated a substantial decline. Bedard et al.[71] investigated total knee arthroplasty transfusion rates from 2007 to 2015 and identified a significant percentage drop from 17.3% to 4.4%. Shoulder arthroplasty procedures have historically displayed lower transfusion requirements than that of the lower limb, with rates previously reported at 8.0%,[72] and more recently at 4.5%.[73]

Considerable efforts have been made to minimise blood loss and avoid the need for blood transfusion, given the risk of associated complications. Blood transfusion may lead to systematic complications including allergic reactions, infection, and transfusion-related acute-lung injury or circulatory overload.[70] All such complications have demonstrated the potential to cause severe morbidity, or subsequent mortality.[70] With regards to shoulder arthroplasty, Grier et al.[74] identified higher odds of complications including myocardial infarction, pneumonia, venous thromboembolism (VTE) and periprosthetic infection in transfused TSA and RTSA patients.

Prognostic factors that can influence the need for blood transfusion need to be better understood. Given the detrimental complications associated with transfusion, research must further investigate and consolidate the findings, specifically in regard to the upper limb.

1.4.3 Infection

Postoperative infection is a detrimental outcome following arthroplasty, and a common cause of revision surgery. Recent figures from the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) identified infection as the second most common cause of revision for total knee arthroplasty (22.5%), and the fourth most common reason for revision of both total hip arthroplasty (17.5%) and TSA (6.1%).[1] Infection necessitated 24.8% of all revision elbow arthroplasty procedures performed in Australia between 2005 and 2015.[75]

SSIs are classed as superficial wound infections and deep wound or periprosthetic joint infections. Standard antibiotic prophylaxis commonly used in orthopaedic procedures include the intravenous administration of cephalosporins, a class of β-lactam antibiotics.[76, 77] Research into antibiotic prophylaxis has suggested obese patients have impaired tissue penetration of some antibiotics, resulting in inadequate tissue concentrations despite an increased clinical dose (2g).[78] In 2013, experts attending an international consensus meeting on SSI made a strong recommendation for weight-adjusted antibiotic dosing, based on the consensus that preoperative antibiotics vary in pharmacokinetics based on patient weight.[79]

1.4.4 Urinary tract infection and pneumonia

Pneumonia and UTIs are minor systematic complications, however have been associated with increased morbidity and mortality.[80, 81] Both are most prevalent in elderly cohorts,[82] and are common postoperative complications following total joint arthroplasty. In the TSA population, UTI and pneumonia have been identified as significant predictors of hospital readmission following surgery.[83] Consequently, such complications are not only a health risk for the patient but place a significant financial burden on the health care system.

1.4.5 Venous thromboembolism

VTEs including deep vein thrombosis (DVT) and PE are rare complications following upper limb arthroplasty. However, the reported incidence of VTE is varied, ranging from 0.2% to 13.0% in shoulder arthroplasty patients.[83-86] Following TEA, DVT incidence is reportedly 0.8%.[65] VTE complications are not only detrimental to the patient but are also associated with increased risk of hospital readmission, and subsequent burden on the health care system.[83]

1.4.6 Dislocation

Combined instability and dislocation is identified as the most common cause for prosthesis revision (reoperation) following TSA and RTSA. In Australia, it accounts for 25.2% and 38.5% of TSA and RTSA revisions, respectively.[1] Comparatively, dislocation rates are less concerning for the TEA cohort, accounting for 3.4% of revisions.[75]

The aetiology of, or risk factors for, dislocation are limited. In regard to RTSA, factors thought to contribute to dislocation risk included surgical factors such as component malposition[87] and surgical approach, as well as design features of the prosthesis.[88] Obesity has also been hypothesised as a potential patient risk factor for dislocation.[89]

1.4.7 Fracture

Fractures during, or following upper limb total joint arthroplasty, are rare complications, accounting for 1.9% of TSA revision procedures in Australia.[1] Incidence is higher for RTSA, and elbow arthroplasty procedures, with fractures responsible for approximately 13% of revision cases.[1, 75] Fracture types affecting upper limb arthroplasty patients include periprosthetic and acromial fractures. Periprosthetic fractures are those that occur in the bone surrounding the implanted prosthetic.[90] In shoulder arthroplasty, periprosthetic fractures commonly occur intraoperatively, and affect the humerus. Acromial fractures can occur along the acromion and scapular spine, and are commonly associated with RTSA.[91]

1.4.8 Pain, function and quality of life

Pain and poor joint function detrimentally impact quality of life (QoL), and are primary symptoms leading to total joint replacement. Shoulder pain for 3 months or more has been linked to depression, anxiety and sleep disturbance.[92] Following arthroplasty, research has demonstrated significant improvements in pain, function and psychological status.[93]

In the general population, obesity has been associated with decreased shoulder function.[94] Furthermore, increasing BMI is correlated with the incidence and severity of rotator cuff tears, a common indication for shoulder arthroplasty.[95] Nevertheless, research has demonstrated improvements in clinical outcomes including pain, range of motion (ROM) and strength following shoulder arthroplasty in high BMI patients.[96] Unfortunately, there is a paucity of literature examining the differences in pain and functional outcomes across BMI groupings.

1.4.9 Unscheduled return to theatre and revision

Revision procedures refer to re-operations of previous primary total shoulder or elbow replacement, where one or more of the prosthetic components are replaced, removed, or another component is added.[1] Revision arthroplasty is a complex procedure that carries a greater risk of complications, and poorer outcomes compared with primary arthroplasty.[97, 98] In Australia, recent one-year cumulative percentage revision rates were reported at 3.0% for TSA and 2.6% for RTSA.[1] These figures increased to 11.2% in TSA, and 6.5% in RTSA, at 9 years post-surgery.[1] The most common reason for revision for both TSA and RTSA patients was instability/dislocation, accounting for 25.2% and 38.5%, respectively.[1] Patients also return to theatre for causes other than revision, such as for irrigation and debridement, which will be investigated with regard to comorbidity.

1.4.10 Mortality

Risk of postoperative mortality following elective upper limb arthroplasty is low. For TSA patients, mortality rates range from 0 to 1.0%,[99, 100] and are comparable to mortality rates following arthroplasty of the hip and knee.[100] Similarly, low mortality rates following TEA have been reported, for example, at 0.62% by 90 days post-surgery.[101] Nevertheless, death following an elective

surgical procedure is a devastating outcome, and potential risk factors for mortality, specifically obesity and diabetes mellitus, have been investigated in this review.

1.5 Significance of the review

The available evidence on the impact of comorbidities such as obesity and diabetes mellitus on upper limb arthroplasty outcomes is inconclusive and contradictory (refer Appendix 1: Protocol).[102] An understanding of the relationship between pre-existing comorbidities and arthroplasty outcomes is essential as it may impact patient selection for different types of orthopaedic surgery. Patients must be better informed of any additional risks associated with a pre-existing chronic disease, as this may influence their decision-making. Orthopaedic surgeons may also consider alternate treatments or further pre-cautionary measures to ensure the safety and effectiveness of the arthroplasty procedure in patients identified at greater risk for poorer outcomes.

To date, research has considered a number of perioperative, short and longer-term complications for patients with comorbid conditions in isolation. An inclusive review, that considers perioperative, as well as mid- and longer-term outcomes, is needed to develop a clear understanding of the impact of obesity and diabetes mellitus on upper limb arthroplasty.

1.6 Review question and objective

The objective of this review was to locate, critically appraise and synthesise the best available evidence investigating the impact of selected comorbidities on upper limb arthroplasty outcomes.

Specifically, the question directing this review was:

> *Are patients with obesity or diabetes mellitus at an increased risk of complications and/or poorer postoperative outcomes following total shoulder, reverse total shoulder and total elbow arthroplasty?*

Chapter 2: Systematic Review Methods

Chapter 2 presents the systematic review methods including the study inclusion criteria and the search strategy performed. Detailed descriptions of the methods of critical appraisal, data extraction and data synthesis processes are also provided.

The originality of the proposed review topic was investigated via a preliminary literature search of the biomedical citations database, PubMed, and a screening of the international registry for systematic reviews, PROSPERO. Preliminary searches indicated that this review topic had not previously been assessed through systematic review methodology, nor was it registered as *under investigation* at the commencement of the literature search for this review (16 April 2016).

The systematic review was undertaken in accordance with an *a priori* protocol (Appendix 1).[102] A deviation from the *a priori* protocol following its publication is described in detail in Section 2.1.1 and 2.1.2. To avoid duplication, this review was prospectively registered in PROSPERO (registration number: CRD42016053299).

2.1 Inclusion criteria

2.1.1 Participants

Adults (18 years or older) who had undergone upper limb arthroplasty, specifically, primary TSA, RTSA and TEA were considered for inclusion in this review.

As the screening process to assess study eligibility progressed, it became apparent that this inclusion criterion, as stated, was difficult to apply to cohorts that included a combination of both upper limb and lower limb arthroplasty patients. Considering lower limb arthroplasty procedures performed on the hip and knee have demonstrated poorer outcomes in diabetic and obese patient populations,[103-106] the inclusion of such data may have negatively skewed or biased the review results. Therefore, the participant inclusion criterion was further refined during the review process. For example, if the primary studies evaluated the impact of diabetes mellitus or obesity on outcomes from a combination of arthroplasty procedures (i.e. hip, knee, shoulder, elbow and/or

hemi-arthroplasty [HA]), they were considered further. Initially, authors of such studies were contacted for specific data on the cohort of interest. If the data was obtainable, it was included, however if the data was not available, or a response was not received, the paper was deemed *eligible for inclusion* if it included ≥70% of the population of interest (TSA, RTSA, TEA). The intention was to conduct subgroup analyses to explore the impact of including such articles (refer Section 2.6). Studies were deemed *ineligible* if <70% of the study cohort comprised the population of interest.

2.1.2 Exposure

The review considered studies that evaluated the influence of comorbidity, namely, obesity and diabetes mellitus, on the arthroplasty outcomes of interest.

Obesity:

BMI is the ratio of weight in kilograms to height in metres squared (kg/m^2).[107] It is an index widely used to classify levels of obesity.[108, 109] The International Classification of adult weight according to BMI is defined by WHO using the following ranges:

- Underweight: < 18.50 kg/m^2
- Normal range: 18.50 – 24.99 kg/m^2
- Overweight: 25.00 – 29.99 kg/m^2
- Obese: ≥ 30.00 kg/m^2

This review defined obesity as a BMI of at least 30.0 kg/m^2. Therefore, the term *non-obese* was used to describe patients categorised with a BMI < 30.0 kg/m^2, and the term *obese* was used to describe patients categorised with a BMI ≥ 30.0 kg/m^2. The obese category is further subdivided into *obese class 1* (BMI 30.0 to 34.9 kg/m^2) and *obese class 2* (BMI ≥ 35.0 kg/m^2), depending on the BMI groups reported in the primary studies. *Morbidly obese* is obese class 3 (BMI of ≥ 40.0 kg/m^2) and *normal range* refers to patients with a BMI < 25.0 kg/m^2.

Diabetes mellitus:

Type 1 and type 2 diabetes mellitus were considered for inclusion. Given that the classification and diagnostic criteria for diabetes mellitus has changed over time, this review considered patients

formally diagnosed with diabetes mellitus using standard criteria valid at the time of the study. Ideally, criteria were described in the article.

During the screening process to determine study eligibility (refer Section 2.3), it became apparent that further clarification of the exposure of interest was required to identify eligible studies. It was decided that primary studies must have considered the impact of diabetes mellitus or obesity on outcomes in isolation. Consequently, studies that reported the impact of multiple comorbidities as a comorbidity score were ineligible for inclusion, regardless of whether diabetes mellitus or obesity was included. This added clarification sought to minimise the effect of confounding variables (i.e. additional comorbidities) and allow for more accurate assessment of the impact of the diabetes mellitus and obesity on outcome.

2.1.3 Outcomes

This review considered studies that reported postoperative complications and outcomes including:

- Operative duration
- LoS
- Blood transfusion
- Infection (SSI and periprosthetic infection)
    - Diagnosed by, but not limited to, laboratory and microbiological testing.
- UTI
    - Diagnosed by, but not limited to, laboratory testing for positive urine culture.
- Pneumonia
    - Diagnosed by, but not limited to, chest X-rays and blood tests.
- VTE (DVT and PE)
    - Diagnosed by, but not limited to, duplex sonography, Doppler ultrasonography or computed tomography scan.
- Dislocation
- Acromial or stem fractures (e.g. periprosthetic fractures)
- Pain: measured using scoring systems such as the Visual Analogue Scale for Pain
- Function: measured by range of motion or using a scoring system such as the Constant-Murley shoulder score.
- QoL: measured using a scoring system such as the Short Form-36

- Unscheduled return to theatre (for causes such as instability or dislocation)
- Revision following primary TSA, RTSA or TEA
- Mortality

2.1.4 Types of studies

This review considered analytical epidemiological study designs, including prospective and retrospective cohort studies, and case-control studies, for inclusion.

2.2 Search strategy

2.2.1 Literature search

The search strategy was developed and conducted in accordance with the Joanna Briggs Institute (JBI) guidelines for searching.[110] A comprehensive three-step search strategy was developed to identify both published and unpublished studies through electronic database and grey literature searching.

2.2.1.1 Bibliographic database search

An initial limited search of PubMed was undertaken to identify both controlled vocabulary and free text terms used to index relevant articles. Index terms and keywords identified from titles and abstracts were then translated and tested for use in the *Cumulative Index of Nursing and Allied Health Literature* (CINAHL) database, and the biomedical and pharmacological database, Embase. Index terms and key words included those that related to the participants of interest (e.g. arthroplasty, replacement and elbow or shoulder, total shoulder or total elbow) and exposure of interest (e.g. comorbidity, obesity, BMI, overweight, diabetes mellitus or hyperglycaemia).

A second search using all identified keywords and index terms was then undertaken across PubMed, CINAHL and Embase on 27 May, 2016. Articles in languages other than English were excluded; no limitation on publication date was employed. Detailed search strategies for each database are available in Appendix 2: Table 2.1.

2.2.1.2 Grey literature search

The grey literature search included a review of relevant national and international conference proceedings, and the European database of grey literature, Open Grey.[111]

Conferences selected as likely sources of eligible studies were based on those listed by the Australian Orthopaedic Association (AOA) that were relevant to the present review topic.[112] Screening was limited to the most recent conference proceedings that were electronically accessible, including the:

- American Academy of Orthopaedic Surgeons Annual Meeting;
- Australian Orthopaedic Association Annual Scientific Meeting;
- Canadian Orthopaedic Association Annual Scientific Meeting;
- British Orthopaedic Association Annual Congress; and the
- European Federation of National Associations of Orthopaedics and Traumatology Congress.

Grey literature search strategies, access dates and URLs are detailed in Appendix 2: Table 2.2. To ensure comprehensive searching of relevant literature, the reference lists of all eligible studies were screened for additional studies.

2.3 Study selection

Citations retrieved from database searches were exported and managed using the bibliographic citation software, Endnote X7 (Thomas Reuters, New York, USA).[113] Endnote software facilitated removal of duplicates and subsequent screening of titles and abstracts to determine eligibility for inclusion. Citations that did not meet the inclusion criteria (refer Section 2.1) were excluded. Full-text articles were retrieved for citations that clearly met the inclusion criteria, and for those with insufficient information to determine eligibility. Full-text studies that did not meet the inclusion criteria (refer Section 2.1) were excluded. In other instances, the first author, and if necessary, subsequent authors were contacted via email if full-text articles could not be retrieved, or if further information to determine eligibility was required. For example, further information was sought when it was difficult to determine:

1. Whether the cohort described in the study included the cohort of interest, specifically TSA, RTSA and TEA patients;
2. Whether the TSA, RTSA and TEA patients included in the cohort were diabetic or obese;
3. Whether the TSA, RTSA and TEA patients included in the cohort were diabetic or obese, and experienced the outcome of interest.

Authors were also contacted for further information when inadequate definitions were used in the full-text article, and it was difficult to determine:

4. What constituted a 'post-operative complication';[114]
5. How 'overweight' was defined.[66]

If authors did not respond and therefore, the eligibility of the studies could not be determined, studies were excluded due to *insufficient information to determine eligibility* (refer Section 3.1.1.1).

Many eligible studies gathered data retrospectively from national databases over defined time periods. Consequently, multiple published articles presented data from the same patient cohort. As data from the same patients could only contribute once to the data synthesis conducted in this review, these articles were further scrutinised prior to inclusion. Of the eligible studies that reported on the same patient cohort, the study that provided the greatest representation of data - by having either analysed the greatest number of years, or multiple outcome measures of interest - was preferentially selected. Furthermore, a study was preferred if the study provided more recent data or readily extractable data. In cases where a study with an overlapping cohort was deemed 'inferior' but provided additional outcomes not reported in the 'superior' included study, the study was included but only data on the additional outcomes were extracted.

2.4 Assessment of methodological quality

Studies selected for retrieval were assessed by two independent reviewers for methodological validity using standardised critical appraisal tools from the JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI) for cohort[115] and case-control[116] studies.

To ensure consistency of interpretation and application of the appraisal instruments, explanatory criteria were developed to facilitate the appraisal process. Explanatory tables detailed the criteria that constituted a *'Yes', 'No', 'Unclear'* or *'Not Applicable'* response to each question outlined in the

critical appraisal tool (refer Appendix 3.). Appraisal was piloted with four studies to determine suitability and consistency in understanding of the application of the tools between each reviewer.

Any disagreements that arose between the reviewers were resolved through discussion and, where necessary for one study,[167] through consultation with a third reviewer. All eligible studies were included in the review irrespective of their methodological quality.

2.5 Data extraction

Data was extracted from included studies using a customised data extraction template (refer Appendix 4.). The following details were extracted from each of the included studies:

- Study's country of origin
- Details of the surgery performed including surgical technique, number of surgeons performing the procedure and the indication for the primary arthroplasty procedure
- Type of arthroplasty procedure: TEA, TSA or RTSA
- Demographic characteristics of participant cohorts including age, gender, level of glycaemic control (i.e. controlled or uncontrolled), type of exposure (obesity or, type 1 or type 2 diabetes mellitus), nationality or ethnicity
- Arthroplasty outcomes including postoperative complications and outcomes

Prior to analysis, all extracted data was cross-checked with study articles to confirm accuracy.

2.5.1 Contacting study authors for further data

A number of included studies reported data in a manner not readily suitable for statistical analysis. As such, four study authors were contacted with a request for further data due to the reasons listed below, however no responses were received:

1. Percentages instead of raw figures were reported, requiring calculation of the number of events to include in data synthesis. As very large sample sizes and small percentages were reported, errors in the rounding of the 'number of events' may have arisen (two studies).[117, 118]
2. Due to variation in BMI groupings between studies, authors were contacted for data on alternative grouping variations (two studies).[119, 120]

3. Definition of the outcome measure *'operative duration'*, to determine whether this referred to the duration the patient was in the operating theatre or the duration of the operation from incision to closure (three studies).[118-120]

2.6 Data synthesis

Quantitative data, where possible, was pooled in statistical meta-analysis using Review Manager (RevMan) Version 5.3 software.[121] Effect sizes with 95% confidence intervals were expressed as odds ratios (OR) for categorical data and weighted mean differences (WMD) for continuous data. As per the study protocol (refer Appendix 1),[102] the intention was to use a random-effects model with a Mantel-Haenszel statistical method for OR,[122] and an inverse variance method for WMD for the meta-analyses.[123] Given this review included observational studies, the random-effects statistical model was deemed most appropriate as it assumes estimated effects across studies follow some distribution, but are not identical.[124] However, recent research suggests that five or more studies are required when using a random-effects model to practically and consistently achieve statistical power greater than the power of the individual studies contributing to the meta-analysis.[125] Consequently, a fixed-effects model was employed for meta-analyses comprising less than five studies. However, when heterogeneity was considerably high across studies in a meta-analysis with less than five studies, both a random-effects and fixed-effects analysis were conducted, to serve as a sensitivity analysis. Where statistical pooling was not possible, findings were presented in narrative form including tables and figures to aid data presentation, where appropriate.

Statistical heterogeneity was assessed using both the standard Chi^2 (χ^2) and I^2. The I^2 statistic is defined as the percentage of total variation across studies due to chance, with values ranging between 0% – 100%.[126] The Cochrane Handbook was used as a guide for the interpretation of I^2: thresholds of 0% to 40% 'might not be important' and indicated low heterogeneity in this review; 30% to 60% 'may represent moderate heterogeneity'; 50% to 90% 'may represent substantial heterogeneity'; and 75% to 100% 'may represent considerable heterogeneity'.[127] Subgroup analysis was employed to explore the impact of different joint arthroplasty procedures in upper limb shoulder arthroplasty (TSA and RTSA) and elbow arthroplasty cohorts. Type of diabetes mellitus could not to be considered as included studies did not separate data accordingly.

The majority of meta-analyses were conducted using unadjusted data (number of events) for a number of reasons. First, to avoid potential heterogeneity attributable to adjustment for different confounding factors between studies.[128] However, this was not possible for some outcomes of interest (i.e. VTE [PE only]), revision and infection) as studies only reported effect estimates (raw data was not available). In order to meta-analyse this data, the standard error (SE) was required.[129] To calculate the SE, the natural log of both the effect estimate and confidence intervals was calculated and the range between the upper and lower confidence intervals was divided by 3.92.[129] This meta-analysis approach used a generic inverse variance method. Second, for the obesity exposure, BMI groupings varied between the included studies. The use of unadjusted data permitted the combination of BMI categories that aligned with classifications used in this review (refer Section 2.1.2), irrespective of categories analysed in the individual studies. Consequently, for all outcomes, we aimed to conduct a single, overall meta-analysis comparing obese (BMI ≥ 30.0) versus non-obese (BMI < 30.0) patients. For categorical variables, event and sample totals were summed for each BMI group of < 30.0 versus ≥ 30.0. Conversely, for continuous variables such as operative duration and LoS, BMI groupings within a study could not be summed to compare in a single, overall BMI < 30.0 versus ≥ 30.0 and consequently, multiple meta-analyses comparing various BMI groupings were conducted. Where various BMI categories did not align across studies, outcomes were combined in the overall meta-analysis comparing obese versus non-obese, despite variations in individual study BMI groupings. For example, Gupta et al.[120] categorised BMI as > 35.0, not specifically > 30.0. Similarly, Pappou et al.[130] categorised BMI as ≥ 40.0, not specifically > 30.0, however data from such studies were included in meta-analyses comparing BMI < 30.0 versus ≥ 30.0. This approach was necessary for meta-analyses conducted for outcomes including mortality, blood transfusion, dislocation, infection, revision, UTI, pain and function. Furthermore, where possible, multiple meta-analyses using the various BMI categories (refer Section 2.1.2) were also conducted for each outcome, allowing exploration of the impact of different levels of BMI on outcome.

A number of studies reported 'no-event' data for outcomes including mortality, dislocation and infection. 'No-event' means no events were reported in both the exposed and non-exposed study arms of a single study. As OR calculations naturally exclude no-event data,[131] calculated effect estimates were not affected by studies reporting 'no-event' outcomes. A number of studies also reported zero-cell counts, that is, no events were observed in one arm of an individual study. Revman software automatically accounts for such zero-cell counts,[132] however, this was not

required in our analysis as the Mantel-Haenszel model was used. The Mantel-Haenszel model only requires zero-cell corrections if the same cell is zero in all the included studies.[132]

Some studies simply reported the percentage of outcome events, without reporting the raw number of events. As raw figures are required for meta-analysis, they were calculated, where possible, from the data available. As a majority of studies reported data from large databases, this created a potential for error in the calculation of the raw number of events. Raw figure calculations were required for studies by Ponce et al.,[133] Jiang et al.,[118] Griffin et al.,[117] and Singh et al.[134] (diabetes mellitus exposure only). A mixed study cohort was reported in one included study.[133] This study included a subset of HA patients, which contributed to less than 30.0% of the cohort total (refer Section 2.1.1). The impact of this study was intended to be assessed using sensitivity analysis, however this was not possible as only two studies were ultimately included in meta-analyses that included this study. A sensitivity analysis was also conducted for meta-analyses heavily weighted with the findings of a single study (> 90.0%). This was necessary for studies that reported on obesity and the outcomes including VTE, fracture and revision.

Chapter 3: Results

3.1 Search results and study selection

Chapter 3 presents the results of the systematic review including the results of the search, study selection, critical appraisal and characteristics of included studies. Results for each outcome are reported independently for each exposure.

3.1.1 Bibliographic database, grey literature and reference list searching

The search of bibliographic databases outlined in Section 2.2.1.1 returned 9596 citations (Figure 3.1; PubMed [*n = 3480]*, Embase [*n = 5272]* and CINAHL [*n = 844])*. The grey literature search retrieved a further 793 titles and/or abstracts, as outlined in Table 3.1. An additional 17 citations were identified via the reference list screening of eligible studies. Following removal of 3203 duplicate citations, a total of 7203 original records were reviewed (Figure 3.1). Initial title and abstract screening resulted in the exclusion of 6943 ineligible citations. A total of 260 studies were identified for full-text retrieval.

Table 3.1. Grey literature search results

Database	**Conference**	**Titles/abstracts searched**	**Likely eligible**
Open Grey		44	0
Conference proceedings	American Academy of Orthopaedic Surgeons Annual Meeting [Internet]; 2016 Mar 1-5; Orlando, Florida.	182	1
	Canadian Orthopaedic Association Annual Scientific Meeting [Internet]; 2016 Jun 16-19; Québec City, Québec.	69	0
	Proceedings of the British Orthopaedic Association Annual Congress [Internet]; 2015 Sep 15-18; Liverpool, England.	148	0
	17th EFFORT (European Federation of National Associations of Orthopaedics and Traumatology)	251	3

	Congress [Internet]; 2016 Jun 1-3; Geneva, Switzerland.		
	Australian Orthopaedic Association Annual Scientific Meeting [Internet]; 2015 Oct 11-15; Brisbane, Queensland.	99	0
TOTALS		**793**	**4***
** Authors of the four records were contacted for further information, however no responses were received.*			

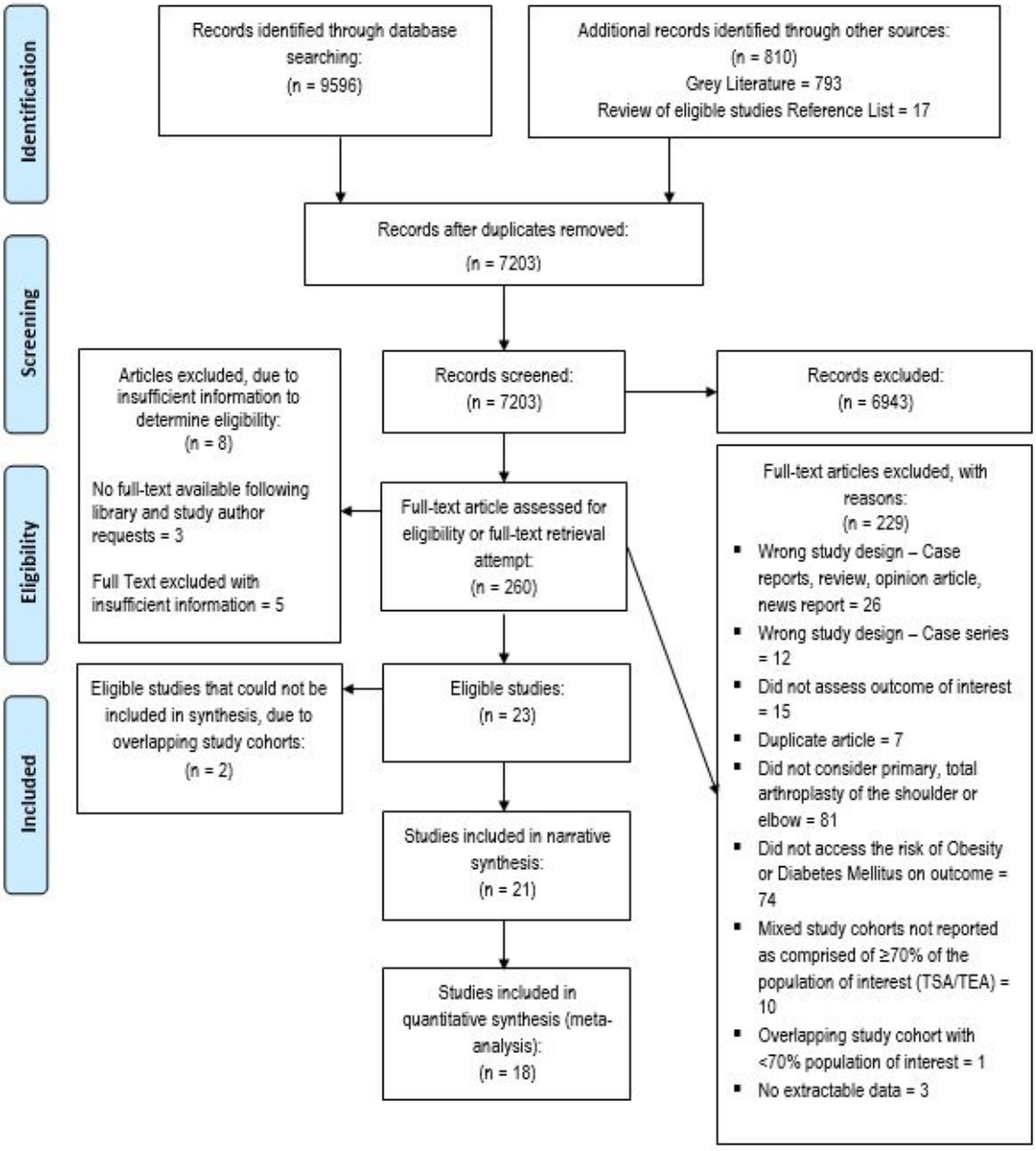


Figure 3.1. *PRISMA flow diagram outlining the study selection and inclusion process*

3.1.1.1 Contacting study authors for further information to determine eligibility

Of the 260 studies identified, nine studies had either no locatable full-text (three studies)[135-137] following document retrieval library requests, or the full-texts provided insufficient information to determine eligibility (six studies).[66, 114, 138-141] No response was received from seven of the nine authors contacted for further information, resulting in the exclusion of the seven studies as their eligibility could not be determined.[66, 114, 135-137, 139, 140] Both studies from the two authors who responded were also excluded: one author could not supply any further information;[138] the other author provided the full-text, however, the study was ineligible for inclusion as the association between BMI and outcome was not assessed.[141]

Four records from the grey literature search were identified as potentially eligible for inclusion (Table 3.1.). Authors of the four records were contacted for further information, however no responses were received. Consequently, no grey literature was further considered for inclusion beyond title and abstract screening.

3.1.1.2 Studies with insufficient or minimal extractable data

Several studies provided insufficient or minimal extractable data in the publication. As such, 18 authors were contacted for further data. Of these, a total of five authors responded, however were either unable to provide further data or advised they would provide a follow-up email, from which no further response was received. Of the non-responders, studies by Ponce et al.,[133] Dunn et al.,[63] Day et al.,[142] Basques et al.,[62] and Singh et al.[143] were included in the review as minimal extractable data was reported in the papers. Of the remaining 13 studies, 10 reported study cohorts with mixed arthroplasty procedures.[144-153] These studies were excluded as they did not report a study population comprising ≥70.0% TSA, RTSA or TEA patients (refer Section 2.1.1) and/or did not present the data for each specific arthroplasty cohort individually to allow for extraction. The three remaining studies did not provide sufficient extractable data and were excluded because they either considered complications in combination[154] or did not present data in a format that allowed accurate data extraction.[155, 156] A further study by Minhas et al.[157] reported on a cohort with <70% TSA study population, however the author was not contacted because the cohort of interest overlapped with another included study.[118]

3.1.1.3 Eligible studies with overlapping cohorts

Studies by Garcia et al.[158] and Werner et al.[97] were eligible for inclusion in the review, however were not included in data synthesis as the reported cohorts overlapped with a more appropriate included study. The study by Garcia et al.[158] collected data on 4751 shoulder arthroplasty patients from a national healthcare database between 2005 and 2013. Jiang et al.[118] collected similar outcome data on an overlapping patient population from the same database, between 2006 and 2013. Despite reporting on a slightly smaller cohort, the study by Jiang et al.[118] was preferably chosen as the authors reported more detailed, extractable data on outcomes of interest. For example, Garcia et al.[158] reported *urinary complications* and *respiratory complications* while Jiang et al.[118] explicitly reported data on UTIs and pneumonia. The second overlapping study by Werner et al.[97] investigated patient factors associated with early revision rates for shoulder arthroplasty patients (TSA/RTSA/HA). Revision rates for the TSA and RTSA subset were also reported in a second publication by Werner and others,[159] which was chosen in preference, given additional outcomes of interest including VTE, dislocation and infection were also reported.

Cohorts described by Pope et al.[160] and Toor et al.[161] did overlap with other included studies, however were included as they reported additional outcomes of interest. Following the removal of eligible studies due to either overlapping study cohorts or no extractable data, 21 eligible articles remained for data synthesis.

3.1.1.4 Summary of eligible studies

Following full-text review, 229 studies were excluded due to reasons outlined in Figure 3.1. An additional eight records were excluded due to *insufficient information to determine eligibility*, following unsuccessful document retrieval requests from the University of Adelaide Barr Smith Library, and requests made to study authors. Twenty-three eligible studies were identified, however two could not be included in synthesis due to overlapping study cohorts,[97, 158] which resulted in 21 studies being included in the review (Figure 3.1).[62, 63, 117-120, 130, 133, 134, 142, 143, 159-168]

3.2 Assessment of methodological quality

The methodological quality of the 21 included studies (20 cohort studies and one case-control) was assessed, with results summarised in Table 3.2.

The majority of cohort studies (17) recruited participants from the same population (Table 3.2; Question 1),[62, 63, 117-119, 133, 134, 143, 159-165, 167, 168] and measured outcomes and/or exposures similarly to assign individuals to study groups (19) (Table 3.2; Question 2).[62, 117-120, 133, 134, 142, 143, 159-168] However, very few studies (three) measured the outcome or exposure used to group participants in a valid and reliable way (Table 3.2; Question 3).[134, 167, 168] These three studies grouped participants by outcome, specifically periprosthetic infection[134, 167] or fracture.[168] Eighteen of the 20 studies identified key confounders, specifically age, gender or comorbidities (Table 3.2; Question 4),[62, 63, 117-120, 133, 134, 142, 143, 159-161, 163-165, 167, 168] and 16 reported strategies to deal with such factors (Table 3.2; Question 5).[62, 63, 117-120, 133, 134, 142, 143, 159-161, 163, 167, 168] In 12 studies, it was deemed *Unclear* whether patients were free of the outcomes, specifically infection, UTI, pneumonia and/or VTE at the start of the study[117-120, 133, 159-164, 167] and *Not Applicable* in seven studies that assessed outcomes irrelevant during the preoperative time period (e.g. operative duration, LoS etc.) (Table 3.2; Question 6).[62, 63, 134, 143, 165, 166, 168] Outcomes were measured in a valid and reliable way in eight of the studies,[62, 63, 118, 134, 143, 163, 167, 168] however it was *Unclear* in 11 studies (Table 3.2; Question 7).[117, 119, 133, 142, 159-162, 164-166] Appropriate follow-up periods varied for each outcome measure, however, all studies reported a follow-up time period that was sufficiently long enough for the outcome to occur (Table 3.2; Question 8).[62, 63, 117-120, 133, 134, 142, 143, 159-168] Critical appraisal Questions 9 and 10 assessed loss to follow-up, however as the majority of studies were retrospective in nature these questions were deemed *Not Applicable*.[62, 63, 117-120, 133, 134, 142, 143, 159-164, 166-168] Statistical methods were appropriately described and used in 16 of the 20 studies (Table 3.2; Question 11).[62, 63, 117-120, 133, 134, 142, 143, 160-163, 167, 168] The most common reason for a lack of appropriate statistical analysis in the remaining four studies was because the potential influence of confounding variables was not addressed.

The single case-control study[130] was also found to be of moderate quality (Table 3.2). The study matched controls, at a minimum, on age, gender, surgical procedure and duration of follow-up (Table 3.2; Question 1), with data for matching collected from the same source population (Table 3.2; Question 2). Equivalent criteria were used for the identification of cases and controls (Table

3.2; Question 3), and confounding variables were identified (Table 3.2; Question 6). The exposures were measured in the same way for each group (e.g. level of obesity was measured by BMI for both groups) (Table 3.2; Question 5), however a description on how the exposure was measured was not reported (e.g. a description of the methods and/or equipment used to measure the height and weight for the calculation of BMI) (Table 3.2; Question 4). A description of how outcomes were assessed or diagnosed was also not reported (Table 3.2; Question 8), however both the time for follow-up and statistical analysis were appropriate (Table 3.2; Question 9; Question 10).

Table 3.2. Assessment of methodological quality of the included studies

Included study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11
Cohort study designs											
Jiang et al. 2016[118]	Y	Y	N	Y	Y	U	Y	Y	NA	NA	Y
Werner et al. 2015[159]	Y	Y	N	Y	N	U	U	Y	NA	NA	N
Pope et al. 2015[160]	Y	Y	N	Y	Y	U	U	Y	NA	NA	Y
Morris et al. 2015[167]	Y	Y	Y	Y	Y	U	Y	Y	NA	NA	Y
Griffin et al. 2015[164]	Y	Y	N	Y	N	U	U	Y	NA	NA	N
Dunn et al. 2015[63]	Y	U	N	Y	Y	NA	Y	Y	NA	NA	Y
Day et al. 2015[142]	N	Y	N	Y	Y	N	U	Y	NA	NA	Y

Basques et al. 2015[62]	Y	Y	N	Y	Y	NA	Y	Y	NA	NA	Y
Toor et al. 2014[161]	Y	Y	N	Y	Y	U	U	Y	NA	NA	Y
Ponce et al. 2014[133]	Y	Y	N	Y	Y	U	U	Y	NA	NA	Y
Gupta et al. 2014[120]	N	Y	N	Y	Y	U	N	Y	NA	NA	Y
Griffin et al. 2014[117]	Y	Y	N	Y	Y	U	U	Y	NA	NA	Y
Chalmers et al. 2014[119]	Y	Y	N	Y	Y	U	U	Y	NA	NA	Y
Baghdadi et al. 2014[162]	Y	Y	N	U	Y	U	U	Y	NA	NA	Y
Li et al. 2013[165]	Y	Y	N	Y	N	NA	U	Y	U	U	N
Mau et al. 2015[166]	N	Y	N	N	N	NA	U	Y	NA	NA	N
Beck et al. 2013[163]	Y	Y	N	Y	Y	U	Y	Y	NA	NA	Y
Singh et al. 2012[134]	Y	Y	Y	Y	Y	NA	Y	Y	NA	NA	Y
Singh et al. 2012[168]	Y	Y	Y	Y	Y	NA	Y	Y	NA	NA	Y

Singh et al, 2011[143]	Y	Y	N	Y	Y	NA	Y	Y	NA	NA	Y
Total Y Score (%)	***85.0***	***95.0***	***15.0***	***90.0***	***80.0***	***0.0***	***40.0***	***100.0***	***0.0***	***0.0***	***80.0***
Total N Score (%)	***15.0***	***0.0***	***85.0***	***5.0***	***20.0***	***5.0***	***5.0***	***0.0***	***0.0***	***0.0***	***20.0***
Total U Score (%)	***0.0***	***5.0***	***0.0***	***5.0***	***0.0***	***60.0***	***55.0***	***0.0***	***5.0***	***5.0***	***0.0***
Total NA Score (%)	***0.0***	***0.0***	***0.0***	***0.0***	***0.0***	***35.0***	***0.0***	***0.0***	***95.0***	***95.0***	***0.0***
Case-control study design											
Pappou et al. 2014[130]	Y	Y	Y	N	Y	Y	NA	N	Y	Y	-

Total columns contain the percentage of cohort studies graded as Yes (Y), No (N), Unclear (U) or Not Applicable (NA) for each critical appraisal question. Cohort and case-control studies are reported separately. See Appendix 3 for appraisal tools explanatory tables.

Appraisal questions for cohort studies:

(1) Were the groups similar and recruited from the same population? (2) Were the variables (exposures/outcomes) measured similarly to assign people to both exposed and unexposed groups? (3) Was the exposure/outcome used to group participants measured in a valid and reliable way? (4) Were confounding factors identified? (5) Were strategies to deal with confounding factors stated? (6) Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)? (7) Were the outcomes measured in a valid and reliable way? (8) Was the follow up time reported and sufficient to be long enough for outcomes to occur? (9) Was follow-up complete, and if not, were the reasons to loss to follow-up described and explored? (10) Were strategies to address incomplete follow-up utilized? (11) Was appropriate statistical analysis used?

Appraisal questions for case-control studies:

(1) Were the groups comparable other than the presence of disease in cases or the absence of disease in controls? (2) Were cases and controls matched appropriately? (3) Were the same criteria used for identification of cases and controls? (4) Was exposure measured in a standard, valid and reliable way? (5) Was exposure measured in the same way for cases and controls? (6) Were confounding factors identified? (7) Were strategies to deal with confounding

factors stated? (8) Were outcomes assessed in a standard, valid and reliable way for cases? (9) Was the exposure period of interest long enough to be meaningful? (10) Was appropriate statistical analysis used?

3.3 Characteristics of included studies

A summary of the characteristics of included studies is presented in Table 3.3. Of the included studies there were 19 retrospective cohort studies,[62, 63, 117-120, 133, 134, 142, 143, 159-164, 166-168] one prospective cohort study[165] and one case-control study.[130] The majority of studies (17) considered TSA and/or RTSA patient populations, while four studies evaluated TEA patients. All the included studies were conducted in the United States of America (USA).

In regard to study settings, the majority of studies retrospectively gathered data from national or multi-institutional databases (Table 3.3). The American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database was utilised by three studies to identify 30-day postoperative complications and outcomes.[62, 63, 118] Inpatient data was collected by four studies from the National Inpatient Sample (NIS), a set of longitudinal hospital inpatient databases in the USA.[117, 133, 160, 161] Two studies gathered data from the PearlDiver healthcare database,[159, 164] and an additional four studies screened the Mayo Clinic Medical Center Total Joint Registry.[134, 143, 162, 168]

Indications for arthroplasty were reported in 13 of the 21 studies (Table 3.3). Common indications included rotator cuff tear or rupture, rotator cuff disease, osteoarthritis, rheumatoid arthritis and traumatic arthropathy. Eight studies reported surgical technique details, mainly specifying the prosthesis used, surgical approach and type of fixation.[130, 134, 162, 163, 165-168] Of the eight, three studies investigated RTSA and specified using the deltopectoral surgical approach.[130, 163, 167] The remaining studies reported using a mixture of cementless and cemented fixation methods. Six studies reported the number of surgeons that performed the arthroplasty procedures, four of which stated a single surgeon.[119, 130, 163, 167] Patients' ethnicity was reported in five studies, with the majority of patient cohorts identified as White or White/Hispanic, ranging from 74.8% to 91.1%.[117, 118, 133, 160, 161] The number of outcomes reported per study ranged from one to 10.

Table 3.3 Summary of characteristics of included studies

Included study	Methods	Exposure, Arthroplasty procedure	Participants	Setting	Complications and postoperative outcomes	
Jiang et al. 2016[118]	**Study design:** Retrospective cohort study **Follow-up:** Up to 30 days **Country of origin:** USA **No. of surgeons performing procedure:** Not reported **Surgical technique:** Not reported	**Exposure:** 1. BMI = 18.5-25 2. BMI = 25-30 3. BMI = 30-35 4. BMI >35 **Procedure:** TSA and RTSA **Indication for procedure:** Not reported	**Sample size:** Total *n = 4267* 1. n = 738 2. n = 1463 3. n = 1126 4. n = 940 **Demographics:** *Age: average yr.* (SD) 1. 72 (11) 2. 71 (10) 3. 69 (10) 4. 67 (9) *Gender: (F: M)* 1. 494: 244 2. 717: 746 3. 574: 552 4. 583: 357 *Ethnicity/Nationality:*	**Setting:** The American College of Surgeons National Surgical Quality Improvement Program database was analysed from 2006 to 2013 for all patients who underwent a primary TSA, including anatomic TSA and reverse TSA. **Exclusions:** Patients were excluded if they had a BMI less than 18.5 kg/m2, lacked documented preoperative height and weight, or had previous shoulder hardware, fracture, pathologic fracture,	**LoS:** Days (SD) 1. 2.1 (1.4) 2. 2.1 (2.9) 3. 2.0 (1.2) 4. 2.1 (1.2) **Blood transfusion:** n (%) 1. 44.3 (6) 2. 52.7 (3.6) 3. 40.5 (3.6) 4. 21.6 (2.3) *Adjusted RR (95% CI); P-Val* 2. 0.68 (0.33–1.41); 0.300 3. 0.82 (0.39–1.71) 0.591 4. 0.41 (0.16–1.05) 0.063 **Operative duration** (Min): Mean (SD) 1. 110 (42) 2. 115 (46)	**Pneumonia:** n (%) 1. 2.95 (0.4) 2. 7.3 (0.5) 3. 6.8 (0.6) 4. 1.88 (0.2) **UTI:** n (%) 1. 11.1 (1.5) 2. 11.7 (0.8) 3. 6.8 (0.6) 4. 12.2 (1.3) **DVT:** n (%) 1. 5.2 (0.7) 2. 1.46 (0.1) 3. 3.4 (0.3) 4. 6.6 (0.7) **PE:** n (%) 1. 3.7 (0.5) 2. 2.9 (0.2) 3. 4.5 (0.4)

			White/Hispanic (%): 1. 86 2. 85 3. 89 4. 94 Black (%): 1. 3 2. 3 3. 3 4. 7 Asian (%): 1. 2 2. < 1 3. < 1 4. < 1 *DM comorbidity: n (%)* 1. 59.0 (8) 2. 175.6 (12) 3. 132.8 (18) 4. 253.8 (27)	tumour, or associated infection.	3. 120 (43) 4. 122 (45) **Return to theatre:** n (%) **(Unknown causes)** 1. 10.3 (1.4) 2. 8.8 (0.6) 3. 7.9 (0.7) 4. 6.6 (0.7) *Adjusted RR (95% CI); P-Val* 2. 0.29 (0.07–1.29); 0.103 3. 0.56 (0.14–2.23); 0.408 4. 0.58 (0.12–2.89); 0.504 **Superficial infection**: n (%) 1. 0.0 (0.0) 2. 1.46 (0.1) 3. 3.4 (0.3) 4. 1.9 (0.2)	4. 3.8 (0.4) **Mortality:** n (%) 1. 0.0 (0) 2. 1.46 (0.1) 3. 3.4 (0.3) 4. 1.88 (0.2) **Deep infection:** n (%) 1. 0.7 (0.1) 2. 1.46 (0.1) 3. 1.1 (0.1) 4. 0.0 (0.0)
Werner et al. 2015[159]	**Study design:** Retrospective cohort study	**Exposure:** 1. Non-obese (BMI < 30) 2. Obese	**Sample size:** Total *n = 144 239* 1. n = 105 661 2. n = 23 864 3. n = 13 759	**Setting:** Patients who underwent TSA or RTSA from 2005 to 2012 were identified by	**Infection (1 Yr.):** n (%) 1. 2083 (2.0) 2. 1177 (4.9) 3. 1284 (9.3) 4. 94 (9.8)	**Revision TSA (8 Yrs.)**: n (%) 1. 3202 (3.0) 2. 1021 (4.3) 3. 653 (4.7)

	Follow-up: Infection, dislocation, component loosening, periprosthetic fracture = 1 year. Revision TSA = up to 8 years. VTE = 90 days medical complications **Country of origin:** USA **No. of surgeons performing procedure:** Not reported	(BMI = 30-39.9) 3. Morbidly obese (BMI = 40-49.9) 4. Super obese (BMI => 50) **Procedure:** TSA and RTSA **Indication for procedure:** Not reported	4. n = 955 **Demographics:** *Age: (%)* **< 65 Years** 1. 6.4 2. 7.8 3. 15.4 4. 27.1 **65 – 80 Years** 1. 68.6 2. 76.9 3. 74.7 4. 68.4 **> 80 Years** 1. 25.0 2. 15.2 3. 9.9 4. 4.5 *Gender: (F: M): n (%)* 1. 62763 (59.4): 42898 (40.6) 2. 15130 (63.4): 8734 (36.6) 3. 9893 (71.9): 3866 (28.1)	ICD-9 procedure codes: 81.80 and 81.88. Patient data was collected from the PearlDiver patient records database. **Exclusions:** No patients undergoing shoulder hemiarthroplasty were included.	*OR (95% CI); P-Val* **4 vs 1:** 3.4 (2.6–4.4); <.0001 **4 vs 2:** 2.3 (1.8–3.0); <.0001 **4 vs 3:** 1.7 (1.3–2.2); <.0001 **Dislocation (1 Yr.):** n (%) 1. 1777 (1.7) 2. 867 (3.6) 3. 666 (4.8) 4. 41 (4.3) *OR (95% CI); P-Val* **4 vs 1:** 1.8 (1.2–2.6); .004 **4 vs 2:** 1.3 (0.9–1.9); .278 **4 vs 3:** 1.0 (0.7–1.5); .941 **VTE (90 Days):** n (%) 1. 786 (0.7) 2. 552 (2.3) 3. 543 (3.9) 4. 47 (4.9)	4. 42 (4.4) *OR (95% CI); P-Val* **4 vs 1:** 1.5 (1.1–2.0); .019 **4 vs 2:** 1.1 (0.8–1.5); .538 **4 vs 3:** 1.0 (0.7–1.4); .97 **Medical complications (90 Days):** n (%) 1. 4295 (4.1) 2. 2967 (12.4) 3. 2630 (19.1) 4. 271 (28.4) *OR (95% CI); P-Val* **4 vs 1:** 2.7 (2.2–3.4) <.0001 **4 vs 2:** 2.1 (1.7–2.6) <.0001 **4 vs 3:** 1.6 (1.3–1.9) <.0001 **PP fracture (1 Yr.):** n (%) 1. 1454 (1.4) 2. 615 (2.6) 3. 368 (2.7) 4. 26 (2.7)

	Surgical technique: Not reported		4. 801 (83.9): 154 (16.1) *Ethnicity/Nationality:* Not reported *DM comorbidity: n (%)* 1. 29662.6 (28.1) 2. 11454.7 (48.0) 3. 8379.2 (60.9) 4. 660.9 (69.2)		*OR (95% CI); P-Val* **4 vs 1:** 2.9 (1.8–4.5); <.0001 **4 vs 2:** 1.9 (1.2–3.0); .008 **4 vs 3:** 1.4 (0.9–2.2); .189	*OR (95% CI); P-Val* **4 vs 1:** 1.4 (0.9–2.2); .222 **4 vs 2:** 1.3 (0.8–2.1); .336 **4 vs 3:** 0.9 (0.6–1.5); .909
Pope et al. 2015[160]	**Study design:** Retrospective cohort study **Follow-up:** Inpatient duration **Country of origin:** USA	**Exposure:** 1. Type 1 or type 2 diabetic group 2. Non-diabetic group **Procedure:** TEA **Indication for procedure:** Not reported	**Sample size:** Total *n = 13698* 1. n = 2270 2. n = 11428 **Demographics:** Age: Mean (SD) 1. 66.37 (26.29) 2. 58.95 (37.52) *Gender: (F: M):* n (%) 1. 1772 (78.07): 498 (21.93) 2. 7530 (66.19):	**Setting:** Patients treated between 1 Jan, 2007 and 31 Dec, 2011, from the NIS for TEA ICD-9 procedure code: 81.84. Within this group, a subpopulation of patients diagnosed with type 1 and type 2 DM was identified based on the ICD-9 Clinical Modification diagnosis codes 250.00 to 250.93. The remainder of the population was	**LoS:** Days (SD) 1. 4.2 (8.5) 2. 3.7 (9.3) P-Val: 0.01 **Blood transfusion:** n (%) 1. 332 (14.62) 2. 962 (8.41) P-Val: <.0001 *Adjusted OR (95% CI); P-Val* 1.108 (0.768–1.1598) **Wound infection:** n (%) 1. 28 (1.60)	**Pneumonia:** n (%) 1. 31 (1.36) 2. 102 (0.89) P-Val: .03 **UTI:** n (%) 1. 152 (6.71) 2. 389 (3.40) P-Val: <.0001

	No. of surgeons performing procedure: Not reported **Surgical technique:** Not reported		3846 (33.81) *Ethnicity/Nationality:* White (%): 1. 75.00 2. 74.62 Black (%): 1. 8.26 2. 8.00 Asian (%): 1. 1.07 2. 1.54 *Obesity comorbidity: n (%)* Not reported	identified as the non-diabetic group. **Exclusions:** None reported	2. 72 (0.83) P-Val: .0007	
Morris et al. 2015[167]	**Study design:** Retrospective cohort study **Follow-up:** minimum 1-year follow-up	**Exposure:** 1. DM 2. No DM 3. Healthy weight BMI < 25 4. Overweight BMI 25 - 30	**Sample size:** Total *n = 301* 1. n = 48 2. n = 253 3. n = 96 4. n = 96 5. n = 109	**Setting:** RTSAs completed by a single surgeon from 2004 to 2011, in a prospectively collected shoulder arthroplasty registry. **Exclusions:**	**Periprosthetic infection:** n (%) 1. 3 (6.3) *OR (95% CI); P-Val* 1. 1.34 (0.23–5.23); .877 3. 6 (6.3) 4. 5 (5.2) 5. 4 (3.7)	

	Country of origin: USA **No. of surgeons performing procedure:** 1 **Surgical technique:** Standard deltopectoral approach using the Aequalis RSA system (Tornier, Inc., Bloomington, MN, USA). Non-antibiotic-loaded Cemented humeral stems were used.	5. Obese BMI > 30 **Procedure:** RTSA **Indication for procedure:** RC tear arthropathies: 144 (47.8%) Failed prior arthroplasties: 61 (20.3) Acute PH fracture: 22 (7.3%) PH non-union/ malunions: 24 (8.0%) OA: 18 (6.0%) Instability arthropathies: 10 (3.3%) Inflammatory arthropathies: 6 (2.0%)	**Demographics:** *Age:* Mean (SD) Total: 68.3 (11.3) *Gender (F: M):* n (%) Total 179 (59.5): 122 (40.5) *Ethnicity/Nationality:* Not reported	All patients with a history of infection in the operative shoulder and all patients undergoing revision of an existing RTSA were excluded.		

		Others: 16 (5.3%).				
Griffin et al. 2015[164]	**Study design:** Retrospective cohort study **Follow-up:** Up to 90 Days; 1 Yr.; 2 Yrs. **Country of origin:** USA **No. of surgeons performing procedure:** Not reported **Surgical technique:** Not reported	**Exposure:** 1. Non-obese (BMI < 30) 2. Obese (BMI = 30-40) 3. Morbidly Obese (BMI > 40) **Procedure:** TEA **Indication for procedure:** Not reported	**Sample size:** Total *n = 7580* 1. n = 5939 2. n = 1030 3. n = 611 **Demographics:** *Age: (%)* **< 65 Years** 1. 17.2 2. 18.7 3. 26.5 **65 – 80 Years** 1. 53.5 2. 65.1 3. 63.7 **> 80 Years** 1. 29.3 2. 16.1 3. 9.8 *Gender (F: M):* n (%)	**Setting:** Data was derived from the Medicare database within the PearlDiver records, screened from 2005 to 2011, using CPT and ICD-9 codes. **Exclusions:** Patients who underwent surgery for revision TEA were excluded, but patients with revision for fracture were included.	**Infection (90 Days):** n (%) 1. 127 (2.1) 2. 48 (4.7) 3. 43 (7.9) *OR (95% CI); P-Val* Obese vs non-obese 2.2 (1.6–3.1); <.0001 Morbidly obese vs non-obese 3.5 (2.4-4.9); <.0001 Morbidly obese vs obese 1.5 (1.0 – 2.4); .042 **VTE (90 Days):** n (%) 1. 41 (0.7) 2. 23 (2.2) 3. 17 (2.8) *OR (95% CI); P-Val* Obese vs non-obese 3.3 (2.0–5.5); <.0001 Morbidly obese vs non-obese 4.1 (2.3–7.3); <.0001	**Revision TEA (2 Yrs.):** n (%) 1. 215 (3.6) 2. 68 (6.6) 3. 48 (7.9) *OR (95% CI); P-Val* Obese vs. non-obese 1.9 (1.4–2.5); <.0001 Morbidly obese vs non-obese 2.3 (1.6–3.1); <.0001 Morbidly obese vs obese 1.2 (0.8–1.8); .391 **Return to theatre:** n (%) *Removal of implant **(6months)*** 1. 45 (0.8) 2. 13 (1.3) 3. 13 (2.1) *OR (95% CI); P-Val* Obese vs non-obese 1.7 (0.9–3.1); .100

			1. 4781 (80.5): 1158 (19.5) 2. 859 (83.4): 171 (16.6) 3. 527 (86.3): 84 (13.7) *Ethnicity/Nationality:* Not reported *DM comorbidity:* n (%) 1. 1906.4 (32.1) 2. 532.5 (51.7) 3. 408.1 (66.8)		Morbidly obese vs obese 1.3 (0.7–2.4); .0485 **Blood transfusion:** n (%) 1. 62 (1.0) 2. 33 (3.2) 3. 37 (6.1) *OR (95% CI); P-Val* Obese vs non-obese 3.1 (2.0–4.8); <.0001 Morbidly obese vs non-obese 6.1 (4.0–9.3); <.0001 Morbidly obese vs obese 1.9 (1.2–3.1); .006 **Dislocation (1 Yr.):** n (%) 1. 144 (2.4) 2. 67 (6.5) 3. 45 (7.4) *OR (95% CI); P-Val* Obese vs non-obese 2.8 (2.1–3.8); <.0001 Morbidly obese vs non-obese 3.2 (2.3–4.5); <.0001 Morbidly obese vs obese 1.1 (0.8–1.7); .571	Morbidly obese vs non-obese 2.8 (1.5–5.3); .001 Morbidly obese vs obese 1.7 (0.8–3.7); .175 *Removal of implant **(1 Yr.)*** 1. 94 (1.6) 2. 23 (2.2) 3. 28 (4.6) *OR (95% CI); P-Val* Obese vs non-obese 1.4 (0.9 – 2.3); .134 Morbidly obese vs non-obese 3.0 (1.9-4.6); < .0001 Morbidly obese vs obese 2.1 (1.2 – 3.7); .008 *Removal of implant* ***(2 Yrs.)*** 1. 129 (2.2) 2. 40 (3.9) 3. 36 (5.9) OR (95% CI); P-Val Obese vs non-obese 1.8 (1.3–2.6); .001

					PP fracture (1 Yr.): n (%) 1. 36 (0.6) 2. 16 (1.6) 3. 14 (2.3) *OR (95% CI); P-Val* Obese vs. non-obese 2.6 (1.4–4.7); .002 Morbidly obese vs non-obese 3.8 (2.1–7.2); <.0001 Morbidly obese vs obese 1.5 (0.7–3.1); .374	Morbidly obese vs non-obese 2.8 (1.9–4.1); < .0001 Morbidly obese vs obese 1.6 (1.0–2.5); .061
Dunn et al. 2015[63]	**Study design:** Retrospective cohort study **Follow-up:** Inpatient duration **Country of origin:** USA	**Exposure:** 1. Diabetes **Procedure:** TSA and RTSA **Indication for procedure:** Not reported	**Sample size:** Total *n = 2004* **Demographics:** *Age:* Mean (SD) Total: 68.8 (11.1) *Gender (F: M):* n (%) Total 1139 (57.0): 859 (43.0) *Ethnicity/Nationality:*	**Setting:** All patients undergoing primary unilateral TSA between 2005 and 2011 were isolated from the National Surgical Quality Improvement Program database. **Exclusions:** Any patients who underwent hemiarthroplasty, resurfacing arthroplasty,	**LoS:** OR (95% CI); P-Val 1.91 (1.33–2.74); .0004	

	No. of surgeons performing procedure: Not reported **Surgical technique:** Not reported		Not reported *Obesity comorbidity:* Mean (SD) 30.3 (6.4)	bilateral TSA, or revision TSA were excluded.		
Day et al. 2015[142]	**Study design:** Retrospective cohort study **Follow-up:** Up to 6 months **Country of origin:** USA **No. of surgeons performing procedure:** Not reported	**Exposure:** 1. Diabetes Mellitus **Procedure:** TSA **Indication for procedure:** Predominately OA	**Sample size:** Total *n = 74203* **Demographics:** *Age; Gender; Ethnicity/Nationality:* Not reported for TSA cohort alone. *Obesity comorbidity:* Did not report obesity measure defined by BMI.	**Setting:** A systematic sample of USA Medicare claims submitted by hospitals and outpatient institutions (Part A) from 1 January, 2004, to 31 December, 2009. ICD-9 CM codes used. **Exclusions:** Patients who were eligible for Medicare benefits because of disability or end-stage renal disease were excluded from the study, thereby retaining	**PE** *Crude relative risk* 1.0 *PE adjusted HR (95% CI)* 1.01 (0.77, 1.32)	

	Surgical technique: Not reported			only those persons aged 65 years and older.		
Basques et al. 2015[62]	**Study design:** Retrospective cohort study **Follow-up:** Up to 30 days **Country of origin:** USA **No. of surgeons performing procedure:** Not reported **Surgical technique:** Not reported	**Exposure:** 1. DM 2. No DM **Procedure:** TSA and RTSA **Indication for procedure:** RA, OA arthropathy, articular cartilage disorder, recurrent dislocation, other joint derangement, unspecified shoulder pain/ disorder, shoulder tendons and bursa, RC	**Sample size:** Total *n = 1505* 1. n = 266 2. n = 1239 **Demographics:** *Age:* Mean (Range) Total 72.8 (60–90) *Gender (F: M):* n (%) Total 886 (58.9): 619 (41.1) *Ethnicity/Nationality:* Not reported *Obesity comorbidity:* n (%) Total	**Setting:** Patients who were 60 years or older and underwent TSA between 2011 and 2012 were identified in the ACS-NSQIP database. TSA patients were identified using Current Procedural Terminology (CPT) code 23472. **Exclusions:** Patients with incomplete perioperative data were excluded from the study.	**Extended LoS:** (> 3 days) *Bivariate analysis:* OR (95% CI); P-Val 2.37 (1.53–3.66); <.001 *Multivariate analysis:* OR (95% CI); P-Val 2.37 (1.53–3.66); <.001	

		rupture, RC sprain, traumatic arthropathy, malunion/ non-union of fracture, PH fracture.	BMI < 30: 802 (53.3) BMI 30-35: 400 (26.6) BMI 35–40: 182 (12.1) BMI ≥40: 121 (8.0)			
Toor et al. 2014[161]	**Study design:** Retrospective cohort study **Follow-up:** Inpatient duration **Country of origin:** USA **No. of surgeons performing procedure:** Not reported	**Exposure:** 1. Type 1 or type 2 diabetic group 2. Non-diabetic Group **Procedure:** TEA **Indication for procedure:** Not reported	**Sample size:** Total *n = 3184* 1. n = 488 2. n = 2696 **Demographics:** *Age:* Mean (SD) 1. 66.78 (11.9) 2. 58.48 (17.21) *Gender (F: M):* n (%) 1. 376 (77.0): 112 (23.0) 2. 1772 (66.3): 902 (33.7) *Ethnicity/Nationality:* White n (%): 1. 299 (76.7) 2. 1551 (74.6)	**Setting:** Data collected from 2005 to 2010, from the NIS for TEA ICD-9-CM procedure code: 81.84. Patients diagnosed with type 1 or type 2 DM were identified. **Exclusions:** Patients were excluded if they had an ICD-9-CM diagnosis code for pathologic fracture, metastatic cancer, or infection of the elbow.	**DVT:** n (%) 1. 2 (0.4) 2. 10 (0.4) *OR (95% CI); P-Val* 1.11 (0.24–5.06); .705 **PE:** n (%) 1. 2 (0.4) 2. 12 (0.4) *OR (95% CI); P-Val* 0.92 (0.21–4.13); >.95 **Return to theatre:** n (%) **Cause:** **Irrigation & debridement** 1. 6 (1.2) 2. 34 (1.3) *OR (95% CI); P-Val*	

	Surgical technique: Not reported		Black n (%): 1. 24 (6.2) 2. 154 (7.4) Asian (%): 1. 6 (1.5) 2. 32 (1.5) *Obesity comorbidity:* n (%) Not reported		0.98 (0.41–2.33); >.95 **Mortality:** n (%) 1. 2 (0.4) 2. 5 (0.2) *OR (95% CI); P-Val* 2.21 (0.43–11.44); .293	
Ponce et al. 2014[133]	**Study design:** Retrospective cohort study **Follow-up:** Inpatient duration **Country of origin:** USA **No. of surgeons**	**Exposure:** 1. Type 1 or type 2 DM 2. No DM **Procedure:** n TSA = 29253 RTSA = 21940 HA = 15292 **Indication for procedure:** Not reported	**Sample size:** Total n = 66 485 1. n = 13 730 2. n = 52 755 **Demographics:** *Age:* Mean (SD) Total: 69 (13) 1. 70 (9.4) 2. 69 (13) *Gender (F: M):* n (%) Total: 38561 (58): 28589 (43)	**Setting:** The study population consisted of adults (≥18 years) undergoing shoulder arthroplasty between 1 January, 2011 and 31 December, 2011, identified from the NIS database. The ICD-9-CM codes of 81.80 (TSA), 81.81 (hemiarthroplasty), and 81.88 (RTSA) were used to identify primary shoulder arthroplasty patients.	**Pneumonia:** n (%) 1. 109.8 (0.8) 2. 316.5 (0.6) *Risk adjusted multivariate analysis: OR (95% CI); P-Val* 1.1 (0.88–1.4); .34 **PE:** n (%) 1. 41.2 (0.3) 2. 105.5 (0.2) *Risk adjusted multivariate analysis: OR (95% CI); P-Val* 1.5 (1.1–2.2); .048	**Transfusion:** n (%) 1. 1510.3 (11.0) 2. 4220.4 (8.0) *Risk adjusted multivariate analysis: OR (95% CI); P-Val* 1.2 (1.1-1.3); <.001 **Mortality (in-hospital):** n (%) 1. 41 (0.3) 2. 53 (0.1)

	performing procedure: Not reported **Surgical technique:** Not reported		1. 8101 (59): 5629 (41) 2. 30070 (57): 22685 (43) *Ethnicity/Nationality:* White %: 1. 77 2. 82 Black %: 1. 6.2 2. 3.8 Asian %: 1. 0.8 2. 0.4 *Obesity comorbidity:* n (%) Total: 9308 (14) 1. 3433 (25) 2. 5803 (11)	Patients were classified as having diabetes (type 1 or type 2, with or without chronic complications) with the use of ICD-9-CM diagnosis codes 250.00 to 250.93. **Exclusions:** None reported	**Perioperative surgical infection:** n (%) 1. 41.2 (0.3) 2. 158.3 (0.3) Risk adjusted multivariate analysis: OR (95% CI); P-Val 0.9 (0.61–1.3); .62	*Risk adjusted multivariate analysis: OR (95% CI); P-Val* 2.1 (1.4–3.4); <.001
Gupta et al. 2014[120]	**Study design:** Retrospective cohort study	**Exposure:** 1. Normal BMI (BMI < 25)	**Sample size:** Total *n = 119* 1. n = 30 2. n = 65	**Setting:** Patients who had undergone primary RTSA with a minimum 90-day	**Operative duration** (Min): Mean (SD) 1. 98 (41) 2. 96 (43)	

	Follow-up: Minimum 90 days **Country of origin:** USA **No. of surgeons performing procedure:** Not reported **Surgical technique:** Not reported	2. Class 1 obesity (BMI = 25 – 35) 3. Class 2 Obesity (BMI > 35) **Procedure:** RTSA **Indication for procedure:** RC tear arthropathy: 45 massive/ irreparable RC tear: 19 End-stage GH arthritis with irreparable RC tear: 35 Inflammatory arthropathy: 6	3. n = 24 **Demographics:** *Age:* Mean (SD) Total: 73.3 (9.8) 1. 75.7 (8.2) 2. 74.1 (9.8) 3. 68.4 (10.5) *Gender (F: M):* n (%) Total: 76 (64): 43 (36) 1. 22 (73): 8 (27) 2. 37 (57): 28 (43) 3. 18 (75): 6 (25) *Ethnicity/Nationality:* Not reported *DM comorbidity:* Authors reported DM comorbidity for all patients that had a complication of interest. Of the outcomes of interest in this review, 1	postoperative follow-up were included. Department of Orthopedic Surgery, Rush University Medical Center, Chicago, IL, USA. **Exclusions:** Patients with previous shoulder arthroplasty, if RTSA was performed as a revision for a failed prior arthroplasty (hemiarthroplasty or TSA), prior deep space infection requiring explantation, or incomplete records.	3. 120 (29) **Blood transfusion:** n (%) 1. 1 (3.3) 2. 2 (3.1) 3. 3 (12.5) **Superficial wound infection:** n (%) 1. 0 (0) 2. 1 (1.5) 3. 0 (0) **Dislocation:** n (%) 1. 1 (3.3) 2. 2 (3.1) 3. 2 (8.3) **Mortality:** n (%) 1. 0 (0) 2. 0 (0) 3. 0 (0)	

		PH malunion with associated irreparable RC tear: 12	patient with a BMI > 40.0 experienced a dislocation.			
Griffin et al. 2014[117]	**Study design:** Retrospective cohort study **Follow-up:** Inpatient duration **Country of origin:** USA **No. of surgeons performing procedure:** Not reported **Surgical technique:** Not reported	**Exposure:** 1. Non-obese (BMI ≤ 29) 2. Obese (BMI = 30 – 39) 3. Morbidly obese (BMI: ≥ 40) **Procedure:** TSA **Indication for procedure:** Not reported	**Sample size:** Total *n = 31 924* 1. n = 29 536 2. n = 1805 3. n = 583 **Demographics:** *Age:* Mean (SD) Total: 68.7 (10.8) 1. 68.3 (10.9) 2. 66.8 (9.2) 3. 64.9 (9.1) *Gender (F: M):* n (%) Total: 17973 (56.3): 13951 (43.7) 1. 16392 (55.5): 13144 (44.5) 2. 1170 (64.8): 635 (35.2) 3. 399 (68.4): 184 (31.6)	**Setting:** The NIS database was used to identify in-hospital data on 39,924 patients who underwent TSA in the US between 1 January, 1998 and 31 December, 2008. CPT and ICD-9 codes were used. **Exclusions:** None reported	**LoS:** Days (SD) Total: 2.57 (1.98) 1. 2.56 (2.0) 2. 2.54 (1.67) 3. 2.84 (1.77) **Mortality:** n (%) Total: 31.9 (0.1) 1. 29.5 (0.1) 2. 1.8 (0.1) 3. 1.2 (0.2)	**Infection:** n (%) Total: 31.9 (0.1) 1. 29.5 (0.1) 2. 1.8 (0.1) 3. 0.0 (0.0) **PE:** n (%) Total: 63.8 (0.2) 1. 59.1 (0.2) 2. 5.4 (0.3) 3. 1.2 (0.2)

			Ethnicity/Nationality: White (%): Total: 91.1 1. 91.5 2. 86.3 3. 83.9 Black (%): Total: 3.9 1. 3.6 2. 6.8 3. 10.1 Other (%): Total: 5.0 1. 4.9 2. 6.9 3. 6.0 *DM comorbidity:* Not reported			
Chalmers et al. 2014[119]	**Study design:** Retrospective cohort study	**Exposure:** 1. Normal BMI: (BMI < 25)	**Sample size:** Total *n = 127* 1. 15 2. 91 3. 21	**Setting:** All patients who underwent TSA by the senior author with a minimum of 90-days	**Operative duration** (Min): Mean 1. 112 2. 111 3. 120	**Infection:** n (%) 1. 0 (0.0) 2. 0 (0.0) 3. 0 (0.0)

	Follow-up: Minimum 90 days **Country of origin:** USA **No. of surgeons performing procedure:** 1 **Surgical technique:** Not reported	2. Obesity class I: (BMI: 25-35) 3. Obesity class II: (BMI: > 35.0) **Procedure:** TSA **Indication for procedure:** n OA: 120 Post-traumatic arthropathy: 4 Instability related arthropathy: 3	**Demographics:** *Age:* Mean 1. 66.3 2. 65.8 3. 65.2 *Gender (F: M):* n (%) 1. 10 (67): 5 (33) 2. 36 (40): 55 (60) 3. 13 (62): 8 (38) *Ethnicity/Nationality:* Not reported *DM comorbidity:* Not reported	of post-operative follow-up. Department of Orthopedic Surgery, Rush University Medical Center, Chicago, Illinois **Exclusions:** History of prior ipsilateral shoulder arthroplasty, or incomplete peri- or post-operative records.	**Blood transfusion:** n (%) 1. 0 (0.0) 2. 2 (2.2) 3. 1 (4.7) **Mortality:** n (%) 1. 0 (0.0) 2. 0 (0.0) 3. 0 (0.0)	**Dislocation:** n (%) 1. 0 (.0) 2. 2 (2.2) 3. 0 (0.0)
Baghdadi et al. 2014[162]	**Study design:** Retrospective cohort study **Follow-up:**	**Exposure:** 1. Non-obese (BMI < 30) 2. Obese: (BMI ≥ 30)	**Sample size:** Total *n = 723* 1. 564 2. 159	**Setting:** Patients who underwent primary TEA using a single implant design (semi-constrained, linked TEAs using the Coonrad/Morrey	**Revision:** Survivorship % *For any reason at 5 Yrs:* 1. 93 (91–95) 2. 90 (83–94) *For any reason at 10 Yrs:* 1. 86 (82–89)	**Revision:** Adjusted HR (95% CI) for BMI per unit increase 1.02 (0.99, 1.05)

	Median: 5.8 years, range: 0 - 25 years **Country of origin:** USA **No. of surgeons performing procedure:** Not reported, but majority (76%) performed by a single surgeon **Surgical technique:** 722 cementless 1 cemented Single Prosthesis: Coonrad/	**Procedure:** TEA **Indication for procedure:** n Inflammatory conditions: 317 Traumatic conditions: 310 Primary osteoarthrosis: 19 Resection of neoplastic lesion: 6 Hemophilic, septic, charcot neuropathic & crystal deposition arthropathy: 10	**Demographics:** *Age:* Mean *(SD) 62.3 (13.7) *Gender (F: M):* n (%) 550 (76): 173 (24) *Ethnicity/Nationality:* Not reported *DM comorbidity:* Not reported	Total Elbow ([Zimmer, Warsaw, Indiana]) performed between 1987 and 2006. **Exclusions:** None reported	2. 70 (60–79) *For any reason at 15 Yrs:* 1. 75 (69–81) 2. 63 (51–74) *Mechanical failure at 5 Yrs:* 1. 95 (93–97) 2. 93 (87–96) *Mechanical failure at 10 Yrs* 1. 88 (84–91) 2. 72 (61–81) *Mechanical failure at 15 Yrs* 1. 77 (71–83) 2. 65 (53–76) *Aseptic loosening at 5 Yrs:* 1. 96 (94–98) 2. 93 (87–97) *Aseptic loosening at 10 Yrs:* 1. 92 (89–95) 2. 81 (70–88) *Aseptic loosening at 15 Yrs.* 1. 85 (80–90)	**Thromboembolic events:** n (%) 1. 1 (0.2) 2. 0 (0.0) **Perioperative mortality (90 Days):** n (%) 1. 3 (0.5) 2. 2 (1.3) **Return to theatre:** n (%) *Surgical wound complications that required additional operation with no component revision* 1. 38 (6.7) 2. 7 (4.4)

	Morrey Total Elbow (Zimmer, Warsaw, Indiana) Tourniquet applied				2. 76 (64–85) *Deep infection at 5 Yrs.* 1. 98 (96–99) 2. 97 (92–99) *Deep infection at 10 Yrs.:* 1. 97 (95–98) 2. 97 (92–99) *Deep infection at 15 Yrs.:* 1. 97 (95–98) 2. 97 (92–99)	
Li et al. 2013[165]	**Study design:** Prospective cohort study **Follow-up:** Up to 2 years **Country origin:** USA **No. of surgeons performing procedure:**	**Exposure:** 1. Normal (BMI < 25) 2. Overweight: (BMI: 25 – 29.9) 3. Obese: (BMI ≥ 30) **Procedure:** TSA **Indication for procedure:**	**Sample size:** Total *n = 76* 1. 26 2. 25 3. 25 **Demographics:** *Age:* Mean *(SD)* 1. 71 (9) 2. 71 (11) 3. 68 (8) *Gender (F: M):* n Total: 49: 27 1. 17: 9 2. 15: 10	**Setting:** Patients had unconstrained anatomic TSA in a single hospital between 1 January, 2009 and 31 January, 2010 were enrolled into the prospective total shoulder registry, grouped according to BMI, and followed prospectively for two years **Exclusions:** Patients had undergone a hemiarthroplasty, RSA or	**Function:** **Preop. vs Post-op (2 Yrs.)** *ASES Score: Mean (SD)* 1. 38.4 (15.5) **vs** 80.2 (19.4) 2. 37.4 (18.1) **vs** 75.2 (24.9) 3. 35.8 (12.5) **vs** 80.0 (20.6) **Quality of life:** **Preop. vs. Post-op (2 Yrs.)** *SF-36 PCS:* Mean (SD)	**LoS:** Days (SD) 1. 2.3 (0.8) 2. 2.5 (1.5) 3. 2.4 (0.8) **Operative duration (Min):** (Incision to closure) Mean (SD) 1. 108.3 (19.5) 2. 115.5 (37.3) 3. 119.7 (37.3) **Blood transfusion:** Units of blood; Mean (SD) 1. 0.2 (0.5)

	Multiple **Surgical technique:** Unconstrained anatomic TSA	OA, RA, or posttraumatic arthritis	3. 18: 8 *Ethnicity/Nationality:* Not reported *DM comorbidity:* Not reported	any revision surgery as the index procedure.	1. 38.3 (6.5) **vs** 53.1 (11.3) 2. 36.1 (8.0) **vs** 39.8 (12.2) 3. 36.3 (8.4) **vs** 40.7 (12.4) *SF-36 MCS:* Mean (SD) 1. 47.4 (14.3) vs. 52.8 (10.0) 2. 49.7 (11.6) vs. 51.7 (11.5) 3. 51.5 (12.5) vs. 52.9 (11.6) **Revision TSA (2 Yrs.):** n (%) 1. 2 (7.7) 2. 0 (0.0) 3. 0 (0.0)	2. 0.2 (0.5) 3. 0.1 (0.4) **Pain:** (points) **Preop. vs. Post-op (2 Yrs.)** *VAS – Pain* 1. Preop.: 62; Post-op: 12 2. Preop.: 68; Post-op: 18 3. Preop.: 66; Post-op: 11 **Return to theatre:** n (%) **Cause: Deep infection** 1. 0 (0.0) 2. 1 (4.0) 3. 0 (0.0)
Mau et al. 2015[166]	**Study design:** Retrospective cohort study	**Exposure:** 1. BMI <25 2. BMI 25 – 35 3. BMI > 35	**Sample size:** *TSA* 1. 110 2. 290 3. 99 *RSA*	**Setting:** Patient data was gathered from a multi-institutional database. Patients were treated using either TSA or RTSA	**TSA Group** **Function:** **Preop. vs. Post-op** *SST:* Mean (SD) 1. 4.3 (2.6) vs 10.5 (2.2) 2. 3.8 (2.7) vs 10.4 (2.4) 3. 3.0 (2.8) vs 10.0 (2.8)	**RSA Group** **Function:** **Preop. vs. Post-op** *SST:* Mean (SD) 1. 2.7 (2.3) vs 10.0 (2.4) 2. 2.8 (2.8) vs 9.9 (2.6) 3. 2.9 (2.9) vs 10.3 (2.2)

	Follow-up: Ave. 39.8 ± 18.7 Months (Minimum 2 years) **Country of origin:** USA **No. of surgeons performing procedure:** 12 **Surgical technique:** Prosthesis: Equinoxe (Exactech, Inc., Gainesville, Florida)	**Procedure:** TSA and RTSA **Indication for procedure:** Degenerative arthritis = 499 RC arthropathy OR OA= 612	1. 196 2. 357 3. 59 **Demographics:** *Age:* Mean (SD) *TSA* 1. 68.1 (9.8) 2. 66 (8.9) 3. 63.7 (7.2) *RTSA* 1. 73.5 (7.7) 2. 71.3 (7.7) 3. 68.9 (8.6) *Gender (F: M):* n 1. 79: 31 2. 134: 156 3. 52: 47 *RTSA* 1. 138: 58 2. 217: 140 3. 34: 25 Ethnicity/Nationality:	with one platform shoulder system. **Exclusions:** None reported	*ULCA:* Mean (SD) 1. 14.8 (3.7) vs 31.3 (5.1) 2. 14.6 (3.9) vs 30.1 (6.0) 3. 12.8 (4.3) vs 30.2 (5.7) *ASES:* Mean (SD) 1. 40.0 (15.0) vs 87.4 (17.7) 2. 38.5 (12.6) vs 84.2 (19.9) 3. 31.1 (15.8) vs 81.2 (21.4) *Constant:* Mean (SD) 1. 39.2 (14.1) vs 73.1 (12.5) 2. 37.8 (12.6) vs 71.2 (15.1) 3. 31.0 (11.6) vs 67.9 (17.4) *SPADI:* Mean (SD) 1. 79.0 (19.1) vs 13.8 (20.4) 2. 80.6 (21.8) vs 18.4 (24.9)	*ULCA:* Mean (SD) 1. 12.1 (3.9) vs 30.1 (5.2) 2. 12.4 (4.2) vs 30.3 (4.9) 3. 12.8 (5.1) vs 30.5 (4.9) *ASES:* Mean (SD) 1. 35.0 (16.0) vs 84.3 (17.3) 2. 32.3 (17.0) vs 84.4 (17.3) 3. 33.0 (21.4) vs 86.0 (15.3) *Constant:* Mean (SD) 1. 30.2 (14.0) vs 71.1 (14.4) 2. 30.1 (14.8) vs 71.5 (15.2) 3. 30.8 (18.2) vs 72.2 (15.1) *SPADI:* Mean (SD) 1. 85.2 (22.1) vs 20.2 (23.8) 2. 83.1 (21.8) vs 21.5 (24.8)

			Not reported DM comorbidity: Not reported		3. 90.0 (21.3) vs 22.1 (26.1) *Act abduction:* Mean (SD)* 1. 83.5 (28.0) vs 122.9 (29.8) 2. 80.2 (27.1) vs 120.1 (30.2) 3. 77.4 (25.7) vs 116.2 (31.9) *Act forward flexion:* Mean (SD)* 1. 100.3 (33.5) vs 144.4 (30.8) 2. 95.8 (30.6) vs 139.9 (32.0) 3. 88.7 (27.3) vs 141.2 (34.2) *IR:* Mean (SD)* 1. 3.3 (1.6) vs 5.7 (1.2) 2. 2.8 (1.5) vs 5.2 (1.4) 3. 2.7 (1.4) vs 4.4 (1.6) *Act ER:* Mean (SD)*	3. 79.2 (25.1) vs 19.9 (20.4) *Act abduction:* Mean (SD)* 1. 60.0 (33.5) vs 102.7 (24.9) 2. 65.0 (35.5) vs 106.1 (26.0) 3. 69.2 (34.1) vs 105.7 (25.7) *Act forward flexion:* Mean (SD)* 1. 80.5 (40.7) vs 140.4 (26.0) 2. 82.7 (41.0) vs 139.6 (28.4) 3. 85.7 (41.2) vs 132.6 (32.6) *IR:* Mean (SD)* 1. 3.1 (1.8) vs 4.9 (1.4) 2. 2.9 (1.8) vs 4.5 (1.7) 3. 2.4 (1.7) vs 4.0 (1.7) *Act ER:* Mean (SD)* 1. 10.7 (21.8) vs 32.3 (13.1)

					1. 17.2 (19.9) vs 50.2 (20.6) 2. 16.2 (19.9) vs 45.7 (20.4) 3. 14.2 (17.1) vs 42.6 (19.7)	2. 13.2 (21.2) vs 32.8 (16.2) 3. 14.5 (21.0) vs 31.1 (14.2)
Beck et al. 2013[163]	**Study design:** Retrospective cohort study **Follow-up:** Minimum 2 years **Country of origin:** USA **No. of surgeons performing procedure:** 1 **Surgical technique:** Deltoid-splitting	**Exposure:** 1. Normal (BMI: 18.5 – 24.9) 2. Overweight: (BMI: 25 – 29.9) 3. Obese: (BMI ≥ 30) **Procedure:** RTSA **Indication for procedure:** RC arthropathy	**Sample size:** Total n = 76 1. 23 2. 36 3. 17 **Demographics:** *Age:* Mean (range) Total: 75 (51 – 88) *Gender (F: M):* n 1. 13: 10 2. 19: 17 3. 12: 5 *Ethnicity/Nationality:* Not reported *DM comorbidity: n (%)* 1. 1 (4.3) 2. 7 (19.4)	**Setting:** Patients undergoing RTSA for rotator cuff arthropathy by a single surgeon from 1 January, 2005 to 1 March, 2010. Inclusion criteria included patient age > 18 years, primary diagnosis of RC arthropathy, minimum 2-year follow-up, and subsequent RTSA by the senior author (G.D.H.). **Exclusions:** Patients with history of infection.	**Function:** Post-op *Act forward flexion:* Mean (SD)* 1. 134 (32) 2. 129 (43) 3. 117 (44) *Act abduction:* Mean (SD)* 1. 99 (26) 2. 100 (41) 3. 86 (27) *Act ER:* Mean (SD)* 1. 26 (15) 2. 33 (17) 3. 23 (18) **Infection:** n (%) 1. 0 (0.0) 2. 2 (5.6) 3. 3 (17.6)	**Operative duration** (Min): Mean (SD) 1. 74 (19) 2. 81 (18) 3. 83 (24) **Pain:** (points) Mean (SD) *VAS – Pain – Post-Op.* 1. 1.5 (1) 2. 2.6 (3) 3. 3.0 (3) **LoS:** Days (SD) 1. 2.7 (1) 2. 2.6 (1) 3. 3.9 (4)

	approach; Deltopectoral approach.		3. 8 (47.1)			
Singh et al. 2012[134]	**Study design:** Retrospective cohort study **Follow-up:** Mean: 7 Yrs. SD = 6 Yrs. Range: (1 day to 31 Years) **Country of origin:** USA **No. of surgeons performing procedure:** Not reported **Surgical technique:**	**Exposure:** 1. BMI < 24.9 2. BMI 25 – 29.9 3. BMI 30 – 34.9 4. BMI 35 – 39.9 5. BMI ≥ 40 6. No DM 7. DM **Procedure:** TSA **Indication for procedure:** RA, OA, trauma, tumour, RC disease, other	**Sample size:** Total *n = 2588* Total with known BMI: n = 2101 1. 475 2. 744 3. 521 4. 235 5. 126 6. 2409 7. 179 **Demographics:** *Age:* Mean (SD) Total: 65 (12) *Gender (F: M):* n 1352: 1236 *Ethnicity/Nationality:* Not reported	**Setting:** Every adult aged 18 years or older with primary TSA performed at the Mayo Clinic Medical Center, Rochester, in a 33-year period from 1976 to 2008. **Exclusions:** None reported	**Deep / Periprosthetic infection:** n (%); HR (95% CI) 1. 4 (0.8); 1.0 (Reference) 2. 5 (0.7); 0.82 (0.22-3.02) 3. 7 (1.3); 1.67 (0.47-5.95) 4. 4 (1.7); 2.48 (0.63-9.83) 5. 2 (1.6); 2.46 (0.45-13.34) 6. 29 (1.2) 7. 3 (1.7)	

	Cemented and cementless fixation		*DM comorbidity:* % With infection: 9.4 Without infection: 6.9			
Pappou et al. 2014[130]	**Study design:** Case-control Study **Follow-up:** Minimum 2 years **Country of origin:** USA **No. of surgeons performing procedure:** 1 **Surgical technique:** Prosthesis: Reverse shoulder	**Exposure:** 1. Obese (BMI ≥ 40) 2. Controls (BMI < 30) **Procedure:** RTSA **Indication for procedure:** RC tear arthropathy = 68 Massive RC tear = 8 RA = 8	**Sample size:** Total *n = 84* 1. 21 2. 63 **Demographics:** *Age:* Mean (range) 1. 69.2 (7.1) 2. 71.1 (6.4) *Gender (F: M):* n 1. 17: 4 2. 50: 13 *Ethnicity/Nationality:* Not reported *DM comorbidity:* Not reported	**Setting:** A prospective database was retrospectively searched for morbidly obese patients with a BMI of ≥40 kg/m2 who had undergone primary RTSA for a reason other than fracture from 1 January, 2003 to 31 December, 2010. Three controls for each morbidly obese patient were matched on the basis of age, sex, surgical indication, and duration of follow-up. **Exclusions:** Patients receiving a RTSA for treatment of a PH fracture, who had incomplete clinical and	**Function:** Mean (SD) **Preop. vs Post-op** *VAS – Function* 1. 2.1 (2.1) vs 6.9 (2.4) 2. 3.6 (2.4) vs 7.8 (2.2) *ASES Score:* Mean (SD) 1. 32.0 (12.8) vs 69.0 (16.0) 2. 39.9 (17.8) vs 78.2 (18.6) *SST:* Mean (SD) 1. 1.1 (1.1) vs 7.0 (3.4) 2. 2.1 (1.9) vs 8.2 (2.9) *Forward flexion:* Mean (SD)* 1. 61 (26) vs 139 (39) 2. 74 (42) vs 153 (31) *Abduction:* Mean (SD)* 1. 56 (20) vs 125 (49)	**Pain:** Mean (SD) **Preop. vs Post-op** *VAS – Pain* 1. 6.6 (1.9) vs 2.2 (2.9) 2. 6.2 (2.2) vs 1.3 (2.2) **Operative duration** (Min): (Incision to dressing) 1. 118 (35) 2. 109 (35) **Acromial fracture**: n (%) 1. 2 (9.5) 2. 1 (1.6) **Revision:** n (%) **Cause: Humeral stem loosening** 1. 0 (0.0) 2. 1 (1.6) (Revision occurred at 75 months post RTSA)

	prosthesis (DJO Surgical) All received deltopectoral approach.			radiographic data, or less than 2-year follow-up.	2. 68 (35) vs 138 (40) *ER:* Mean (SD)* 1. 11 (25) vs 54 (35) 2. 26 (26) vs 55 (33) *IR: (vertebral levels)* 1. L5 (2) vs T12 (2) 2. L3 (2) vs T12 (2)	**Superficial wound infection:** n (%) 1. 1 (4.8) 2. 0 (0.0) **UTI:** n (%) 1. 0 (0.0) 2. 1 (1.6) **LoS:** Days (SD) 1. 3.1 (2.6) 2. 2.6 (1.3)
Singh et al. 2012[168]	**Study design:** Retrospective cohort study **Follow-up:** Mean: 7 years Range: 1 day -31 years **Country of origin:** USA **No. of surgeons**	**Exposure:** 1. BMI = < 24 2. BMI = 25-29.9 3. BMI = 30-35.9 4. BMI = 35-39.9 5. BMI ≥ 40 **Procedure:** TSA **Indication for procedure:** RA = 452 Trauma-related = 374 OA = 1640	**Sample size:** Total *n = 2588* 1. 475 2. 744 3. 521 4. 235 5. 126 **Demographics:** *Age:* Mean (median) Total: 65 (67) *Gender (F: M):* n 1372: 1216	**Setting:** Every patient who had had a primary shoulder arthroplasty performed when they were eighteen years of age or older at the Mayo Clinic Medical Center, Rochester, Minnesota, in a thirty-three-year period from 1976 to 2008. Periprosthetic shoulder fractures were identified from the total joint registry. **Exclusions:**	**PP fracture:** n (%) 1. 7 (1.5) 2. 1 (0.1) 3. 2 (0.4) 4. 3 (1.3) 5. 2 (1.6)	

	performing procedure: Not reported **Surgical technique:** Cemented implants: 2485 No cement: 103	Other = 122	*Ethnicity/Nationality:* Not reported *DM comorbidity:* Not reported	Not reported		
Singh et al. 2011[143]	**Study design:** Retrospective cohort study **Follow-up:** Up to 20 years **Country of origin:** USA **No. of surgeons**	**Exposure:** Total BMI: Mean (SD) 30 (6) **Procedure:** TSA **Indication for procedure:** n RA = 452 Trauma = 374 Tumour = 37 OA = 1640 RC Disease = 40	**Sample size:** Total *n = 2588* **Demographics:** *Age:* Mean (SD) Total: 65 (12) *Gender (F: M):* n (%) Total 1163 (53): 1044 (47) *Ethnicity/Nationality:* Not reported	**Setting:** All patients who had undergone TSA between January 1976 and December 2008 at the Mayo Clinic Medical Centre, Rochester, Minnesota. BMI data only available from 1987 onwards. **Exclusion:** Not reported	**Revision:** *Univariate regression analysis:* HR (95% CI) 1.01 (0.99,1.04) P-Val: 0.29	

	performing procedure: Not reported **Surgical technique:** Not reported	Other = 30	DM comorbidity: *Not reported*			

Act *= Active;* ***ASES*** *= American Shoulder and Elbow Score;* ***BMI*** *= Body Mass Index kg/m²;* ***DM*** *= diabetes mellitus;* ***DVT*** *= deep vein thrombosis;* ***ER*** *= external rotation (degrees);* ***F*** *= Female;* ***GH*** *= Glenohumeral;* ***HR*** *= hazard ratio;* ***HA*** *= Hemi-arthroplasty;* ***ICD-9*** *= International Classification of Diseases, Ninth Revision codes;* ***IR:*** *internal rotation (degrees);* ***LoS*** *= length of stay;* ***M*** *= Male;* ***Min*** *= minutes;* ***NIS*** *= Nationwide Inpatient Sample;* ***n*** *= number of arthroplasties;* ***OA*** *= osteoarthritis;* ***OR*** *= odds ratio;* ***PE*** *= pulmonary embolism;* ***PH*** *= proximal humeral;* ***P-Val*** *= P-Value;* ***RA*** *= rheumatoid arthritis;* ***RC*** *= rotator cuff;* ***RR*** *= relative risk;* ***RTSA*** *= reverse total shoulder arthroplasty;;* ***SD*** *= standard deviation;* ***SST*** *= Simple Shoulder Test;* ***TEA*** *= total elbow arthroplasty;* ***TSA*** *= total shoulder arthroplasty;* ***UK*** *= United Kingdom;* ***USA*** *= United States of America;* ***UTI*** *= urinary tract infection;* ***Yr.*** *= Year.*

******* *All range of motion measurements (forward flexion, abduction, ER, IR) are measured in degrees unless otherwise stated.*

3.4 Exposure: obesity and diabetes mellitus

Of the 21 included studies, 15 evaluated the influence of obesity on arthroplasty outcomes (Table 3.3).[117-120, 130, 134, 143, 159, 162-168] Thirteen of the 15 studies considered arthroplasty of the shoulder joint, while two assessed TEA. A total of 198 010 patients were included across the studies that evaluated obesity, the majority of which were female (60.9%; 120 660). Most patients were also 65 years of age or older across all of the included studies (refer Table 3.3). Seven studies reported on whether the obese cohort had a diabetic comorbidity,[118, 120, 134, 159, 163, 164, 167] however it could not be determined whether patients with diabetes mellitus experienced an outcome of interest. Follow-up duration varied across study and outcome. Maximum follow-up periods per study included the inpatient duration (from hospital admission to discharge),[117] up to 30 days,[118] a minimum of 90 days,[119, 120] 1 year[167] and 2 years;[130, 163] up to 2 years[164, 165], 8 years,[159] and 20 years;[143] a median of 5.8 years (range: 0 – 25 years),[162] and mean follow-ups of 39.8 (SD = 18.7 months)[166] and 7 years (range: 1 day – 31 years).[134, 168]

Eight of the 21 included studies evaluated the influence of diabetes mellitus on arthroplasty outcomes, reporting on a total of 164 553 patients (Table 3.3). Dissimilar to obesity studies, gender ratio was relatively equal across studies that reported it, with slightly more males (51.7%; 46 755 males) than females included. Six studies considered arthroplasty of the shoulder joint,[62, 63, 133, 134, 142, 167] while two assessed TEA.[160, 161] Further categorisation by level of glycaemic control or type of diabetes mellitus was not provided, however four studies indicated the percentage of the cohort who were obese.[62, 133, 134, 167] Follow-up intervals varied and included duration as an inpatient (from hospital admission to discharge),[63, 133, 160, 161] up to 30 days,[62] up to 6 months,[142] a minimum of 1 year,[167] and 7 years (range: 1 day – 31 years).[134]

3.5 Complications and postoperative outcomes

A summary of all calculated effect estimates is provided in Appendix 5.

3.5.1 Operative duration

Obesity

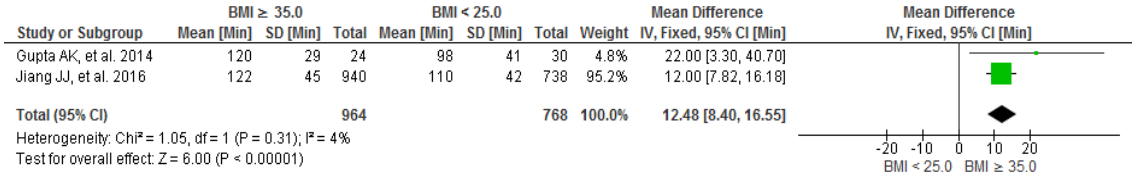
Six studies including a total of 398 TSA/RTSA patients evaluated the influence of obesity on operative duration (Table 3.3).[118-120, 130, 163, 165] Two of the six studies could not be included in meta-analyses as they did not report a measure of variance with the mean operative time,[119] or reported a BMI group that was not comparable with the BMI groupings in the other included studies.[130] Three individual meta-analyses were conducted (Figure 3.2).

Operative duration was not clearly defined by all studies combined in the following meta-analyses. Jiang et al.[118] gathered data from the ACS NSQIP, which reported *'total operation time in minutes'*, with separate classifications for '*duration patient is in the room'* and '*duration of anesthesia in minutes'.* Both Chalmers et al.[119] and Gupta et al.[120] simply reported *'length of procedure in minutes'*, while Beck et al.[163] described this outcome as *'surgery time (min)'.* Further detail was provided by Pappou et al.[130] who defined operative duration as *'incision to dressing'*, and Li et al.[165] who stated surgical time was from *'incision to closure as documented by the anesthesia records'.*

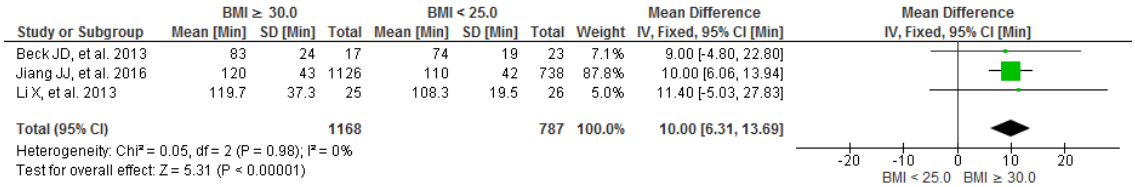
Obese class 2 TSA/RTSA patients had a statistically significant greater mean operative duration time than TSA/RTSA patients with a BMI in the normal range. The WMD was 12.48 minutes (95% CI [8.40, 16.55]), indicating patients with a BMI ≥ 35.0 experienced longer operative durations than patients with a BMI < 25.0 (Figure 3.2: Panel A). Similarly, obese TSA/RTSA patients had a statistically significant greater mean surgical duration time, on average 10.00 minutes longer, than TSA/RTSA patients with a BMI in the normal range (BMI < 25.0) (Figure 3.2: Panel B).

Obese TSA/RTSA patients also displayed a statistically significant greater mean operative duration time than TSA/RTSA patients with a BMI in the overweight range. The WMD was 4.78 minutes (95% CI [1.50, 8.07]), indicating obese patients experienced longer operative durations than overweight patients (Figure 3.2: Panel C). Variability between studies for each meta-analysis was not statistically significant (Figure 3.2).

Panel A



Panel B



Panel C

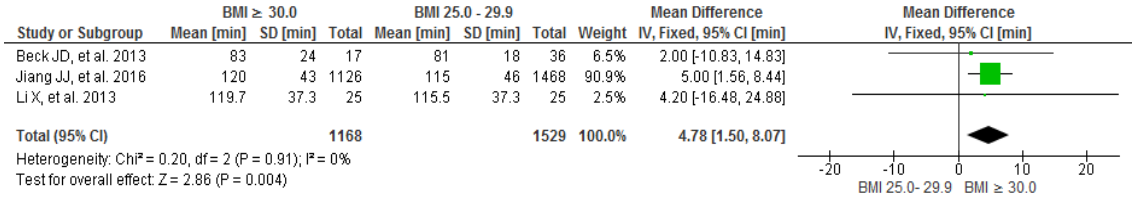


Figure 3.2. *Forest plots of differences in operative duration (minutes) across various BMI groupings. (IV:* inverse variance*; CI: confidence interval; df: degrees of freedom; Min: minutes).*

Panel A: Obese class 2 (BMI ≥ 35.0) versus normal BMI (BMI < 25.0) total shoulder arthroplasty (TSA) and reverse total shoulder arthroplasty (RTSA) patients.

Panel B: Obese (BMI ≥ 30.0) versus normal BMI (BMI < 25.0) TSA/RTSA patients.

Panel C: Obese (BMI ≥ 30.0) versus overweight (BMI 25.0 – 29.9) TSA/RTSA patients.

Diabetes mellitus

No studies investigated the impact of diabetes mellitus on operative duration.

3.5.2 Length of stay

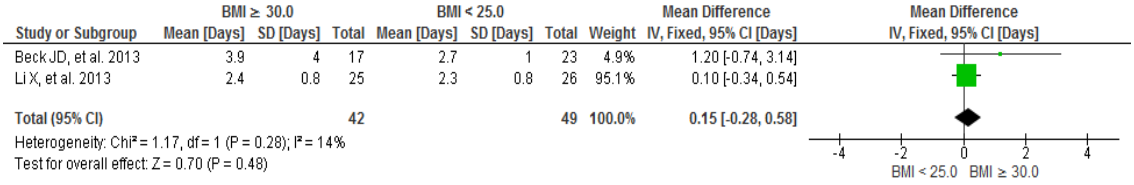
Obesity

Five studies with a total of 36 427 TSA/RTSA patients evaluated the influence of obesity on LoS (Table 3.3).[117, 118, 130, 163, 165] One study could not be included in the statistical analysis due to non-comparable BMI groupings.[118] No statistically significant difference in LoS (days) was observed between obese TSA/RTSA patients and patients with a BMI in the normal range (WMD = 0.15; 95% CI [-0.28, 0.58]). Analysis of heterogeneity revealed low statistical variability between studies (I^2, 14%) that was not statistically significant ($\chi^2 = 1.17$, P = 0.28) (Figure 3.3: Panel A).

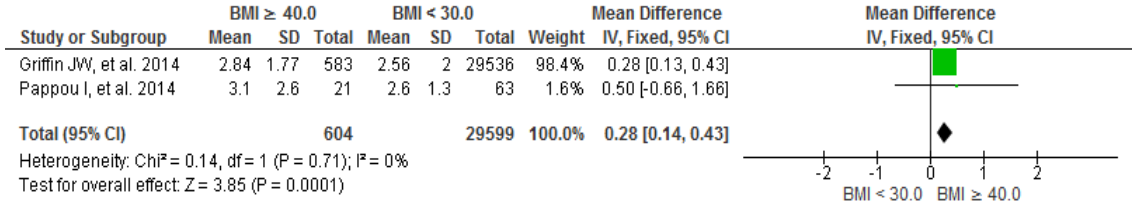
Morbidly obese patients had a small, yet statistically significant increase in LoS of 0.28 days (6.72 hours) (95% CI [0.14, 0.43]) in comparison to non-obese patients. Two different study designs (a case series[117] and case-control study[130]) were combined, however no statistical heterogeneity was observed (I^2, 0%) (Figure 3.3: Panel B).

No statistically significant increased odds in LoS were observed in obese compared to overweight TSA/RTSA patients (MD = 0.05; 95% CI [-0.58, 0.68]); the I^2 statistic indicated moderate heterogeneity between studies (I^2, 45%), however this was not statistically significant ($\chi^2 = 1.81$, P = 0.18) (Figure 3.3: Panel C).

Panel A



Panel B



Panel C

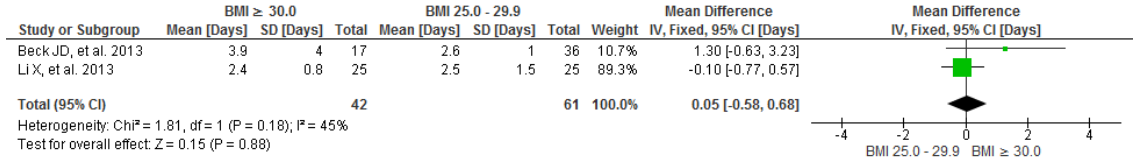


Figure 3.3. *Forest plots of differences in length of stay (days) across various BMI groupings. (IV: inverse variance; CI: confidence interval; df: degrees of freedom).*

Panel A: Obese (BMI ≥ 30.0) versus normal BMI (BMI < 25.0) total shoulder arthroplasty (TSA) and reverse total shoulder arthroplasty (RTSA) patients.

Panel B: Morbidly obese (BMI ≥ 40.0) versus non-obese (BMI < 30.0) TSA/RTSA patients.

Panel C: Obese (BMI ≥ 30.0) versus overweight (BMI 25.0 – 29.9) TSA/RTSA patients.

Diabetes mellitus

Two TSA/RTSA studies[62, 63] and one TEA study[160] investigated the influence of diabetes mellitus on LoS. However, as data were expressed as both risk estimates, calculated from a mixture of dichotomous and continuous methods, and raw figures in the various studies, a meta-analysis could not be conducted.

Dunn et al.[63] identified diabetes mellitus as a patient variable that contributed to increasing the duration of hospital stay (OR = 1.91; 95% CI [1.33, 2.74]; P = .0004), with a mean LoS of 2.2 days (SD = 1.7) in TSA/RTSA patients.[63] Similarly, Basques et al.[62] identified through multivariate analysis that extended LoS (> 3 days) was significantly associated with a history of diabetes mellitus (OR = 2.37; 95% CI [1.53, 3.66]; P < .001). In regard to TEA, Pope et al.[160] reported that diabetic patients had a significantly longer LoS with a mean of 4.2 days (SD = 8.5), compared to non-diabetics, with a mean of 3.7 days (SD = 9.3) (P = 0.01) (Table 3.3).

3.5.3 Blood transfusion

Obesity

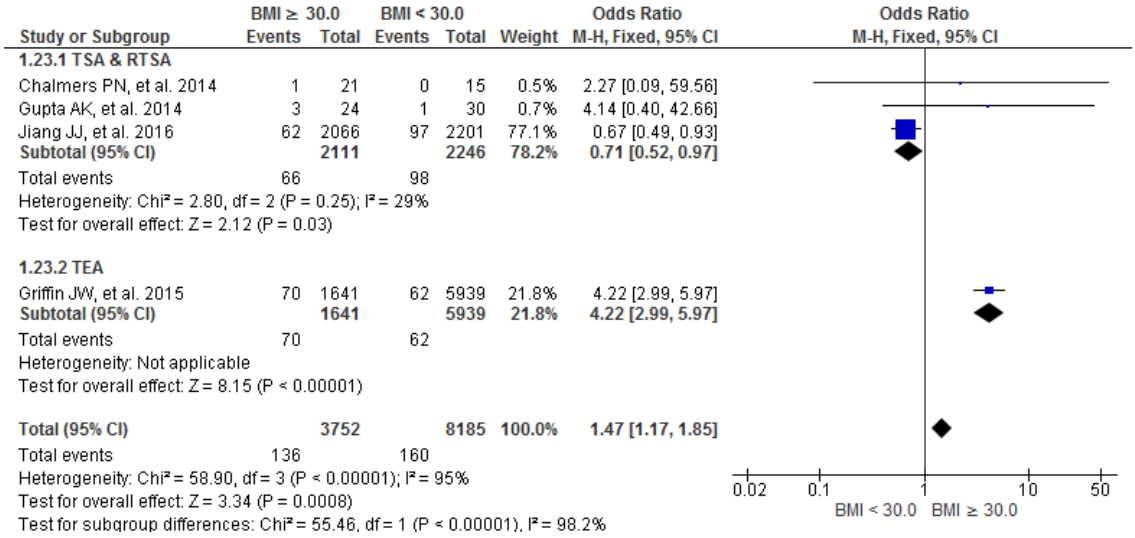
Four TSA/RTSA studies[118-120, 165] and one TEA study[164] including 12 169 patients, evaluated the influence of obesity on the incidence of blood transfusion (Table 3.3). One of the five studies could not be included in meta-analysis as it reported the units of blood transfused for each BMI group without specifying the number of patients that required a blood transfusion.[165] Due to this, and variations in BMI groupings, a total of 11 937 patients contributed to the analysis.

A meta-analysis using a fixed-effects model suggested that obese patients receiving TSA, RTSA and TEA had 1.47 times greater odds of blood transfusion compared to non-obese patients (Figure 3.4: Panel A). However, substantial statistical heterogeneity (I^2, 95%) was observed between studies. A subsequent meta-analysis using a random-effects model was performed, indicating no difference in odds of blood transfusion between obese versus non-obese patients, however high statistical heterogeneity was once again observed (Figure 3.4: Panel B). The high variability between studies may be attributable to differences across shoulder and elbow arthroplasty cohorts. The results indicate that obese TEA patients are more susceptible to blood loss, however this

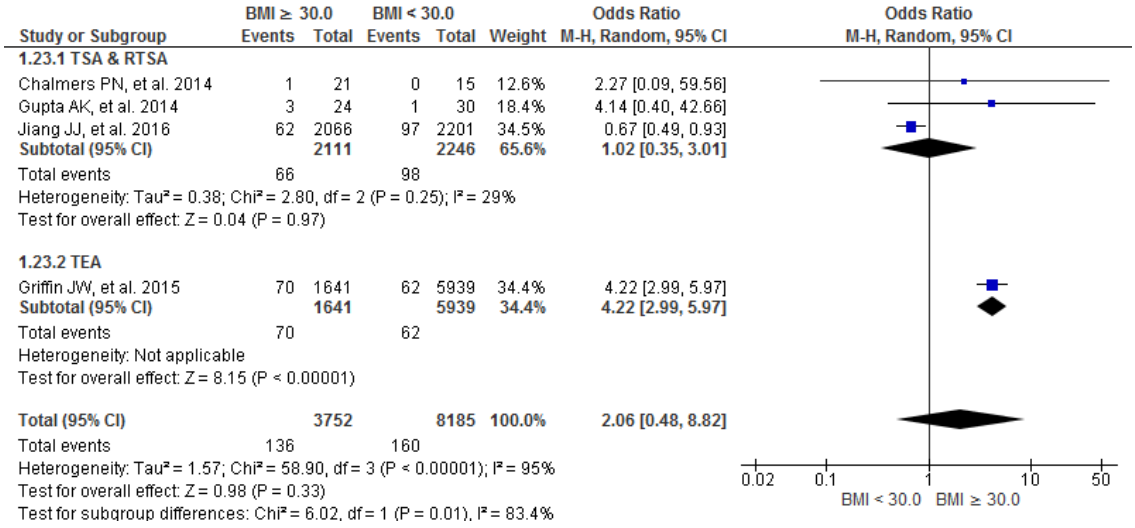
would not be expected clinically. Due to the heterogeneity observed, a sensitivity analysis was conducted that excluded the TEA study and employed different statistical models.[164] An analysis using a fixed-effects model revealed greater odds of blood transfusion in non-obese compared to obese TSA/RTSA patients (OR = 0.71; 95% CI [0.52, 0.97]). Employing a random-effects analysis revealed no difference in odds of blood transfusion in obese versus non-obese TSA/RTSA patients (OR = 1.02; 95% CI [0.35, 3.01]). Both analyses demonstrated low statistical heterogeneity (I^2, 29%), which was not statistically significant (χ^2 = 2.08, P = 0.25). Overall, the heterogeneity of meta-analyses with TSA/RTSA and TEA studies was too high to draw meaningful conclusions. A sensitivity analysis that only assessed TSA/RTSA patients revealed that the odds of blood transfusion was 29% less in obese compared to non-obese patients.

A meta-analysis using a fixed-effects model shows that the odds of blood transfusion was 0.46 in obese class 2 TSA/RTSA patients compared to patients with a BMI in the normal range (Figure 3.4: Panel C). Conversely, when a random-effects model was used, no statistically significant increase in odds were observed (Figure 3.4: Panel D). The I^2 statistic suggested moderate heterogeneity between studies (I^2, 59%), however this was not statistically significant (χ^2 = 4.83, P = 0.09).

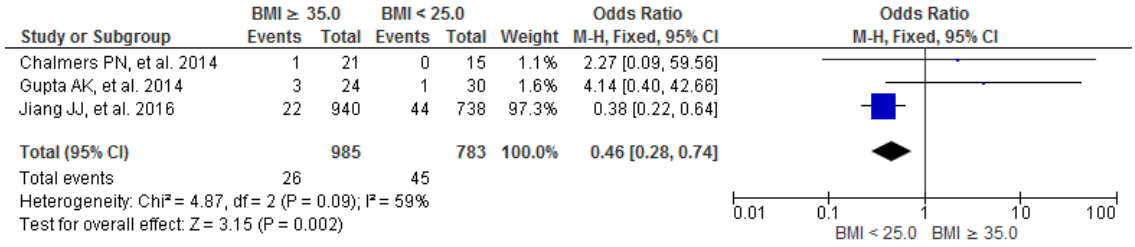
Panel A



Panel B



Panel C



Panel D

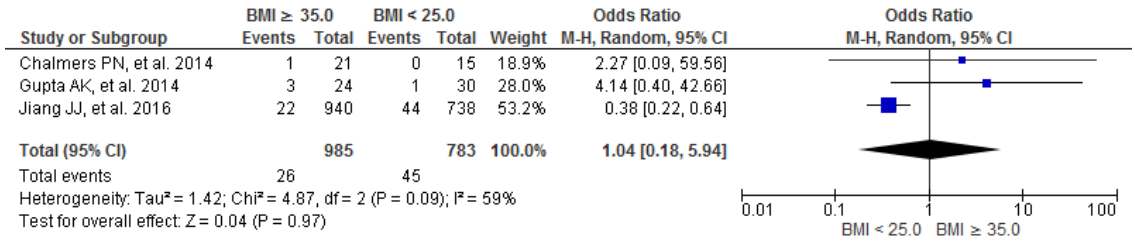


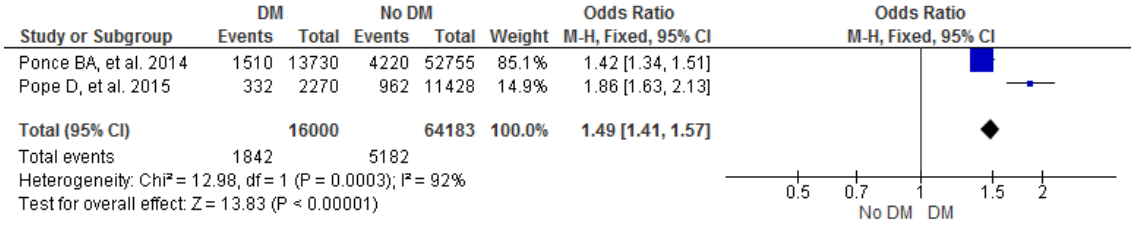
Figure 3.4. *Forest plot of the odds of blood transfusion in various BMI groups. Subgroup analysis was conducted for arthroplasty joint type (total shoulder arthroplasty [TSA] and reverse total shoulder arthroplasty [RTSA], or total elbow arthroplasty [TEA]) (M-H: Mantel-Haenszel; CI: confidence interval; df: degrees of freedom; IV:* inverse variance*).*
Panel A: Fixed-effects model; obese (BMI ≥ 30.0) versus non-obese (BMI < 30.0) TSA/RTSA and TEA patients.
Panel B: Random-effects model; obese (BMI ≥ 30.0) versus non-obese (BMI < 30.0) TSA/RTSA and TEA patients.
Panel C: Fixed-effects model; obese class 2 (BMI ≥ 35.0) versus normal range (BMI < 25.0) TSA/RTSA patients.
Panel D: Random-effects model; obese class 2 (BMI ≥ 35.0) versus normal range (BMI < 25.0) TSA/RTSA patients.

Diabetes mellitus

Two studies investigated the impact of diabetes mellitus on blood transfusion: the first was a TSA/RTSA study that included a subset of HA patients (< 30.0% of the total cohort); [27] the second a TEA study.[160] Both retrospective cohort studies gathered data from the NIS, and reported on a total of 80 183 TSA/RTSA/HA and TEA patients (Table 3.3).

Results of meta-analysis suggest that diabetic upper limb arthroplasty patients had statistically significant increased odds of blood transfusion compared to non-diabetic patients (OR = 1.49; 95% CI [1.41, 1.57]) (Figure 3.5: Panel A). Considerable statistical heterogeneity between studies was observed (I^2, 92%), which may be because each study reported on arthroplasty procedures of different joints. A subsequent meta-analysis using a random-effects model was performed as a sensitivity analysis, however high statistical heterogeneity was once again observed (Figure 3.5: Panel B). Despite statistically significant heterogenity ($\chi^2 = 12.98$, P = 0.0003), both studies provide compelling evidence that diabetics are at greater risk for blood transfusion.

Panel A



Panel B

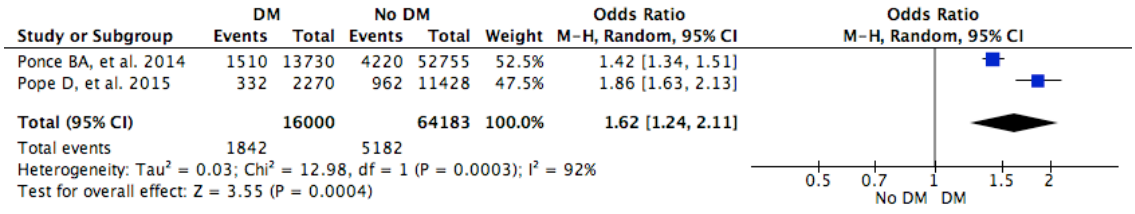


Figure 3.5. *Forest plot of the odds of blood transfusion in diabetic versus non-diabetic upper limb arthroplasty patients. Follow-up period: inpatient duration. (M-H: Mantel-Haenszel; CI: confidence interval; df: degrees of freedom). Panel A: Fixed-effects model; Panel B: Random-effects model.*

3.5.4 Infection

Obesity

Ten TSA/RTSA studies[117-120, 130, 159, 163, 165, 167, 168] and one TEA study[164] evaluated the influence of obesity on infection. Infection was further classified by studies as follows: superficial infection,[118, 120, 130] deep infection,[118, 165] superficial and deep infection combined,[119, 163] periprosthetic infection[134, 167] or no further specification.[117, 159, 164] Postoperative follow-up duration varied in each study and included the inpatient duration,[117] up to 30 days,[118] within 1 year,[159] minimum 1 year,[167] up to 90 days,[164] a minimum 90 days,[119, 120] up to 2 years,[165] a minimum 2 years,[130, 163] and a mean follow-up of 7 years (SD = 6 years)[134] (Table 3.3). Combined, the studies reported on a total of 190 894 TSA/RTSA and TEA patients. However, it should be noted that two[119, 120] of the 11 studies did not contribute to the calculated effect estimate as they reported no infection events for both obese and non-obese groups (Figure 3.6; Panel A). Consequently, this and the variations in BMI groupings, resulted in data from a total of 190 648 patients being included in the data synthesis and contributing to the effect estimate.

Meta-analysis revealed that the odds of infection were 2.37 times greater in obese compared to non-obese TSA, RTSA and TEA patients (Figure 3.6: Panel A). Subgroup analysis indicated a small difference between the overall effect size when compared to shoulder arthroplasty procedures (TSA/RTSA) alone (OR = 1.94; 95% CI [1.04, 3.62]). This suggests that TEA patients may be at slightly greater odds of infection than shoulder arthroplasty patients, however conclusions are limited as only one TEA study was analysed. Heterogeneity between studies was substantial (I^2, 61%) and statistically significant (χ^2 = 20.39, P = 0.009), also limiting plausible conclusions. The heterogeneity observed could be due to the inclusion of studies that reported on different arthroplasty joints, types of infection, study sites, and had differing orthopaedic surgeons.

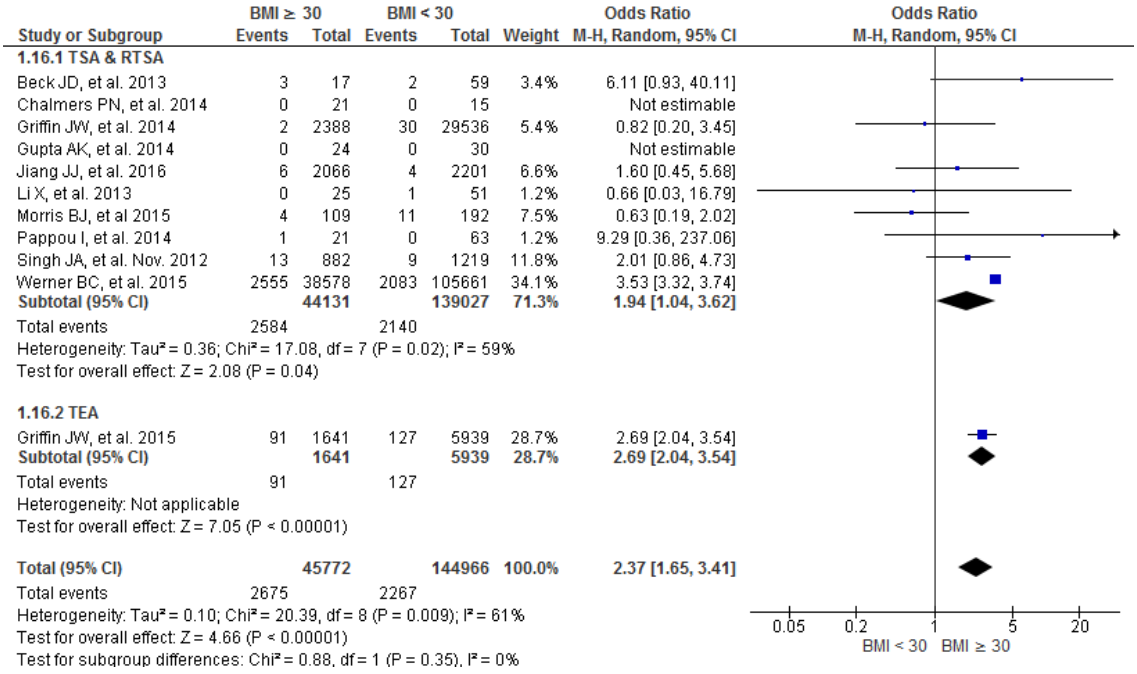
Type of infection, specifically periprosthetic infection, was further considered. A second meta-analysis was conducted using the more appropriate fixed-effects statistical model, given only two studies were included in the analysis (refer Section 2.6). Results identified no statistically significant increase in odds of periprosthetic infection between obese versus non-obese TSA/RTSA patients (OR = 1.31; 95% CI [0.68, 2.55]) (Figure 3.6: Panel B). Statistical heterogeneity between studies was substantial (I^2, 59%), however not statistically significant (χ^2 = 2.45, P = 0.12). Both studies assessed shoulder arthroplasty patients and were of similar methodological quality (Table 3.2).

Both studies identified confounding variables across BMI groups, which may account for the heterogeneity observed in this analysis.

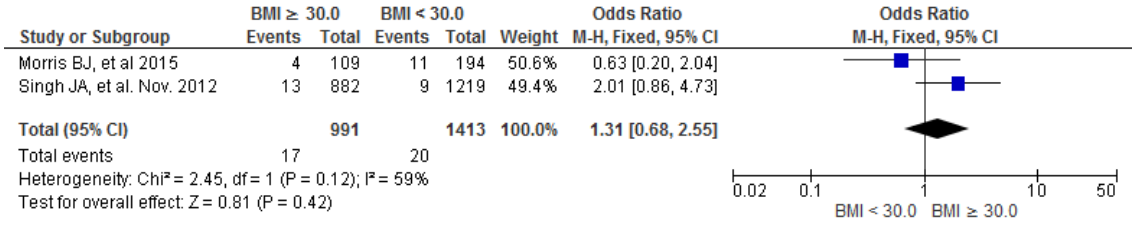
Obese shoulder arthroplasty patients were not at statistically increased odds of infection, whether that be any infection, or specifically periprosthetic infection (OR = 1.11; 95% CI [0.50, 2.50]), when compared to patients with a BMI in the normal range (OR = 1.50; 95% CI [0.74, 3.05]) (Figure 3.6: Panel C). Statistical heterogeneity between studies was low (I^2, 25%), and not statistically significant ($\chi^2 = 4.02$, P = 0.26).

A meta-analysis using a fixed-effects model revealed that morbidly obese TSA, RTSA and TEA patients had 5.04 times increased odds of infection compared to non-obese patients. Moderate statistical heterogeneity was observed between studies; however, it was not statistically significant. Subgroup analysis indicated a minimal difference between the overall effect size compared to shoulder arthroplasty procedures (TSA and RTSA) alone (Figure 3.6: Panel D).

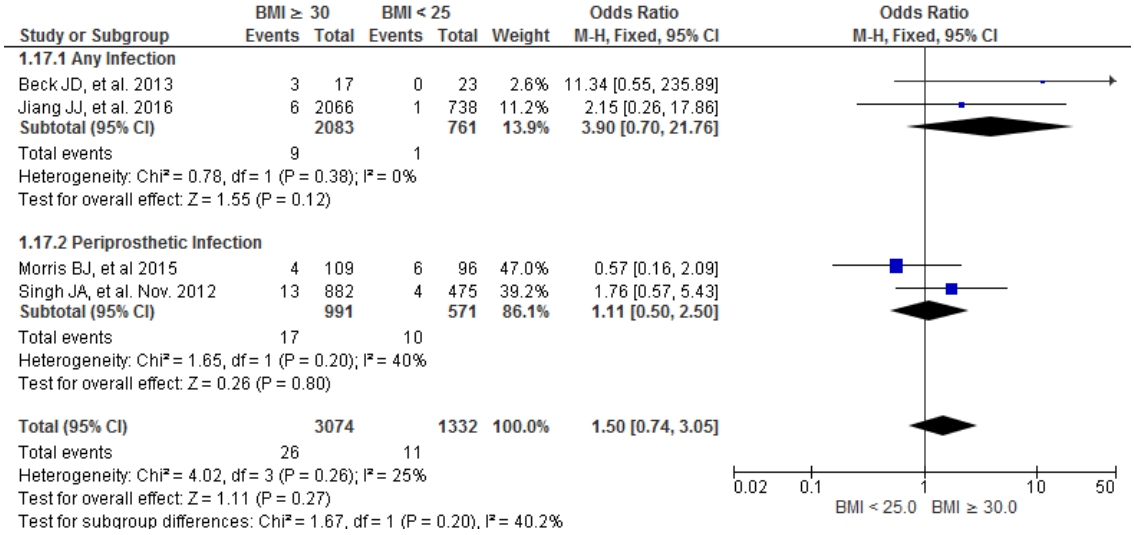
Panel A



Panel B



Panel C



Panel D

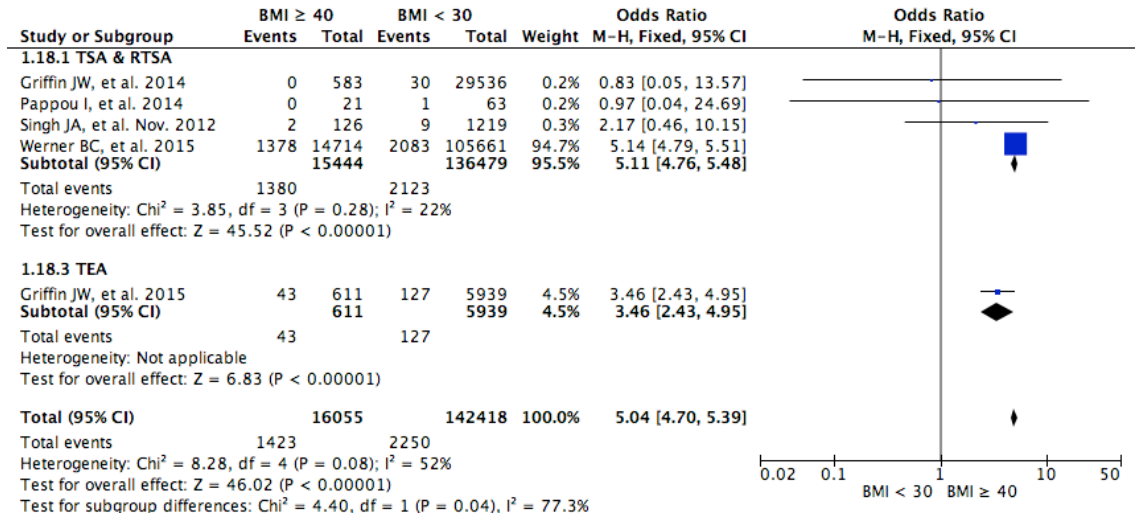


Figure 3.6. *Forest plots of the odds of infection in various BMI groups. Follow-up periods: inpatient duration, up to 30 days, within 1 year, minimum 1 year, up to 90 days, minimum 90 days, up to 2 years, minimum 2 years, and a mean follow-up of 7 years (SD = 6 years). (M-H: Mantel-Haenszel; CI: confidence interval; df: degrees of freedom).*

Panel A: Forest plot of the odds of infection in obese (BMI ≥ 30.0) versus non-obese (BMI < 30.0) upper limb arthroplasty patients. Subgroup analysis was conducted for periprosthetic infection, and arthroplasty joint type (total shoulder arthroplasty [TSA] and reverse total shoulder arthroplasty [RTSA], or total elbow arthroplasty [TEA]) (random-effects model).

Panel B: Forest plot of the odds of periprosthetic infection in obese (BMI ≥ 30.0) versus non-obese (BMI < 30.0) TSA/RTSA patients.

Panel C: Forest plot of the risk of infection in obese (BMI ≥ 30.0) versus normal (BMI < 25.0) TSA/RTSA patients. Subgroup analysis was conducted for periprosthetic infection.

Panel D: Fixed-effects model: morbidly obese (BMI ≥ 40.0) versus non-obese (BMI < 30.0) TSA/RTSA and TEA patients. Subgroup analysis was conducted for arthroplasty joint type (TSA and RTSA, or TEA).

Diabetes mellitus

Three TSA/RTSA studies[133, 134, 167] and one TEA study[160] investigated the impact of diabetes mellitus on infection. One study could not be used in the analysis due to insufficient data, however suggested diabetes mellitus did not impact on odds of infection.[167]

The remaining studies were combined in a statistical meta-analysis, which revealed no effect due to the exposure. However, analysis indicated substantial heterogeneity (I^2, 65%), limiting plausible inference. The results of the subgroup analysis presented in Figure 3.7 indicate that the heterogeneity observed was due to combining studies that reported on different arthroplasty joints.

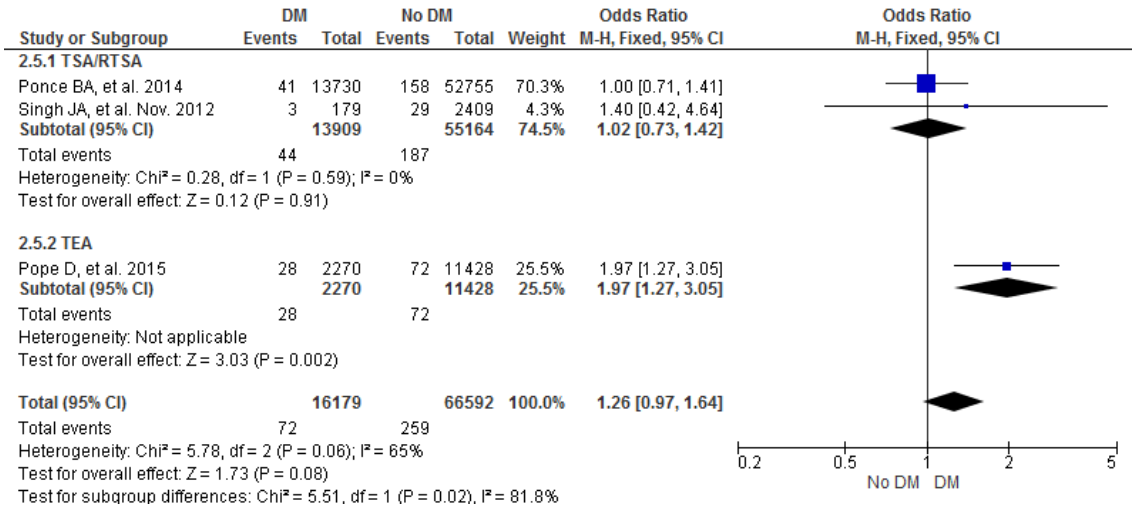


Figure 3.7 *Forest plot of the odds of infection in diabetic versus non-diabetic patients. Follow-up period: inpatient duration and a mean follow-up of 7 years (SD = 6 years). (M-H: Mantel-Haenszel; CI: confidence interval; df: degrees of freedom).*

3.5.5 Urinary tract infection

Obesity

One case-control study[130] and one retrospective cohort study[118] evaluated the influence of obesity on UTI. The studies had a combined sample size of 4351 TSA/RTSA patients, with follow-up periods of up to 30 days[118] and a minimum of 2 years[130] (Table 3.3). No statistically significant difference in odds of UTI was identified between obese compared to non-obese TSA/RTSA patients. Furthermore, no statistical heterogeneity (I^2, 0%) was observed despite the combining of

studies with differing study designs, study sites and orthopaedic surgeons (Figure 3.8.); this however, is expected given the large variance in the study by Pappou and others.[130]

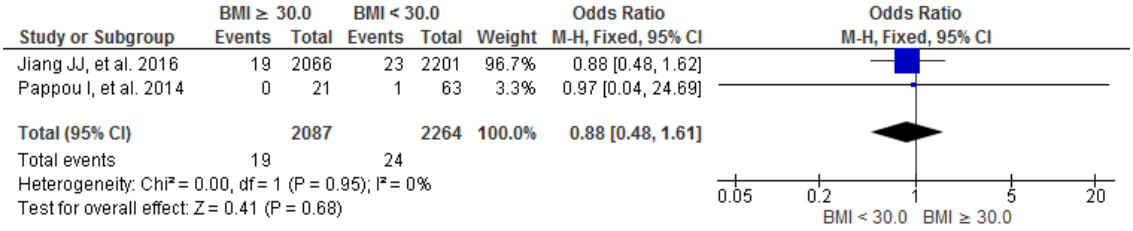


Figure 3.8. *Forest plot of the odds of urinary tract infection in obese (BMI ≥ 30.0) versus non-obese (BMI < 30.0) total shoulder arthroplasty and reverse total shoulder arthroplatsy patients. Follow-up period: up to 30 days and a minimum of 2 years. (M-H: Mantel-Haenszel; CI: confidence interval; df: degrees of freedom).*

Diabetes mellitus

Of the eight studies that addressed diabetes mellitus, only one TEA study[160] investigated the impact of this comorbidity on UTI. Pope et al.[160] found that diabetic patients had significantly higher rates of UTI than non-diabetic patients (6.7% versus 3.4%; P < .0001) during the inpatient follow-up period.

3.5.6 Pneumonia

Obesity

Of the 15 studies that evaluated obesity on arthroplasty outcomes, one TSA/RTSA study[118] investigated the impact of this comorbidity on pneumonia. Jiang et al.[118] used a follow-up period of up to 30-days post-surgery, and found no statistically significant difference between BMI groups (18.5-25; 25-30; 30-35; >35) on complications of pneumonia.

Diabetes mellitus

One TSA/RTSA/HA study[133] and one TEA study[160] investigated the impact of diabetes mellitus on pneumonia. Both studies gathered data from the NIS, and consequently, reported risk of pneumonia for the inpatient follow-up period. Combined, the studies reported on a total of 80 183 TSA/RTSA and TEA patients.

Meta-analysis revealed that diabetic TSA, RTSA and TEA patients had 1.38 times greater odds of pneumonia compared to non-diabetic patients (Figure 3.9.). No statistical heterogeneity was observed despite the two included studies reporting on arthroplasty procedures of different joints (shoulder and elbow).

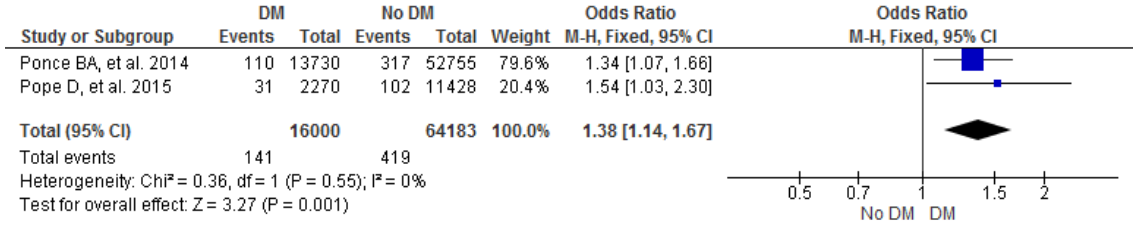


Figure 3.9. *Forest plot of the odds of pnemonia in diabetic versus non-diabetic total shoulder arthroplasty, reverse total shoulder arthroplasty and total elbow arthroplasty patients. Follow-up period: inpatient duration. (M-H: Mantel-Haenszel; CI: confidence interval; df: degrees of freedom).*

3.5.7 Venous thromboembolism

Obesity

Three TSA/RTSA studies[117, 118, 159] and two TEA studies[162, 164] evaluated the influence of obesity on VTE. The VTE outcome reflects data from studies that reported a DVT and/or PE. Combined, the studies reported on a total of 188 733 TSA/RTSA and TEA patients (Table 3.3). Postoperative follow-up included the inpatient duration,[117] up to 30 days,[118] up to 90 days,[159, 164] and a median follow-up duration of 5.8 years (range: 0 – 25 years).[162]

The present analysis for the VTE outcome involved combining the events of DVT and PE. A limitation of the meta-analyses conducted for this outcome is an overestimation of the occurance of VTE for one included study.[118] As Jiang et al.[118] reported DVT and PE events individually, it cannot be determined from the information provided whether there was an overlap in individuals that experienced both a DVT and PE, potentially resulting in the count of a VTE occuring more than once in the same individual within the study cohort.

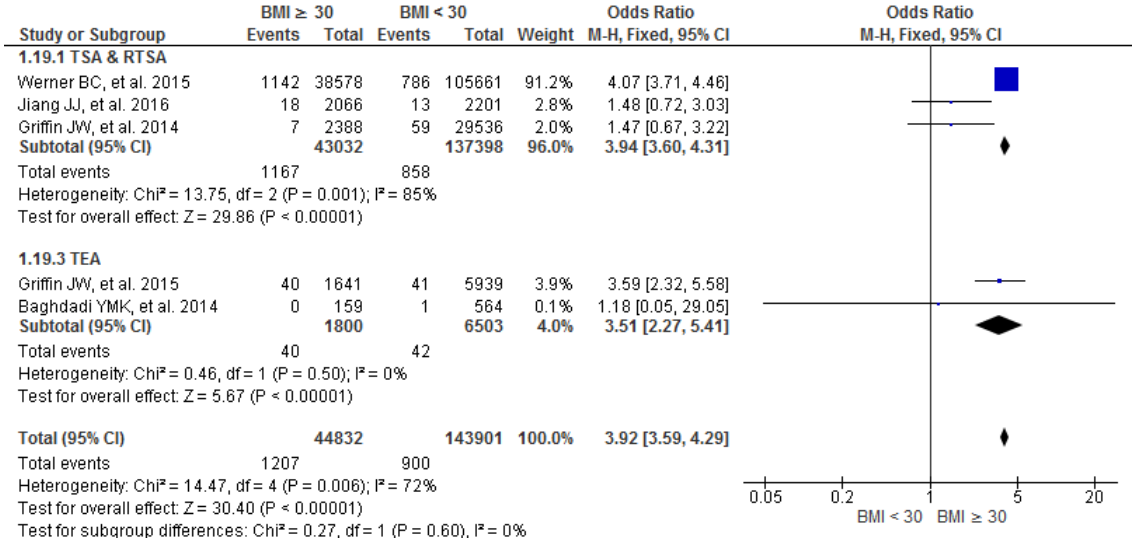
A meta-analysis using a fixed-effects model revealed that the odds of VTE were 3.92 times greater in obese compared to non-obese TSA, RTSA and TEA patients (Figure 3.10: Panel A). Subgroup

analysis identified a negligible difference between the overall effect size compared to the one TEA study alone (OR = 3.51; 95% CI [2.27, 5.41]). As the meta-analysis was heavily weighted with the findings from Werner et al.,[159] a sensitivity analysis was required. Findings were similar, with the odds of VTE 2.40 times greater in obese compared to non-obese patients (95% CI [1.72, 3.36]). Although not statistically significant (χ^2 = 6.69, P = 0.08), substantial heterogeneity was identified between studies, limiting conclusions that can be drawn (I^2, 72%). Consequently, a meta-analysis using a random-effects model was conducted as a sensitivity analysis. Results were consistent, revealing 2.64 times greater odds of VTE in obese compared to non-obese patients (Figure 3.10: Panel B). The heterogeneity observed may be due to a range of factors including combining studies that reported on different arthroplasty joints, types of VTE, study sites, and had differing orthopaedic surgeons.

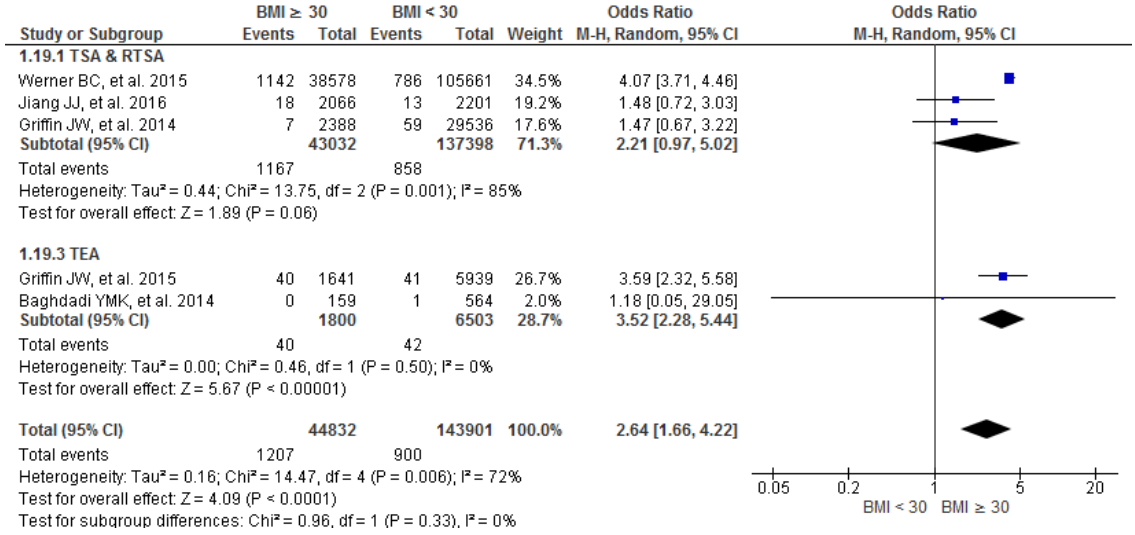
Morbidly obese TSA, RTSA and TEA patients had 5.46 times greater odds of VTE compared to non-obese patients (Figure 3.10: Panel C). Once again, the analysis was heavily weighted on the findings from Werner et al.,[159] however a sensitivity analysis presented similar results (OR = 3.35; 95% CI [1.97, 5.71]). The I^2 statistic identified moderate heterogeneity, however this was not statistically significant (I^2, 55%). This may be due to a range of factors including combining studies that reported on different arthroplasty joints, types of VTE, study sites, and had differing orthopaedic surgeons.

Overall, results identified increased odds of VTE in patients with increasing BMI from ≥ 30.0 (OR = 3.92; 95% CI [3.59, 4.28]) to ≥ 40.0 (OR = 5.46; 95% CI [4.91, 6.07]), compared to non-obese patients.

Panel A



Panel B



Panel C

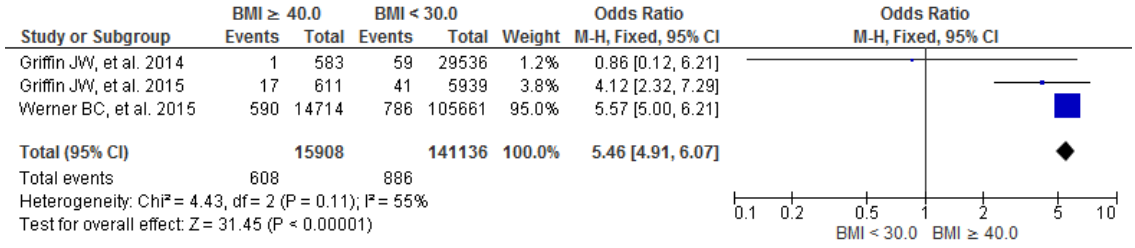


Figure 3.10. *Forest plot of the odds of venous thromboembolism (VTE) in various BMI groups. Follow-up periods: inpatient duration, up to 30 days, up to 90 days and a median follow-up duration of 5.8 years (range: 0 – 25 years). (M-H: Mantel-Haenszel; CI: confidence interval; df: degrees of freedom; IV: inverse variance).*

Panel A: Fixed-effects model: obese (BMI ≥ 30.0) versus non-obese (BMI < 30.0) total shoulder arthroplasty (TSA), reverse total shoulder arthroplasty (RTSA) and total elbow arthroplasty (TEA) patients. Subgroup analysis was conducted for arthroplasty joint type (TSA/RTSA, or TEA).

Panel B: Random-effects model: obese (BMI ≥ 30.0) versus non-obese (BMI < 30.0) TSA, RTSA and TEA patients. Subgroup analysis was conducted for arthroplasty joint type (TSA/RTSA, or TEA).
Panel C: Morbidly obese (BMI ≥ 40.0) versus non-obese (BMI < 30.0) TSA/RTSA and TEA patients.

Diabetes mellitus and venous thromboembolism (pulmonary embolism only)

One TSA/RTSA study[133] and one TEA study[160], with a combined sample size of 69 669 patients, evaluated the impact of diabetes mellitus on VTE, specifically PE. An additional study by Day et al.[142] also evaluated PE and reported an adjusted hazard ratio of 1.01 (0.77, 1.32) (Table 3.3). Risk estimates from three studies were combined in meta-analysis (refer Section 2.6), which revealed no effect due to exposure (Figure 3.11). Despite combining studies that assessed different joint procedures (TEA, or TSA/RTSA/HA), only moderate statistical heterogeneity was observed and was not statistically significant (Figure 3.11). This was expected given the large variance in the analysed studies.

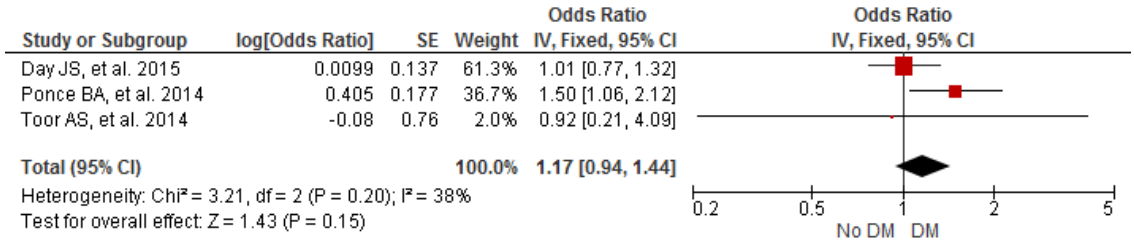


Figure 3.11. *Forest plot of the odds of pulmonary embolism in diabetic versus non-diabetic total shoulder arthroplasty, reverse total shoulder arthroplasty and total elbow arthroplasty patients. Follow-up period: inpatient duration and up to 6 months. (IV: inverse variance; CI: confidence interval; df: degrees of freedom).*

3.5.8 Dislocation

Obesity

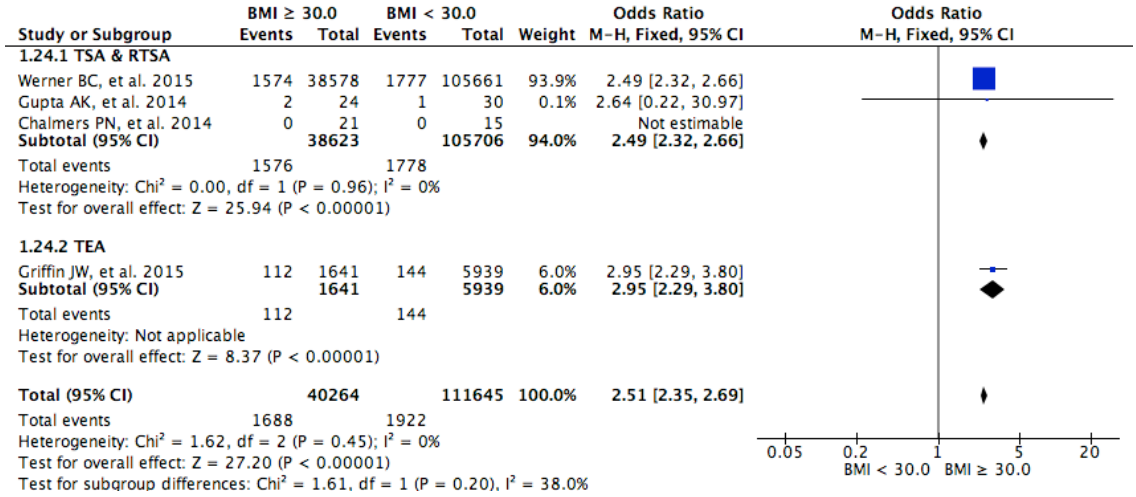
Three TSA/RTSA studies[119, 120, 159] and one TEA study[164] evaluated the influence of obesity on joint dislocation. The studies had a combined sample size of 152 065 patients (Table 3.3). One[119] of the four studies did not contribute to the effect estimate as it reported no dislocations for both obese and non-obese BMI groups. Postoperative follow-up duration varied with each study and included either a minimum of 90 days[120] or up to 1 year.[159, 164]

Obese patients had statistically significant greater odds of dislocation compared to non-obese patients. The effect estimate indicated that the odds of postoperative dislocation were 2.51 times (95% CI [2.35, 2.69]) greater in obese, compared to non-obese patients. Subgroup analysis identified a negligible difference between the effect size of shoulder and elbow arthroplasty studies combined (OR = 2.51; 95% CI [2.35, 2.69]) compared to shoulder arthroplasty procedures (TSA and RTSA) alone (OR = 2.49; 95% CI [2.32, 2.66]) (Figure 3.12: Panel A). This indicates that the type of joint arthroplasty procedure in the upper limb did not influence risk of dislocation. No statistically significant heterogeneity was observed (χ^2 = 1.62, P = 0.45) and I^2 identified no statistical heterogeneity between the studies, despite the inclusion of a small number of studies that each reported on different arthroplasty procedures (shoulder and elbow).

Morbidly obese patients had statistically significant greater odds of dislocation compared to non-obese patients (Figure 3.12: Panel B). The effect estimate indicated that the odds of postoperative dislocation were 2.96 times (95% CI [2.72, 3.23]) greater in morbidly obese compared to non-obese patients (Figure 3.12: Panel B). The I^2 revealed no statistical heterogeneity between studies, despite the inclusion of only two studies that each reported on different arthroplasty procedures (shoulder and elbow).

In summary, results revealed increased odds of dislocation in patients with increasing BMI from ≥ 30.0 (OR = 2.51; 95% CI [2.35, 2.69]) to > 40.0 (OR = 2.96; 95% CI [2.26, 3.23]), compared to non-obese patients.

Panel A



Panel B

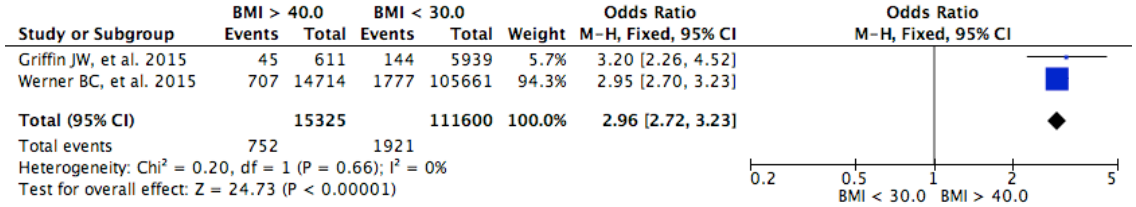


Figure 3.12. *Forest plots of the odds of dislocation in various BMI groups. Follow-up periods:* minimum 90 days and up to 1 year. *(M-H: Mantel-Haenszel; CI: confidence interval; df: degrees of freedom).*

Panel A: Obese (BMI ≥ 30.0) versus non-obese (BMI < 30.0). Subgroup analysis was conducted for arthroplasty joint type (total shoulder arthroplasty [TSA] and reverse total shoulder arthroplasty [RTSA], or total elbow arthroplasty [TEA]).

Panel B: Morbidly obese (BMI > 40.0) versus non-obese (BMI < 30.0) TSA/RTSA and TEA patients.

Diabetes mellitus

No studies investigated the impact of diabetes mellitus on dislocation.

3.5.9 Fracture

Obesity

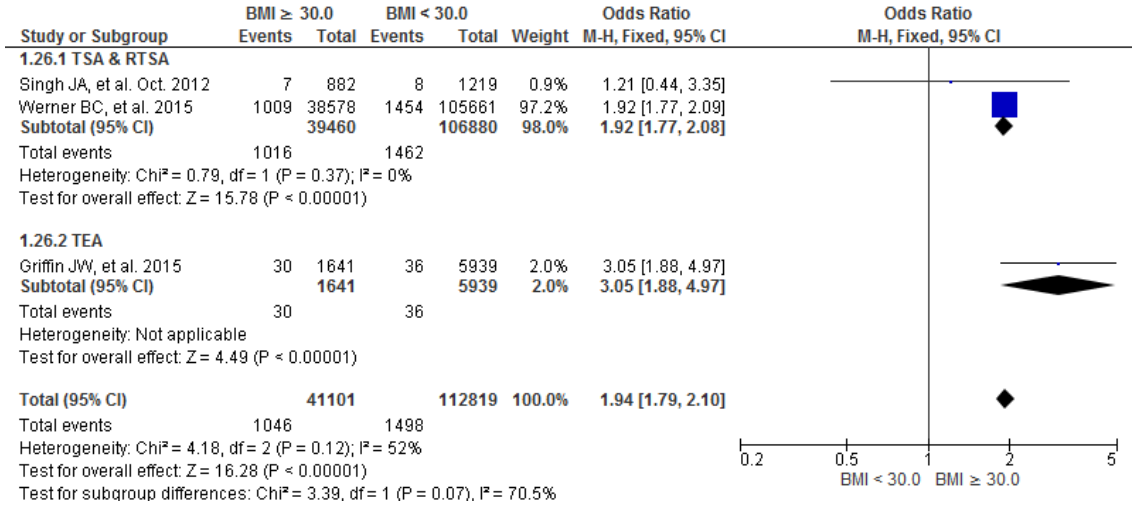
Three TSA/RTSA studies[130, 159, 168] and one TEA study[164] evaluated the influence of obesity on fracture and together had a combined sample size of 154 004 patients. Three studies reported on periprosthetic fracture[159, 164, 168] and one study on acromial fracture[130] (Table 3.3). Postoperative

follow-up duration varied in each study and included up to 1 year,[159, 164] a minimum 2 years[130] and a mean follow-up of 7 years (range: 1 day – 31 years).[168]

Analysis revealed that obese TSA, RTSA and TEA patients had 1.94 times greater odds of periprosthetic fracture than non-obese patients (Figure 3.13: Panel A). Subgroup analysis identified a difference between the overall effect estimate compared to TEA alone (OR = 3.05; 95% CI [1.88, 4.97]). This included study[164] suggested that obese TEA patients may be at an increased risk of periprosthetic fracture compared to obese TSA/RTSA patients (Figure 3.13: Panel A). As the meta-analysis was heavily weighted with the findings from Werner et al.,[159] a sensitivity analysis was required. Findings were similar, with the odds of periprosthetic fracture 2.49 times (95% CI [1.60, 3.88]) greater in obese compared to non-obese patients. The I^2 statistic for the meta-analysis identified moderate to substantial heterogeneity (I^2, 52%), however this was not statistically significant ($\chi^2 = 4.18$, P = 0.12). Once again, this may be due to combining studies that reported on different arthroplasty joints across various study sites and had differing orthopaedic surgeons.

Furthermore, one study reported the incidence of acromial fracture between morbidly obese and non-obese RTSA patients, who were followed-up for a minimum of 2 years.[130] This study was combined with studies that reported on periprosthetic fracture to provide an overall analysis on the odds for fracture. Results revealed that morbidly obese patients had 2.01 times greater odds of fracture compared to non-obese patients (OR = 2.01; 95% CI [1.80, 2.25]) (Figure 3.13: Panel B). The I^2 statistic identified moderate heterogeneity (I^2, 42%), however this was not statistically significant ($\chi^2 = 5.12$, P = 0.16). Once again, analysis was heavily weighted on the findings from Werner et al.,[159] and a sensitivity analysis presented even greater odds of fracture for morbidly obese compared to non-obese patients (OR = 3.74; 95% CI [2.14, 6.55]).

Panel A



Panel B

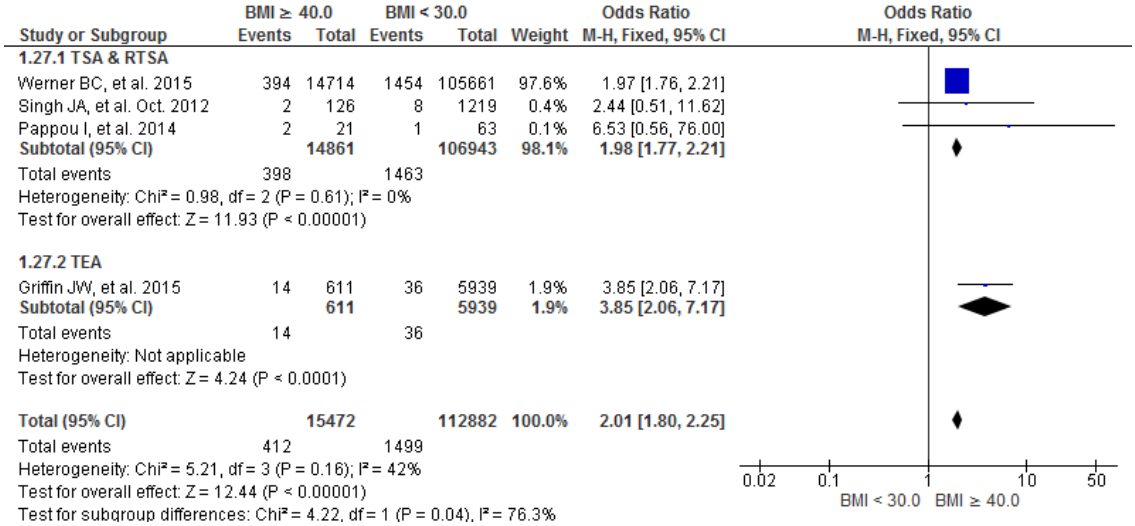


Figure 3.13. *Forest plot of the odds of fracture (acromial or periprosthetic) in various BMI groupings. Subgroup analysis was conducted for arthroplasty joint type. Follow-up periods: up to 1 year, minimum 2 years and a mean follow-up of 7 years (range: 1 day – 31 years) (M-H: Mantel-Haenszel; CI: confidence interval; df: degrees of freedom).*

Panel A: Periprosthetic fracture in obese (BMI ≥ 30.0) versus non-obese (BMI < 30.0) total shoulder arthroplasty (TSA), reverse total shoulder arthroplasty (RTSA) and total elbow arthroplasty (TEA) patients.

Panel B: Fracture (acromial or periprosthetic) in morbidly obese (BMI ≥ 40.0) versus non-obese (BMI < 30.0) TSA/RTSA and TEA patients.

Diabetes mellitus

No studies investigated the impact of diabetes mellitus on fracture.

3.5.10 Pain

Obesity

Three TSA/RTSA studies[130, 163, 165] investigated the influence of obesity on pain. All three studies measured pain using the Visual Analogue Scale for Pain (VAS – P), which is a horizontal line, 10 centimetres in length,[165] and anchored with two verbal descriptors (0 = *'no pain at all'* to 10 = '*pain as bad as it can be',* or similar).[130] Li et al.[165] reported the mean pain scores for preoperative and postoperative time points, however did not report a measure of variance (i.e. standard deviation). Consequently, this data could not be included in the analysis. The retrospective cohort study[163] and case-control[130] reported on a total of 160 TSA/RTSA patients, however only 124 patients were combined in statistical meta-analysis due to variation in BMI groupings. Both studies reported a minimum 2-year follow-up period.

Obese RTSA patients had a statistically significant increase in pain compared to non-obese RTSA patients. The WMD was 1.13 (95% CI [0.21, 2.06]), indicating patients with a BMI ≥ 30.0 experienced slightly greater postoperative pain scores than patients with a BMI < 30.0 (Figure 3.14). No statistical heterogeneity was found, despite the small number of studies included and the variation in study designs. Figure 3.14 shows that the VAS – P mean range was 1.3 to 3, indicating that both groups experienced no pain,[169] or mild pain. Recent research has suggested that a minimum clinically important difference (MCID) for the VAS – P in shoulder arthroplasty patients is 1.4,[170] indicating that although a WMD on the VAS – P was observed between obese and non-obese, it was not clinically relevant.

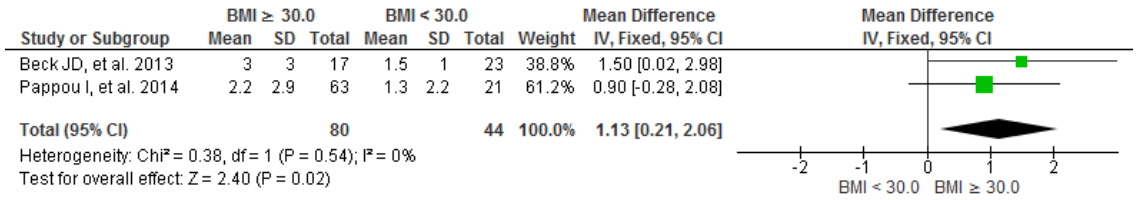


Figure 3.14. *Weighted mean difference in postoperative pain scores between obese (BMI ≥ 30.0) versus non-obese (BMI < 30.0) reverse total shoulder arthroplasty patients. Postoperative pain was measured using the Visual Analogue Scale for Pain (0 to 10 scale, 0 = no pain) Follow-up period: minimum 2 years. (IV: inverse variance; CI: confidence interval; df: degrees of freedom; Min: minutes).*

Diabetes mellitus

No studies investigated the impact of diabetes mellitus on pain.

3.5.11 Function

Obesity

Four TSA/RTSA studies[130, 163, 165, 166] investigated the influence of obesity on function. Each study measured function using various methods including patient or clinician reported scoring systems, and ROM measures such as forward flexion, abduction, external rotation and/or internal rotation (Table 3.3).

3.5.11.1 Functional measure: American Shoulder and Elbow Surgeons Questionnaire (ASES)

Three studies[130, 165, 166] used the American Shoulder and Elbow Surgeons Questionnaire (ASES) at follow-up time points of up to 2 years,[165] and a minimum of 2 years post-surgery.[130, 166] The ASES is a validated questionnaire that provides a standardised measure of shoulder function.[171] It was developed by Richards and others[171] in 1994, and has been described as a baseline measure of shoulder function applicable to all patients, regardless of diagnosis. The score comprises a patient self-evaluation section measuring pain, instability and activities of daily living, in addition to a physician functional assessment of ROM, signs, strength and instability.[171] Only the patient self-evaluation contributes to the total ASES score. A previously published mean normative value for the ASES scoring system for individuals without shoulder disease is 92.2 (SD = 14.5)[172] and the MCID on the ASES self-report section is 6.4 ASES points.[173] The score is interpreted on a '*0 = worst* to *100 = best'* scale.[174] The three studies were combined in a statistical meta-analysis to determine the influence of BMI on the ASES functional score.

No statistically significant difference in ASES functional measure scores was found between obese and non-obese TSA/RTSA patients (Figure 3.15). Heterogeneity was not statistically significant (χ^2 = 5.14, P = 0.08), however the I^2 statistic identified substantial statistical heterogeneity between studies (I^2, 61%), limiting plausible conclusions. Postoperative ASES means ranged from 69 to 86 in obese patients, and from 78.2 to 84.3 in non-obese patients, with higher scores aligned with better self-reports of pain, instability and activities of daily living.

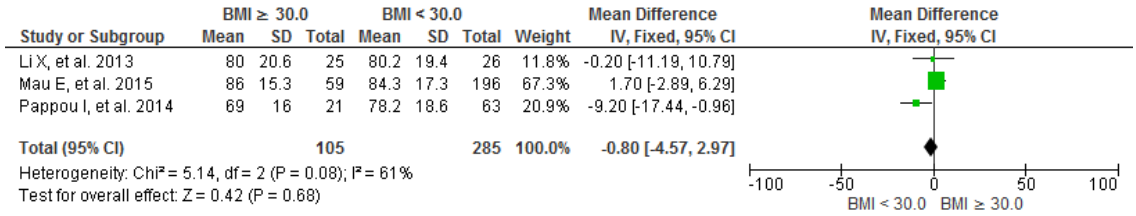


Figure 3.15. *Weighted mean difference in Americam Shoulder and Elbow Surgeons functional scores in obese (BMI ≥ 30.0) versus non-obese (BMI < 30.0) total shoulder arthroplasty and reverse total shoulder arthroplasty patients. (IV: inverse variance; CI: confidence interval; df: degrees of freedom).*

3.5.11.2 Functional measure: abduction range of motion

Three studies[130, 163, 166] reported ROM measurements for a follow-up time period of, at minimum, 2 years. Two studies[163, 166] indicated that ROM measurements were active movements, however this was not specified in the remaining study.[130] One study described obtaining active ROM data via goniometric measurement,[163] while the other study specified that external rotation measurements were taken with the arm at the patient's side.[166]

It should be noted that Mau et al.[166] reported TSA and RTSA data separately. As the RTSA subset constituted a greater proportion of the overall study sample, the data from the RTSA subset was calculated in the meta-analysis. No statistically significant WMD was observed in abduction ROM between obese and non-obese RTSA patients (Figure 3.16). Moderate statistical heterogeneity between studies was present (I^2, 53%), however this was not statistically significant ($\chi^2 = 4.21$, P = 0.12).

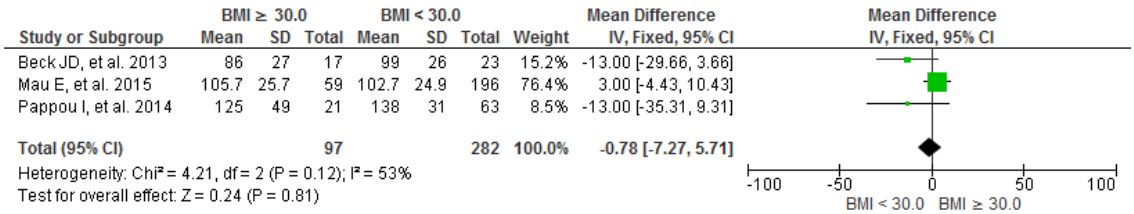


Figure 3.16. *Weighted mean difference in abduction between obese (BMI ≥ 30.0) versus non-obese (BMI < 30.0) reverse total shoulder arthroplasty patients. Follow-up period: minimum 2 years. (IV: inverse variance CI: confidence interval; df: degrees of freedom). Please note that studies by Mau et al.[166] and Beck et al.[163] defined range of motion meaurements as active movements.*

3.5.11.1 Functional measure: external rotation range of motion

Meta-analysis revealed no statistically significant difference in external rotation ROM between obese and non-obese RTSA patients (Figure 3.17). As expected, no statistical heterogeneity was observed (I^2, 0%) given the large variance in the analysed studies.

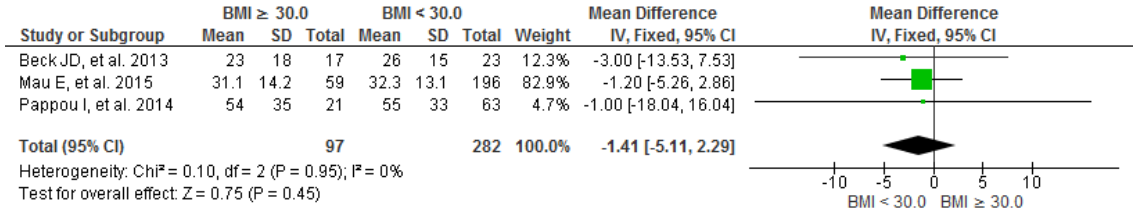


Figure 3.17. *Weighted mean difference in external rotation between obese (BMI ≥ 30.0) versus non-obese (BMI < 30.0) reverse total shoulder arthroplasty patients. Follow-up period: minimum 2 years. (IV: inverse variance; CI: confidence interval; df: degrees of freedom). Please note that studies by Mau et al.[166] and Beck et al.[163] defined range of motion meaurements as active movements.*

Diabetes mellitus

No studies investigated the impact of diabetes mellitus on function.

3.5.12 Quality of life

Obesity

Of the 15 studies that evaluated obesity on arthroplasty outcomes, only one TSA study[165] investigated the impact of this comorbidity on QoL. Li et al.[165] measured QoL using the Short Form-36 (SF – 36) Physical Component Summary (PCS) and the Mental Component Summary (MCS) at 2 years post-surgery. Each summary component was scored on a 0 to 100 point scale, with higher scores on the SF-36 indicating a more favourable health state, or better QoL.[175] Study authors found a significant difference in mean SF-36 PCS scores, with means of at 53.1, 39.8 and 40.7 reported for normal, overweight and obese patients, respectively (see Table 3.3 for SD). This indicates that patients with a BMI of < 25.0 had an improvement of 13.0, or 13.9 points greater than overweight and obese patients ($p < 0.05$).[165] The authors concluded that obese and overweight TSA patients failed to reach the amount of physical function improvement achieved by

normal BMI patients.[165] In addition, no statistically significant difference was reported on SF-36 MCS scores between the three BMI groups (< 25; 25 - 29.9; >30).[165]

Diabetes mellitus

No studies investigated the impact of diabetes mellitus on QoL.

3.5.13 Unscheduled return to theatre

Obesity

Three studies[118, 162, 165] reported on unscheduled return to theatre, with or without defining whether this was due to the need for revision joint replacement surgery or other causes. Studies that did report this information, found the cause for return to theatre included deep infection[165] and wound complications that required additional operation with no revison of prosthetic components.[162] Analysis in this section does not include studies that explicitly stated that the return to theatre was due to 'revision surgery', which is addressed subsequently in Section 3.5.14. Postoperative follow-up duration varied in each study and included up to 30 days,[118] up to 2 years,[165] and at a median of 5.8 years (range: 0 – 25 years).[162] A total of 5066 upper limb arthroplasty patients were included.

The odds of an unscheduled return to theatre were no different between obese and non-obese TSA, RTSA and TEA patients (OR = 0.74; 95% CI [0.44, 1.24]). Subgroup analysis identified a negligible difference between the overall effect estimate compared to shoulder arthroplasty procedures (TSA and RTSA) alone, indicating that the type of joint arthroplasty procedure in the upper limb did not influence the odds of return to theatre (Figure 3.17). No statistical heterogeneity was observed (I^2, 0%) despite combining studies that reported on arthroplasty procedures of different joints (shoulder and elbow) across various study sites and with differing orthopaedic surgeons; this however, was expected given the large variance in the study by Li et al.[165]

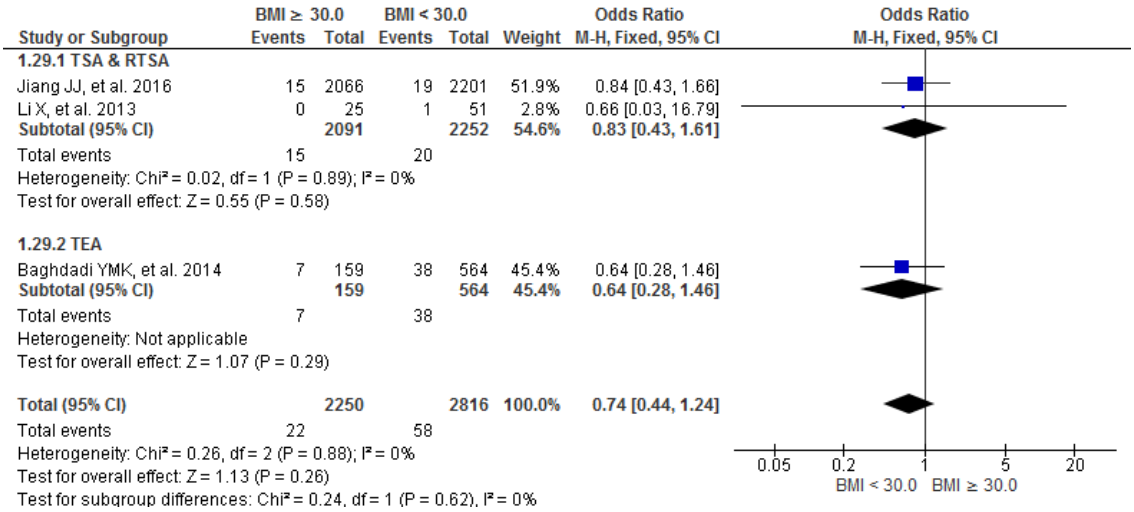


Figure 3.17. *Forest plot of the odds of unscheduled return to theatre in obese (BMI ≥ 30.0) versus non-obese (BMI < 30.0) total shoulder arthroplasty (TSA), reverse total shoulder arthroplasty (RTSA) and total elbow arthroplasty (TEA) patients. Subgroup analysis was conducted for arthroplasty joint type. Follow-up period: up to 30 days, up to 2 years and a median of 5.8 years (range: 0 – 25 years) (M-H: Mantel-Haenszel; CI: confidence interval; df: degrees of freedom).*

Diabetes mellitus

Of the eight studies that addressed diabetes mellitus, one TEA study[161] investigated the impact of this comorbidity on unscheduled return to theatre for irrigation and debridement. Toor et al.[161] found no statistically significant difference in irrigation and debridement occurrence between diabetic and non-diabetic TEA patients (OR = 0.98; 95% CI [0.41-2.33]).

3.5.14 Revision

Obesity

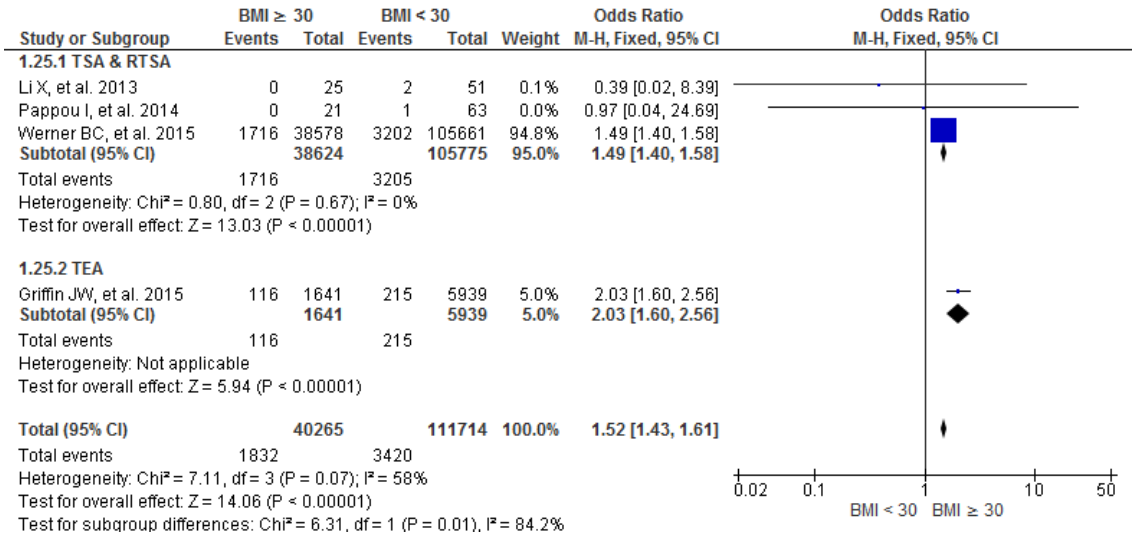
Four TSA/RTSA studies[130, 143, 159, 165] and two TEA studies[162, 164] evaluated the influence of obesity on need for revision surgery. One of the six studies could not be included in the meta-analysis as it did not report the number of revisions for the obese and non-obese groups, and alternatively, reported Kaplan-Meier survival estimates as well as adjusted hazard ratios.[162] A further study also reported a hazard ratio (HR = 1.01; 95% CI [0.99, 1.04]) revealing no association between risk of revision and each additional unit of BMI.[143]

The four remaining studies reported on a total of 151 979 TSA/RTSA and TEA patients (Table 3.3), and were combined in a statistical meta-analysis. Postoperative follow-up duration varied across studies and included up to 2 years,[164, 165] a minimum of 2 years[130] and up to 8 years.[159]

Analysis revealed that obese TSA, RTSA and TEA patients had 1.52 times greater odds of undergoing revision compared to non-obese patients at, up to 8 years post-surgery (Figure 3.18: Panel A). As this analysis was heavily weighted with the findings from Werner et al.,[159] a sensitivity analysis was required. Findings were similar, with the odds of revision 1.99 times greater in obese compared to non-obese patients (95% CI [1.58, 2.50]). Furthermore, morbidly obese TSA, RTSA and TEA patients had 1.62 times greater odds of undergoing revision compared to non-obese patients at, up to 8 years post-surgery (Figure 3.18: Panel B). Again, a sensitively analysis was conducted as the meta-analysis was heavily weighted with the findings of a single study[159] (OR = 3.74; 95% CI [2.14, 6.55]).

The I^2 statistic for both meta-analyses identified moderate heterogeneity (I^2, 58% and 55%), however heterogeneity was not statistically significant (Figure 3.18). In summary, odds of revision increased from 1.52 to 1.62 in patients with increasing BMI, from ≥ 30.0 to ≥ 40.0, when compared to non-obese patients.

Panel A



Panel B

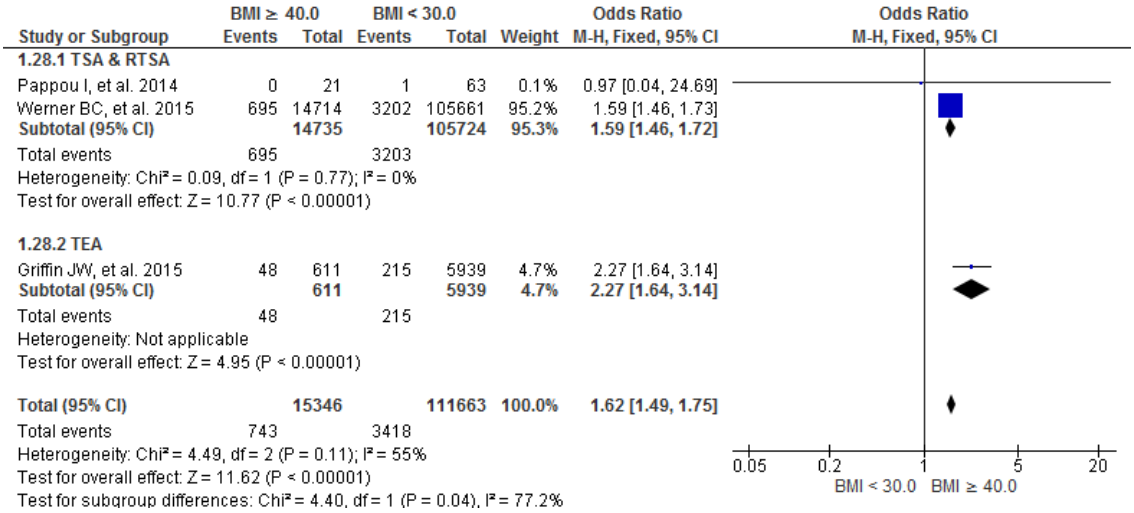


Figure 3.18. *Forest plot of the odds of revision in various BMI groups. Follow-up period: up to 2 years, a minimum of 2 years and up to 8 years.Subgroup analysis was conducted for arthroplasty joint type (total shoulder arthroplasty [TSA] and reverse total shoulder arthroplasty [RTSA], or total elbow arthroplasty [TEA]) (M-H: Mantel-Haenszel; CI: confidence interval; df: degrees of freedom; IV: inverse variance).*

Panel A: Obese (BMI ≥ 30.0) versus non-obese (BMI < 30.0) TSA/RTSA and TEA patients.

Panel B: Morbidly obese (BMI ≥ 40.0) versus non-obese (BMI < 30.0) TSA/RTSA and TEA patients.

Diabetes mellitus

No studies investigated the impact of diabetes mellitus on revision surgery.

3.5.15 Mortality

Obesity

Four TSA/RTSA studies[117-120] and one TEA study[162], including 37 103 participants, evaluated the influence of obesity on mortality. Two[119, 120] of the five studies did not contribute to the effect estimate as they reported no deaths for both obese and non-obese groups, resulting in a total of 36 914 patients available for meta-analysis. Postoperative follow-up duration varied in each study, and included the inpatient duration,[117] up to 30 days,[118] a minimum 90 days[119, 120] and a median of 5.8 years (range: 0 – 25 years)[162] (Table 3.3).

Meta-analysis revealed that obese patients receiving TSA, RTSA and TEA were not at statistically increased odds of mortality compared to non-obese patients (Figure 3.19). Subgroup analysis

identified a negligible difference between the overall effect size compared to shoulder arthroplasty procedures (TSA/RTSA) alone (Figure 3.19). The available evidence suggests that type of joint arthroplasty procedure in the upper limb did not influence risk of mortality. No statistically significant (χ^2 = 0.07, P = 0.71) heterogeneity (I^2, 0%) was observed despite studies being combined that reported on arthroplasty procedures of different joints (shoulder and elbow) across various study sites, and with differing follow-up durations and numerous orthopaedic surgeons (Figure 3.19).

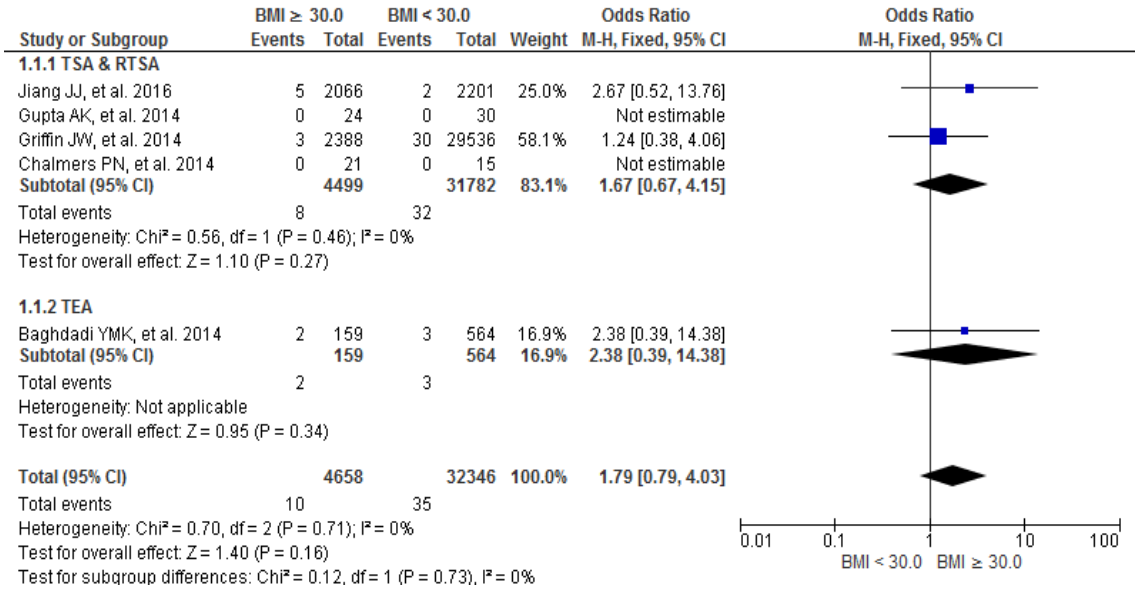


Figure 3.19. *Forest plot of the odds of mortality in obese (BMI ≥ 30.0) versus non-obese (BMI < 30.0) patients following arthroplasty. Subgroup analysis was conducted for arthroplasty joint type (total shoulder arthroplasty [TSA] and reverse total shoulder arthroplasty [RTSA], or total elbow arthroplasty [TEA]). Follow-up periods: inpatient duration, up to 30 days, a minimum 90 days, and a median of 5.8 years (range: 0 – 25 years) (M-H: Mantel-Haenszel; CI: confidence interval; df: degrees of freedom).*

Diabetes mellitus

One study investigating TSA/RTSA[133] and one investigating TEA[161] evaluated the influence of diabetes mellitus on odds of mortality. Both studies were retrospective cohort studies that gathered data from the NIS, and consequently reported mortality risk for the inpatient follow-up duration. The studies comprised a combined sample size of 69 669 patients (Table 3.3).

Results of meta-analysis revealed that diabetic TSA, RTSA and TEA patients had 2.93 times greater odds of mortality compared to non-diabetic patients (Figure 3.20). A meta-analysis identified no statistical heterogeneity (I^2, 0%) despite combining a small number of studies that

reported on arthroplasty procedures of different joints (shoulder and elbow), and the inclusion of a study with a mixed study cohort (HA subset; < 30.0% of the total cohort population) (Figure 3.20). However, the lack of statistical heterogeneity observed is expected given the combination of a small study with large variance, and a large, precise study.

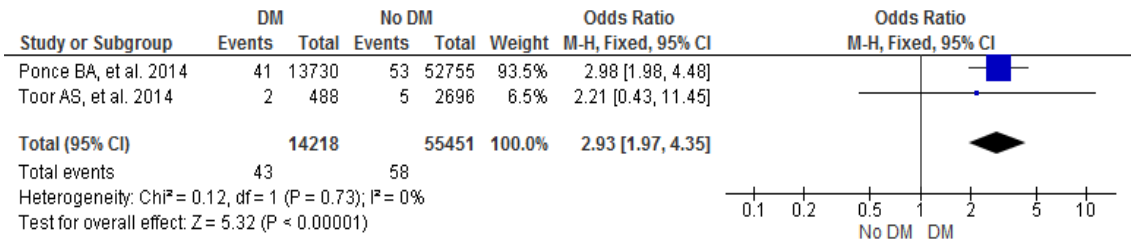


Figure 3.20. *Forest plot of the odds of mortality in diabetic versus non-diabetic upper limb arthroplasty patients. Follow-up periods: inpatient duration (DM: diabetes mellitus; M-H: Mantel-Haenszel; CI: confidence interval; df: degrees of freedom).*

Chapter 4: Discussion

Chapter 4 discusses the results for each exposure of interest in context of the broader orthopaedic literature. Limitations of the systematic review are considered, and implications of the review findings for clinical practice and future research are highlighted.

4.1 Effect of obesity on arthroplasty outcomes

The results of the systematic review presented in this thesis suggest that obesity significantly increased operative duration of upper limb arthroplasty procedures, and increased the odds of other detrimental outcomes and complications occurring, including revision, VTE, dislocation, fracture and infection. Obese patients (BMI ≥ 30.0 kg/m^2) reported significantly higher levels of pain than their non-obese (BMI < 30.0 kg/m^2) counterparts, however the difference was not clinically relevant. The review findings also revealed no difference in periprosthetic infection, LoS, UTI, function, unscheduled return to theatre or mortality between obese patients who had undergone upper limb arthroplasty procedures and their non-obese or normal weight (BMI < 25.0 kg/m^2) counterparts. Morbid obesity (BMI of ≥ 40.0 kg/m^2) made a small, yet statistically significant, difference on mean LoS. The effect of obesity on the incidence of blood transfusion was inconclusive and minimal evidence was available for pneumonia and QoL.

4.1.1 Significant effect of obesity on operative duration, infection, venous thromboembolism, revision, dislocation, fracture and pain

The review findings suggest that operative duration increases by some 10 to 13 minutes, with increasing BMI for obese TSA and RTSA patients. This is comparable to findings in the lower limb population. Bradley et al.[58] identified a linear relationship between theatre time required for total hip and knee arthroplasty, and BMI, indicating that a 5-point increase in BMI could increase theatre time by approximately seven minutes. Studies that have further sub-grouped intraoperative time measurements into categories such as 'total room time' and 'surgery time', have also demonstrated a linear relationship between BMI and time for both total hip arthroplasty,[61, 176] and total knee

arthroplasty.[56] In contrast, Lozano et al.[177] observed that longer surgical times were not required for total knee arthroplasty patients with a BMI ≥ 35.00 kg/m^2.

A recent study on lower limb arthroplasty reported an increased risk of wound complications, including superficial infection, with operative durations greater than 120 minutes.[54] Increased operative duration typically required in high BMI upper limb arthroplasty patients may also explain the increased likelihood of infection observed in this review. Review findings revealed greater risk of infection with increasing BMI, from 2.4 times in obese to greater than five times in morbidly obese patients, when compared with non-obese patients. Conversely, there was no increase in risk of periprosthetic infection in obese patients, compared to their non-obese counterparts. Despite the difference between morbidly obese, obese and non-obese patients observed in this review, when patients with a BMI in the normal range were considered, surprisingly, statistical significance disappeared. Obese shoulder arthroplasty patients were not at an increased risk of infection, whether that be any infection, or specifically periprosthetic infection, when compared to patients in a normal BMI range.

Similar risks of infection have been demonstrated in lower limb arthroplasty cohorts. The prevalence of infection in obese total knee and hip arthroplasty patients is increasing,[178] with much evidence identifying obesity as a significant risk factor. A large systematic review on the total knee arthroplasty population demonstrated risk of infection increased with increasing BMI, and reported odds of infection ranging from 1.45 (95% CI [1.13, 1.84]) in obese up to 4.01 (95% CI [2.26, 7.11]) in morbidly obese, when compared to non-obese patients.[179] However, when the analysis was broken down further to focus on deep infection, significantly greater odds were observed between morbidly obese and non-obese, however not in obese patients overall.[179] Conversely, a recent study found no difference in rates of wound infection across non-obese, obese and morbidly obese total knee arthroplasty patients, however this study was limited by a short in-hospital follow-up duration.[180] More recent meta-analyses specifically focused on periprosthetic infection in mixed joint arthroplasty populations have also been conducted. Kong et al.[181] identified obesity as a risk factor for periprosthetic joint infection (OR = 1.54; 95% CI [1.25, 1.90]), while Kunutsor et al.[182] demonstrated that risk increased in patients with a BMI over 40kg/m^2. Antibiotic prophylaxis recommendations aim to provide weight-adjusted dosing for a number of antibiotics, however some researchers suggest that evidence for adequate dosing is not yet available.[76] The majority of studies included in this review did not report on the antibiotic prophylactic regimes used.

Consequently, whether weight-adjusted antibiotic dosing was used, or whether the type of antibiotic or dosing regime was uniform across studies, remains unknown.

Review results revealed that obese RTSA, TSA and TEA patients were at nearly four times greater risk of VTE than non-obese patients. Furthermore, the odds ratio reached 5.5 in morbidly obese patients, which is consistent with current views and previous findings. For example, Werner et al.[159] concluded that an increased risk of VTE in high BMI patients was 'not surprising' given the potential difficulty of mobilisation with increasing BMI, combined with the loss of an extremity to assist with the mobilisation. Similar findings have also been found in the total knee arthroplasty population. Si et al.[179] reported that odds of DVT increased with increasing BMI, from 2.70 in obese to 8.19 in morbidly obese, when compared to non-obese patients, however, interestingly, no greater risk for PE was observed.[179]

Following resolution of any early complications, joint prostheses are ideally expected to function for 15 to 20 years before a revision is required. Unfortunately, the present review findings suggest that obese and morbidly obese upper limb arthroplasty patients are at greater risk of revision. Revision was reported in studies with follow-up durations of up to 2 years,[164, 165] up to 8 years[159] and a minimum of 2 years.[130] The study with a minimum 2-year follow-up reported that the revision was performed 6.3 years post primary arthroplasty.[130] A revision required within these study follow-up periods (< 10 years) is indicative of early to mid-term failure of the prosthesis, which is a severely detrimental outcome. Similar risks of revision have also been demonstrated in the lower limb arthroplasty population, with obese total knee arthroplasty patients reportedly having 1.60 times (95% CI [1.07, 2.40] greater odds of revision compared to non-obese patients, in studies with a follow-up duration of 5 years or more.[179]

Common causes of prosthesis revision following TSA and RTSA are instability and dislocation.[1] This review found a greater risk of dislocation following TSA, RTSA and TEA with increasing BMI, with morbidly obese patients demonstrating nearly three times greater odds of dislocation compared to non-obese patients. Two studies reported a dislocation within one year,[159, 164] whereas the remaining study simply stated a minimum 90-day follow-up without specifying how long after the arthroplasty procedure the dislocation occurred.[120] With regard to RTSA, instability of the joint can be caused by inadequate tensioning of the deltoid muscle and conjoint tendon.[89] Chalmers et al.[89] suggest that obesity contributes to instability by hindering accurate intraoperative soft tissue tensioning. A heightened risk of dislocation with increasing BMI has also been reported

in the lower limb arthroplasty population. For example, obese total hip arthroplasty patients have 2.08 times greater risk of dislocation.[176] More recently, Wager et al.[183] reported a linear relationship between risk of early dislocation and BMI in a total hip arthroplasty population.

Other less common causes of revision surgery include periprosthetic and acromial fractures. This review found that both obese and morbidly obese TSA, RTSA and TEA patients had approximately two times greater odds of fracture, and in particular periprosthetic fracture, than non-obese patients. Unfortunately, most of the studies reporting incidence of fracture did not specify whether the fracture occurred intraoperatively or postoperatively. If there was a greater risk of intraoperative fracture in high BMI patients, it may suggest greater technical difficulties of the procedure in obese, however this could not be determined or explored further.

Shoulder pain for 3 months or longer has been linked to depression,[92] anxiety and sleep disturbance, which have been demonstrated to improve following arthroplasty.[93] Review findings suggest that obese RTSA patients reported slightly greater postoperative pain scores than non-obese patients, at a WMD of 1.13 on the VAS – P scale. As the MCID of the VAS – P is greater than this (1.4 in the shoulder arthroplasty population),[170] this finding has minimal clinical relevance. Furthermore, the VAS – P mean range was 1.3 to 3, indicating that both the obese and non-obese groups experienced no pain, or only mild pain, postoperatively. Similarly, the present review findings correspond with research on pain relief and obesity in the lower limb. Most recently, Li et al.[184] found that patients across all BMI groups, from normal through to morbidly obese, showed substantial improvements in pain at six months.[184]

4.1.2 No significant effect of obesity on length of stay, function, urinary tract infection, unscheduled return to theatre and mortality

Findings demonstrated little impact of obesity on LoS, with morbidly obese patients demonstrating a small increase of 6.72 hours in comparison to non-obese patients. This finding is comparable with some research that has investigated the impact of obesity following lower limb arthroplasty. Although most evidence suggests that obesity does not influence LoS following either total hip[185, 186] or total knee[57, 59, 177] arthroplasty, some studies have suggested otherwise.[58, 187]

No mean difference in function, as measured by the ASES questionnaire, active abduction and external rotation was found between obese and non-obese TSA and RTSA patients. Similarly, no greater risk of UTI between obese and non-obese TSA and RTSA patients was found. In contrast, greater odds of UTI have been observed in the obese total knee arthroplasty patient population.[188]

Similarly, obese patients receiving TSA, RTSA and TEA were not at increased risk of unscheduled return to theatre or mortality compared to non-obese patients. These findings are comparable with the results of a systematic review that found no significant difference in perioperative morality rates across obese and non-obese total knee arthroplasty groups,[179] however primary research published after the conduct of this systematic review found that morbid obesity was an independent risk factor for in-hospital mortality in this population.[189]

4.1.3 Minimal influence or inconclusive evidence on the impact of obesity on blood transfusion, quality of life and pneumonia

Blood transfusion has been associated with a number of additional complications such as infection and VTE in upper limb arthroplasty patients.[74] This review showed that obese patients have an increased likelihood of blood transfusion, however substantial heterogeneity between studies was observed, limiting any conclusions that can be drawn. Conversely, normal BMI patients demonstrated greater risk of blood transfusion compared to obese class 2 patients. Interestingly, a similar finding has been observed in the lower limb, with obese and morbidly obese total knee arthroplasty patients demonstrating lower rates of transfusion compared to their non-obese counterparts.[180] Overall, evidence for risk of blood transfusion presented here was heterogeneous, and effect estimates varied greatly depending on the statistical model used for synthesis. Consequently, the impact of obesity on need for blood transfusion in upper limb arthroplasty remains inconclusive.

Of the included studies, only one reported the impact of obesity on QoL. This study found that patients with a BMI of < 25.0 improved 13-14 points more than overweight and obese patients on the SF-36 PCS sub-score.[165] There is limited evidence available on what constitutes a MCID on the SF-36 following upper limb arthroplasty surgery. However, minimum clinically important improvements following treatments for other conditions such as rheumatoid arthritis have been

identified at 7.2 for the PCS score,[190] which suggests that an improvement of 13 points or greater may be clinically relevant.

A single study found no statistically significant difference on the incidence of pneumonia between BMI groups.[118] Similarly there is a paucity of evidence on the effects of obesity on pneumonia in the knee arthroplasty literature.

4.1.4 New evidence in obesity and upper limb arthroplasty

Four new studies eligible for this review, which reported on a number of outcomes of interest were published after the search for this review was conducted (27 May, 2016).[74, 191-193]

Similar to the results of this review, a recent study by Wagner et al.[193] found a strong association between BMI and superficial infection but no relationship between BMI and periprosthetic infection in a mixed shoulder arthroplasty population (TSA, RTSA and HA). Furthermore, for every 1-unit increase in BMI greater than, or equal to 30, there was a five per cent increased risk of revision due to mechanical failure.[193] However, no significant associations were found between BMI groups and outcomes including reoperation and revision (all reasons).[193] Contrary to the results presented here, this study examined the risk of periprosthetic fracture and found no association with obese and non-obese categories.[193] Furthermore, Wagner et al.[193] suggested no significant associations between BMI and risk of VTE, or dislocation, however findings were based on a small sample of patients that experienced the VTE (23 patients) or dislocation (61 patients).

The present review findings also corroborate with results from a retrospective cohort study by Anakwenze et al.[191] that found no association between high BMI and one-year mortality in TSA and RTSA patients. However, no association was found between high BMI and risk of aseptic revision or three-year deep infection, which conflicts with the current review findings.[191]

The majority of findings from another retrospective cohort study by Vincent et al.[192] which investigated the mid-term functional outcomes and QoL of obese patients following TSA and RTSA were also consistent with the current review results. The study reported improvements in postoperative ASES scores and active external rotation across all BMI categories.[192] However, lower levels of improvement in active external rotation were noted.[192] Vincent et al.[192] also reported

no significant effects of obesity on additional patient reported outcome measures of function, pain and general health including the Shoulder Pain and Disability Index (SPADI), University of California at Los Angeles Shoulder Rating scale (ULCA), Constant score and Short Form-12 (SF – 12). However, lower SF – 12 scores were found in morbidly obese patients.

The final study identified also presented findings consistent with the results of this review, reporting no association between obesity and higher odds of blood transfusion in shoulder arthroplasty patients.[74]

4.1.5 Limitations of research in obesity upper limb arthroplasty studies

Inferences regarding operative duration are limited due to methodological shortcomings and confounding factors in the studies included in this review. Little information and consistency in the definition of operative duration was provided across the included studies. Surgeons with greater experience and a high volume of annual procedures have been associated with shorter operative durations.[51] Furthermore, evidence suggests that operative duration is affected by additional patient factors such as gender, primary indication and surgical history of the affected shoulder.[51]

Patient factors can also impact on a number of outcomes investigated in this review. Younger age (less than 65 years), has been significantly associated with early revision.[97] Correspondingly, younger age, male gender and traumatic arthroplasty have been found to increase risk of infection.[194] As discussed, further limitations regarding infection include the lack of description of antibiotic prophylactic regimes used in the included studies. Additional risk factors identified for periprosthetic fracture of the humerus have included increasing age, female gender and rheumatoid arthritis.[90] Furthermore, surgical technique and implant type was not uniform across included studies, which may have influenced outcomes such as dislocation.

A number of factors can influence the incidence of VTE, potentially limiting the findings presented here. First, there is a paucity of evidence on the use of VTE prophylaxis.[195, 196] Consequently, the American Academy of Orthopaedic Surgeons has provided a consensus opinion on the routine use of perioperative mechanical and/or chemical VTE prophylaxis following shoulder arthroplasty, however guidelines for prophylactic treatment could not be developed.[195] The absence of universal guidelines may result in different prophylaxis regimes being implemented across hospital sites.

Furthermore, prior history of VTE[142, 197] and increasing age[198] have shown to increase the risk of VTE in arthroplasty cohorts, and could not be controlled for in the data synthesis.

4.2 Effects of diabetes mellitus on arthroplasty outcomes

Diabetes mellitus significantly increased the risk of mortality, pneumonia and blood transfusion in obese patients undergoing upper limb arthroplasty in the present review, however had no effect on PE in these patients. Results of meta-analysis revealed that diabetic TSA, RTSA and TEA patients had nearly three times greater risk of mortality as an inpatient, and had 1.38 times greater odds of developing pneumonia, compared to non-diabetic patients. Similar results have been found in lower limb arthroplasty patients, with uncontrolled diabetes mellitus identified as a risk factor for mortality during the initial hospitalisation period.[199] Furthermore, a recent study found that type 2 diabetic total knee arthroplasty patients had in-hospital mortality rates nearly four times higher than their non-diabetic counterparts.[200] Risk factors for pneumonia have been extensively studied in lower limb arthroplasty patients, with diabetes mellitus consistently flagged.[199, 201]

This review also found evidence that diabetic patients are at greater risk of blood transfusion, which is a concern given transfused patients have higher odds of further complications. Such findings are consistent with lower limb arthroplasty studies, which suggest diabetic total knee and total hip arthroplasty patients have an increased risk of blood transfusion.[199, 201]

Results of meta-analysis revealed no difference in the risk of PE between diabetic and non-diabetic TSA, RTSA and TEA patients. A 2013 systematic review examining the incidence of venous thromboembolic complications following any shoulder surgery identified diabetes mellitus as a risk factor for VTE, however this finding was simply based on the high incidence of VTE reported in the diabetic population.[202] Research in diabetes and lower limb arthroplasty has demonstrated contradictory evidence to the results found for the upper limb population presented here. Both Wang et al.[203] and Zhao et al.[204] identified a significantly greater incidence of DVT in diabetic patients, up to 14 days post total knee arthroplasty. A meta-analysis that included these studies together with four additional studies found an association between diabetes mellitus and increased risk of DVT (OR = 1.36; 95% CI [1.07, 1.72]).[104] In contrast, a more recent study identified no greater risk of DVT in diabetic total knee arthroplasty patients, however was limited by a small

sample size.[205] In regard to total hip arthroplasty, current evidence suggests there is no association between diabetic patients and DVT or PE.[103]

Results of meta-analysis revealed no difference in the odds of infection between diabetic and non-diabetic TSA, RTSA and TEA patients, however, substantial heterogeneity limits this finding and consequently, the impact of diabetes mellitus on postoperative infection remains inconclusive. In contrast to these findings, extensive research has associated diabetes mellitus with infection following arthroplasty of the lower limb. A meta-analysis involving total hip arthroplasty patients, which was heavily weighted on the findings from one included study,[206] concluded that diabetics had two times greater odds of established SSI (95% CI [1.52, 2.76]) than non-diabetics.[103] Similar findings were also observed in studies focused on deep or periprosthetic infection. A systematic review on the total knee arthroplasty population identified 1.61 (95% CI [1.3, 1.88]) increased odds of deep infection in diabetics, compared to their non-diabetic counterparts.[105] Furthermore, a more recent systematic review involving a combined total hip and total knee arthroplasty population identified diabetes as a significant risk factor for periprosthetic infection (OR 1.26; 95% CI [1.15, 1.38).[207]

Some authors have suggested that hyperglycaemia is responsible for the increased infection risk sometimes observed in the diabetic population. Mraovic et al.[49] found that the risk of infection increased three-fold in non-diabetic total knee and hip arthroplasty patients with postoperative hyperglycaemia (Day 1: blood glucose > 200mg/dl). This year, the Healthcare Infection Control Practices Advisory Committee (HICPAC) of the Centers for Disease Control and Prevention released their 2017 Guideline for the Prevention of Surgical Site Infection. In this report, joint arthroplasty procedures were recognised as those for which SSI posed the greatest human and financial burden.[208, 209] Furthermore, this report made a strong recommendation, that is supported by high to moderate quality evidence, to 'implement perioperative glycemic control and use blood glucose target levels less than 200 mg/dL in patients with and without diabetes'.[208(p787)] This highlights the importance of perioperative glycaemic control for the prevention of SSI in all patients, regardless of their diabetes mellitus status. This review aimed to consider level of glycaemic control, however such detailed information was not available in the included studies.

The relationship between diabetes mellitus and LoS could not be assessed statistically in this review, however individual studies indicated longer LoS in the diabetic population. Basque and others[62] suggest that increased LoS may be due to the management of diabetes, which

complicates postoperative care. In regard to UTIs, only one TEA study considered the impact of diabetes mellitus, suggesting higher rates of UTI in the diabetic group.[160] Comparatively, diabetes mellitus has been consistently identified as a risk factor for UTI following lower limb arthroplasty.[103, 199, 201]

There was also limited evidence of the impact of diabetes mellitus on unscheduled return to theatre. No evidence was found on the effects of diabetes mellitus on the outcomes of operative duration, dislocation, fracture, pain, function, QoL, and revision.

4.2.1 New evidence in diabetes mellitus and upper limb arthroplasty

An additional study meeting the review inclusion criteria was published after the search for this review was conducted (27 May, 2016). This study, by Grier et al.[74] reported increased odds of blood transfusion of 1.80 [95% CI [1.63, 1.98] in diabetics with chronic complications, and 1.48 [95% CI [1.39, 1.56] in diabetics without chronic complications, compared to non-diabetics. These findings were consistent with the results of the present review.

4.2.2 Limitations of research in diabetes mellitus upper limb arthroplasty studies

A major limitation of the included studies that focused on diabetes mellitus was that they reported data grouped by diabetes diagnosis without reporting the criteria used for diagnosis, the type of diabetes, or the level of glycaemic control at time of surgery. As discussed, level of glycaemic control is an important variable that was not reported by the included studies.

4.3 Limitations of research in the field

In addition to the limitations discussed for each exposure (refer Section 4.1.5 and Section 4.2.2), a further inherent limitation is the low level of evidence of research in this field. Orthopaedic research commonly involves investigation of outcomes and adverse events following surgical treatment. As surgical treatments typically cannot be controlled for ethical reasons, such research is commonly conducted using observational study designs.[210] Methodological issues inherent in observational studies that may have impacted on the results of the present review include confounding factors (refer Section 4.1.5 and Section 4.2.2) and potential information bias, or error

in measurement.[210] This latter issue is highlighted in the critical appraisal findings in this review (refer Section 3.2), which identified that few studies measured the outcome or exposure used to group participants in a valid and reliable way, potentially leading to such a bias. As the majority of studies retrospectively gathered data from multi-institutional databases, data could not be validated against primary sources, leading to the potential for human error in coding and inaccurate data collection from included studies. A further inadequacy of measurement tools in this field is the use of BMI to define obesity, with limitations of its use discussed in Section 1.2.1.

4.4 Limitations of the systematic review

The comprehensive search strategy, with no publication date limits, was designed to locate all the available evidence, however, despite this, the restriction to include only English-language studies leaves the review at risk of language bias. Previous studies have found that non-English studies are particularly relevant in some medical specialties, including rheumatology and orthopaedics.[211] However, recent evidence and views suggest a diminished impact of the language bias,[212, 213] presumably due to a shift towards the publication of studies in English.[212] Consequently, the impact of a language bias, if any, on review results is unknown.

The screening of abstracts and the selection of studies for inclusion in this review was performed by only one reviewer, which can potentially cause errors of omission. Similarly, despite cross-checking all extracted data with study articles prior to analysis, data extraction was only conducted by a single reviewer, increasing the risk for errors in data handling. Furthermore, a number of datasets that were eligible for inclusion could not be analysed as they were presented in a study with a mixed cohort, and the study author was not able to provide the raw data. The review was also limited due to the exclusion of eight studies for which there was insufficient information to determine eligibility,[66, 114, 135-140] despite efforts made to attain the information through contact with study authors and the university library.

4.5 Implications for future research

A major limitation identified through the review process was the lack of description and/or justification for the terminology used in the included studies. For example, studies rarely specified the equipment and tests used to measure and diagnose each exposure (i.e. group by BMI,

diagnosis of diabetes mellitus). Such detail would increase confidence in outcome comparisons across studies and is a key area for future improvement. Similarly, studies reporting VTE incidence and infection rates should also describe the VTE and antibiotic prophylaxis regimes used to improve comparability across studies in this field.

Studies investigating diabetes mellitus should specify the level of glycaemic control, given available evidence suggests this to be a relevant concern that may influence patient outcomes. Finally, this review identified a paucity of evidence on the TEA population, which may suggest that further research of this population is needed, however it is likely a reflection of the prevalence of the procedure, with respect to other joint arthroplasty surgery.

4.6 Implications for practice

Surgeons should consider advising obese patients of the greater risk of complications including VTE, infection, dislocation, fracture and revision when undertaking elective upper limb arthroplasty. Given obesity was also found to potentially increase the risk of VTE and infection, treating surgeons could consider alternative treatment options, or take precautionary measures, such as using adjusted prophylaxis regimes, when treating obese arthroplasty patients. Similarly, the greater risk of mortality, transfusion and pneumonia should be described to diabetic upper limb arthroplasty patients prior to surgery. Further knowledge of additional risks associated with pre-existing obesity and diabetes mellitus allows the patient and surgeon to make a shared and well-informed decision regarding whether the benefits of upper limb arthroplasty outweigh the potential risk of complications prior to proceeding with surgery. However, these implications for practice must be considered in light of the nature of the research used to inform them and the methodological shortcomings described in this review.

4.7 Conclusions

With the number of upper limb arthroplasty procedures predicted to rise, risk factors that predispose patients to greater complications and poorer outcomes must be thoroughly investigated. This systematic review found that obesity significantly increased operative duration and increased the risk of revision, VTE, dislocation, fracture and infection. Diabetes mellitus was found to increase the risk of mortality, blood transfusion and pneumonia, however had no effect on

PE. Inconsistency in how outcomes were described across the included studies limits the findings, which should be considered in light of confounding variables such as the influence of patient and surgical factors.

Appendix 1: Systematic review protocol[102]

Review Manuscript Title:

The influence of diabetes mellitus and obesity on upper limb arthroplasty outcomes: a systematic review protocol

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Review question/objective

The objective of this review is to locate and synthesize the best available evidence investigating the impact of selected comorbidities on upper limb arthroplasty outcomes.

The review question is, are patients with Diabetes Mellitus or Obesity at increased risk of complications and/or poorer postoperative outcomes following Total Shoulder, Reverse Total Shoulder and Total Elbow Arthroplasty?

Background

Joint arthroplasty refers to the partial or total artificial replacement of a joint used to alleviate pain and physical dysfunction associated with end-stage degenerative disease, joint malformation or trauma.[1] It is an effective treatment commonly used in the medical care of the elderly population, with the median age of 70 – 74 years reported for male and female shoulder arthroplasty patients in 2015, respectively[2].

Obese and overweight in adults are highly prevalent in the Australian population, with the conditions most commonly present in the elderly.[3] In 2011 – 12, 75.0% of Australians aged 65-74 years were overweight or obese.[3] Similarly, diabetes mellitus has been identified as more

commonly present in older age groups, affecting 15.0% of Australians aged 65 – 74 years.[3] As displayed, risks of developing chronic diseases such as diabetes mellitus or obesity escalate with age, increasing the possibility of comorbid patients presenting for elective orthopaedic surgery. The incidence of such conditions is on the rise,[4] and further consideration of their impact on patient outcomes following arthroplasty is imperative.

The amount of research investigating the influence of comorbidity on perioperative and long-term outcomes following lower limb arthroplasty is increasing. Pre-existing diabetes mellitus has been associated with an increased risk of perioperative mortality,[5] deep vein thrombosis,[6] deep infection and poorer long-term function,[7] following Total Knee Arthroplasty. Similarly, diabetes mellitus and obesity are prevalent morbidities of hip arthroplasty patients and have been identified as risk factors for periprosthetic joint infection.[8, 9] Research concerning the influence of comorbidity on upper limb arthroplasty outcome is both sparse and contradictory.

Obesity

Risk associated with Total Shoulder Arthroplasty (TSA) outcomes in obese patients is the most widely studied, yet most controversial upper limb cohort, given the mixed findings reported. Morbidly obese patients (Body Mass Index [BMI] > 40 kg/m^2) generally stay longer in hospital postoperatively, however, in-hospital mortality, pulmonary embolism, infection and cardiac complication rates did not appear to differ from their non-obese or obese counterparts.[10] More recently, Jiang et al.[11] considered the 30-day complication profile of 4796 patients categorized by BMI class; a greater BMI was associated with longer surgical times, however, no association between BMI class and complications after surgery, for example blood transfusions, were identified.[11] Conversely, Werner *et al.*[12] identified obesity as a patient factor associated with early revision of shoulder arthroplasty. Furthermore, an increased risk of postoperative complication has been reported in patients with a BMI > 50 kg/m.[2,13] These patients were classed as ”superobese” and experienced significantly higher rates of infection within a year, venous thromboembolism, dislocation and revision compared with, at minimum, one of the non-obese, obese or morbidly obese comparator groups.[13] Super-obesity was not associated with periprosthetic fracture and postoperative stiffness.[13]

The influence of obesity on mid-term outcomes following TSA has also been investigated. Linberg *et al.*[14] followed a cohort of morbidly obese shoulder arthroplasty patients, reporting improvements in pain and function, as measured at two years post-surgery. A more recent, comparative study

identified increases in quality of life, pain and fatigue scores amongst TSA patients across all BMI classes.[15] Despite these improvements, authors noted that overall physical function in obese (30 kg/m^2) and overweight (25- 29.9 kg/m^2) patients did not significantly improve following TSA, with such patients failing to achieve improvement levels as those reached in the 'normal weight' patient population (<25 kg/m^2).[15] Studies investigating the relationship between Reverse TSA (rTSA) and Obesity have also presented mixed findings. Gupta *et al.*[16] reviewed 119 patients with a minimum 90-day follow-up, categorised by BMI. Patients with a BMI exceeding 35 kg/m^2 presented higher rates of overall complication, specifically blood loss and consequent blood transfusion.[16] On the contrary, evidence also supports rTSA as an effective procedure for the morbidly obese,[17] with no increased risk for complications such as periprosthetic infection.[18]

Unlike shoulder arthroplasty, research investigating the impact of Obesity on outcome following Total Elbow Arthroplasty (TEA) is limited, yet comparable. Within the 90-day postoperative period, Griffin *et al.*[19] identified a higher rate of venous thromboembolism and infection in obese and morbidly obese TEA patients. Postoperatively, a one year onward, dislocation and revision also occurred at a greater rate in the morbidity obese group.[19] Similarly, Baghdadi *et al.*[20] also identified a significantly higher rate of TEA revision in severely obese patients when compared to the non-obese patient group.

Diabetes Mellitus

Diabetic patients undergoing TEA have reportedly endured significantly longer hospital length of stay and higher rates of perioperative complications than their non-diabetic counterparts.[21] Reported complications have included increased rates of pneumonia, myocardial infarction and transfusion requirements.[21] Further findings have also identified diabetes mellitus as an independent risk factor for urinary tract infection following TEA.[22] The influence of diabetes mellitus on shoulder arthroplasty patients has also been investigated. Pounce *et al.*[23] identified an association between diabetes mellitus, in-hospital death and perioperative complications following shoulder arthroplasty.[23]

The available evidence regarding the impact of comorbidities such as obesity and diabetes mellitus on upper limb arthroplasty outcomes appears to be inconclusive and contradictory. An understanding of the relationship between pre-existing comorbidities and arthroplasty outcomes is essential as it may impact patient selection for different types of orthopaedic surgery. Patients must be better informed of any additional risks associated with a pre-existing chronic disease, as this

may influence their decision-making process. Orthopaedic surgeons may also consider further alternate treatments or pre-cautionary measures to ensure the safety and effectiveness of the arthroplasty procedure in patients identified as at greater risk for poorer outcome.

To date, research has considered a number of peri-operative, short and longer term complications for patients with comorbid conditions in isolation. An inclusive review with consideration of peri-operative, as well as mid and longer term outcomes is now needed to develop a clear understanding of the impact of comorbidities on upper limb arthroplasty. A preliminary literature database search in PubMed, in addition to a screening of the review registry PROSPERO, indicated that this topic has not previously been assessed through systematic review methodology, nor is currently under investigation. The primary objective of this systematic review is to investigate the impact of diabetes mellitus or obesity on complications and postoperative outcomes in TSA, rTSA and TEA patients.

Keywords

Comorbidity; Diabetes Mellitus; Elbow Arthroplasty; Obesity; Shoulder Arthroplasty.

Inclusion criteria

Types of participants

This review will consider studies that include adults (18 years or older) who have undergone upper limb arthroplasty, specifically primary TSA, rTSA and TEA.

Exposure

This review will consider studies that evaluate the influence of comorbidity on the arthroplasty outcomes. Comorbidities to be considered will include the presence of either:

1. Obesity

The World Health Organization uses BMI as an index of weight-for-height.[24] BMI is commonly used to classify levels of obesity and is categorized under the following ranges:

- Normal Weight: <25kg/m^2

- Overweight: 25 – 29.9 kg/m^2
- Obese: 30 – 39.9 kg/m^2
- Morbidly Obese: ≥ 40 kg/m^2

This review will categorize obesity as a BMI of at least 30 kg/m^2.

2. Diabetes Mellitus

Type 1 and Type 2 diabetes mellitus will be considered. Given classification and diagnostic criteria for diabetes mellitus may change over time, we will consider patients formally diagnosed with diabetes mellitus using standard criteria valid at the time of the beginning of the study. Criteria should ideally be described in the article.

Outcomes

This review will consider studies that report the postoperative complications and outcomes including:

- *Infection (surgical site infection and periprosthetic infection)*
  - Diagnosed by, but not limited, to laboratory and microbiological testing.
- *Urinary tract infections*
  - Diagnosed by, but not limited to, laboratory testing for positive urine culture.
- *Blood Transfusion*
- *Pneumonia*
  - Diagnosed by, but not limited to, chest x-rays and blood tests.
- *Venous Thromboembolism (Deep Vein Thrombosis and Pulmonary Embolism)*
  - Diagnosed by, but not limited to Duplex Sonography, Doopler Ultrasonography or Computed Tomography Scan.
- *Acromial or Stem Fractures* (For example Periprosthetic fractures).
- *Length of Stay*
- *Operative Duration*

- *Pain:* as measured by scoring systems such as the Visual Analogue Scale for Pain.
- *Function:* as measured by Range of Motion or on scoring systems such as the Constant – Murley Shoulder Score.
- *Quality of Life:* as measured by scoring systems such as the Short Form-36.
- *Dislocation*
- *Unscheduled return to theatre (For causes such as instability or dislocation).*
- *Revision* following primary Total Shoulder or Elbow arthroplasty.
- *Mortality*

Types of studies

This review will consider analytical epidemiological study designs including prospective and retrospective cohort studies and case-control studies for inclusion.

Search strategy

The search strategy aims to find both published and unpublished studies. A three-step search strategy will be utilized in this review. An initial limited search of PubMed and CINAHL will be undertaken followed by analysis of the text words contained in the title and abstract, and of the index terms used to describe the article. A second search using all identified keywords and index terms will then be undertaken across all included databases. Thirdly, the reference list of all identified reports and articles will be searched for additional studies. Studies published in English will be considered for inclusion and no limitation on publication date will be assigned.
The databases to be searched include:

- PubMed
- CINAHL
- Embase

The grey literature search, or search for unpublished studies, will include:
1. *National and international conference proceedings*.

Conferences chosen for review will be based on those listed by the Australian Orthopaedic Association (AOA) of which are relevant to the present review topic and provide electronically accessible proceedings. The conference proceedings of the most recent conference will be screened. Conferences will include:

- American Academy of Orthopaedic Surgeons Annual Meeting
- Australian Orthopaedic Association Annual Scientific Meeting
- Canadian Orthopaedic Association Annual Scientific Meeting
- British Orthopaedic Association Annual Congress
- European Federation of National Associations of Orthopaedics and Traumatology Congress

2. *Open Grey – European database of grey literature*

Initial keywords and search filters to be used will be:

1. Arthroplasty OR Replacement OR total shoulder OR total elbow
2. Comorbidity OR Obesity OR Body Mass Index OR overweight OR Diabetes Mellitus
3. Outcome OR perioperative OR midterm OR long term OR infection OR length of stay OR urinary tract infection OR mortality OR venous thrombosis OR fracture OR function OR quality of life OR pain OR revision OR complication.
4. 1 AND 2 AND 3

Assessment of methodological quality

Papers selected for retrieval will be assessed by two independent reviewers for methodological validity prior to inclusion in the review using standardized critical appraisal instruments from the Joanna Briggs Institute System for the Unified Management, Assessment and Review of Information (JBI-SUMARI) (Appendix I). However, methodological quality of papers will not influence eligibility for inclusion. Any disagreements that arise between the reviewers will be resolved through discussion, or with a third reviewer. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis flowchart will be used to report study selection and inclusion in the review.[25]

Data collection

The data extracted will include specific details about the interventions, populations, study methods and outcomes of significance to the review question and objective. The following components will be extracted from each of the studies:

- Country origin of study.
- Details of surgery performed
- Type of arthroplasty procedure: Total Elbow, Total Shoulder or Reverse Total Shoulder.
- Demographics and characteristics of participant cohorts including age, sex, level of glycaemic control (i.e. controlled or not controlled), type 1 or type 2 diabetes mellitus, nationality or ethnicity, indication for primary arthroplasty and function.
- Arthroplasty outcomes, including postoperative complications and outcomes.

Data synthesis

Quantitative data will, where possible, be pooled in statistical meta-analysis using JBI-SUMARI. All results will be subject to double data entry. Effect sizes expressed as odds ratios (for categorical data) and weighted mean differences (for continuous data) and their 95% confidence intervals will be calculated for analysis. A random effects model will be used and heterogeneity will be assessed statistically using the standard χ^2 and I^2. Where statistical pooling is not possible the findings will be presented in narrative form, including tables and figures to aid in data presentation, wherever appropriate.

Where possible, subgroup analysis may be conducted to further explore the different levels of BMI, type of diabetes mellitus, differences in surgical treatment groups or level of methodological quality of included studies.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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Statement of Authorship

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Principal Author

Name of Principal Author (Candidate)	Annika Theodoulou
Contribution to the Paper	Performed literature review, prepared the manuscript and acted as corresponding author.
Overall percentage (%)	85%
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.
Signature	Date: 5 Feb 18

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);

ii. permission is granted for the candidate in include the publication in the thesis; and

iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

Name of Co-Author	Jeganath Krishnan
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Contribution to the Paper	Review of appropriate systematic review methodology; Review and edit of manuscript.
Signature	Date: 9/1/17.

Please cut and paste additional co-author panels here as required.

Appendix 2: Search Strategies

Table 2.1 Bibliographic database search strategies*

PubMed database	
Search	*Query*
#1	(((Arthroplasty[mh:noexp] OR Arthroplasty, Replacement[mh:noexp] OR Arthroplasty, Replacement, Elbow[mh] OR Arthroplast*[tw] OR Total shoulder[tw] OR Total elbow[tw] OR (replacement*[tw] AND (Elbow[tw] OR shoulder[tw]))))
#2	((Comorbidity[mh] OR Comorbid*[tw] OR Obesity[mh:noexp] OR Obesity, Morbid[mh] OR Obesit*[tw] OR Obese[tw] OR Body Mass Index[mh] OR Body Mass Index[tw] OR BMI[tw] OR Overweight[mh:noexp] OR Overweight[tw] OR Diabetes Mellitus[mh:noexp] OR Diabetes Mellitus, Type 2[mh:noexp] OR Diabet*[tw] OR Hyperglycemia[mh] OR Hyperglycem*[tw]))
#3	(#1 AND #2) AND English[lang]
Cumulative Index of Nursing and Allied Health Literature (CINAHL) database	
Search	*Query*
S1	MH Arthroplasty OR MH Arthroplasty, Replacement OR MH Arthroplasty, Replacement, Elbow OR Ti Arthroplast* OR AB Arthroplast* OR TI "Total shoulder" OR AB "Total shoulder" OR TI "Total elbow" OR AB "Total elbow" OR (TI replacement* AND (Ti Elbow OR Ti shoulder)) OR (AB replacement* AND (AB Elbow OR AB shoulder))
S2	MH Comorbidity OR MH Obesity OR MH Obesity, Morbid OR TI Obesit* OR AB Obesit* OR TI Obese OR AB Obese OR MH "Body Mass Index" OR TI "Body Mass Index" OR AB "Body Mass Index" OR TI bmi OR AB bmi OR TI Overweight OR AB Overweight MH Diabetes Mellitus OR MH Diabetes Mellitus, Type 2 OR MH Diabetes

	Mellitus, Type 1 OR TI Diabet* OR AB Diabet* OR TI Comorbid* OR AB Comorbid* OR TI Hyperglycem* OR AB Hyperglycem* OR MH Hyperglycemia
S3	S1 AND S2 **Narrow by Language**: - English
Embase database	
Search	*Query*
#1	'arthroplasty'/de OR 'elbow arthroplasty'/de OR 'shoulder arthroplasty'/de OR 'reverse shoulder arthroplasty'/de OR arthroplast* OR 'total shoulder' OR 'total elbow' OR ('replacement*' AND (elbow OR shoulder))
#2	'comorbidity'/de OR comorbid* OR 'obesity'/de OR 'morbid obesity'/de OR obesit* OR 'obese' OR 'body mass'/de OR 'body mass index' OR 'bmi' OR 'overweight' OR 'diabetes mellitus'/de OR 'insulin dependent diabetes mellitus'/de OR 'non insulin dependent diabetes mellitus'/de OR diabet* OR “hyperglycemia”/de OR hyperglycem*
#3	#1 AND #2 AND [english]/lim
** All searches were performed on 27 May 2016.*	

Table 2.2 Grey literature search strategies

Grey literature source	Date cited	Website URL
Database		
Open Grey *Search strategy*: *((shoulder replacement) OR (elbow replacement) OR (shoulder arthroplasty) OR (elbow arthroplasty) OR (total elbow) OR (total shoulder)*	1 September 2016	http://www.opengrey.eu/
Conference proceedings		
American Academy of Orthopaedic Surgeons Annual Meeting [Internet]; 2016 Mar 1-5; Orlando, Florida.	31 August 2016	http://www.aaos.org
Canadian Orthopaedic Association Annual Scientific Meeting [Internet]; 2016 Jun 16-19; Québec City, Québec.	31 August 2016	http://www.coa-aco.org/annual-meetings/meeting-archives/quebec-city-2016.html
Proceedings of the British Orthopaedic Association Annual Congress [Internet]; 2015 Sep 15-18; Liverpool, England.	1 September 2016	http://congress.boa.ac.uk/liverpool-2015/#tab-id-1
17th EFFORT (European Federation of National Associations of Orthopaedics and Traumatology) Congress [Internet]; 2016 Jun 1-3; Geneva, Switzerland.	1 September 2016	https://www.efort.org/geneva2016/scientific-content/advanced-scientific-programme/
Australian Orthopaedic Association Annual Scientific Meeting [Internet]; 2015 Oct 11-15; Brisbane, Queensland.	21 September 2016	https://www.aoa.org.au/ (Password protected eProceedings)

Appendix 3. JBI Critical Appraisal Explanatory Tables

Table 3.1. Cohort studies explanatory table

Question 1. Were the groups similar and recruited from the same population?	
Yes	All participants were recruited from a population who received a total shoulder, reverse total shoulder or total elbow arthroplasty over a defined period of time or population (i.e. cases from a single surgeon). Baseline characteristics including age and gender were reported. Selection criteria were defined.
No	All participants did not receive a total shoulder, reverse total shoulder or total elbow arthroplasty or were not recruited from a defined period of time or population. Baseline characteristics including age and gender were not reported. Selection criteria were not defined.
Unclear	Description of above unclear or unsatisfactory.
Not Applicable	Not applicable.
Question 2. Were the variables (exposures/outcomes) measured similarly to assign people to both exposed and unexposed groups?	
Yes	<u>Obesity</u> Authors use BMI to assign each patient to a group. <u>Diabetes Mellitus</u> Authors use the diagnosis of diabetes mellitus to assign each patient to a group. <u>Outcome Measure</u>

	All patients were grouped on the basis of the presence or absence of a postoperative outcome.
No	The variable used to assign patients was not the same, or not measured similarly across groups.
Unclear	Description of above unclear or unsatisfactory.
Not Applicable	
Question 3. Was the exposure/outcome used to group participants measured in a valid and reliable way?	
Yes	<u>Obesity</u> Methods of measurement of height and weight, and calculation of BMI are described. Methods described are valid and reliable, and may include calibrated scales and repeated measures. <u>Diabetes Mellitus</u> Methods described for the diagnosis of diabetes mellitus are valid and reliable, such as diagnosis via blood test. <u>Outcome Measure</u> The outcome measure must be clearly defined and based on existing definitions or diagnostic criteria (i.e. a dislocation outcome may be identified via radiograph).
No	Methods of measurement of height, weight and diagnosis of diabetes mellitus or an outcome measure are not reported, invalid or unreliable.
Unclear	Description of above unclear or unsatisfactory.
Not Applicable	Not Applicable.
Question 4. Were confounding factors identified?	

Yes	Key confounders (i.e. age, gender or comorbidities) are identified.
No	Authors do not report presence or absence of confounding factors.
Unclear	Authors do not specifically report the presence or absence of confounding factors, but purely describe that they would be statistically accounted for, if present. Description of above is unclear or unsatisfactory.
Not Applicable	
Question 5. Were strategies to deal with confounding factors stated?	
Yes	Subgroup analysis or multivariate analysis was conducted to adjust for confounding variables.
No	Strategies to deal with confounding variables are not discussed.
Unclear	Description of above unclear or unsatisfactory.
Not Applicable	
Question 6. Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	
Yes	<u>Studies that assess outcome measures: infection, UTI, pneumonia and VTE</u> Groups/participants were reported as free of perioperative and postoperative complications including infection, UTI, pneumonia and VTE preoperatively.
No	<u>Studies that assess outcome measures: infection, UTI, pneumonia and VTE</u> Groups/participants were reported as not free of perioperative and postoperative complications including infection, UTI, pneumonia and VTE preoperatively.
Unclear	<u>Studies that assess outcome measures: infection, UTI, pneumonia and VTE</u>

	No information is provided concerning the presence of infection, UTI, pneumonia and VTE preoperatively.
Not Applicable	Studies that assess the following outcome measures are not applicable during the preoperative time period and include periprosthetic or surgical site infection, blood transfusion, fractures, LoS, operative duration, dislocation, unscheduled return to theatre, revision and mortality. Studies that assess postoperative outcomes such as pain, function and QoL are common symptoms experienced that lead to the intervention of interest and thus the presence of these outcomes preoperatively is not applicable.
Question 7. Were the outcomes measured in a valid and reliable way?	
Yes	Outcomes are measured using standardised medical tests, methods or instruments for outcomes including infection, UTI, pneumonia, VTE, acromial or stem fractures. Alternatively, authors provide a reference to the description of a standardised method from which the outcome was measured (i.e. in ACS NSQIP database analysis studies). Authors reference or report on the reliability and/or validity of the measurement tools they use for outcomes including: pain, function and QoL. Outcomes including blood transfusion, dislocation, unscheduled return to theatre, revision or mortality, are reported as simply having occurred. LoS is reported in days, and operative duration is reported in minutes.
No	Outcomes were not measured, referenced of reported as described above.
Unclear	Description of above unclear or unsatisfactory.
Not Applicable	
Question 8. Was the follow up time reported and sufficient to be long enough for outcomes to occur?	
Yes	Follow-up time period is clearly defined for each outcome measure.

	Follow-up time period is adequate for each outcome to present itself: - Minimum in-hospital duration for outcomes including infection, UTI, pneumonia, VTE, QoL, function and mortality. - No minimum follow-up time period required for the outcomes including pain, unscheduled return to theatre or revision. - Not applicable for the outcomes including blood transfusion, acromial or stem fractures, LoS, operative duration.
No	Follow-up time period is not clearly defined or adequate for the outcome to present itself.
Unclear	Description of above unclear or unsatisfactory.
Not Applicable	
Question 9. Was follow-up complete, and if not, were the reasons to loss to follow-up described and explored?	
Yes	Follow-up was complete, and if not, reasons for loss to follow-up were reported.
No	Follow-up was not complete and reasons for loss to follow-up were not reported.
Unclear	Description of above unclear or unsatisfactory.
Not Applicable	Not applicable.
Question 10. Were strategies to address incomplete follow-up utilized?	
Yes	Strategies to address incomplete follow-up were reported.
No	Strategies to address incomplete follow-up were not reported.
Unclear	Description of above unclear or unsatisfactory.

Not Applicable	Retrospective study design
Question 11. Was appropriate statistical analysis used?	
Yes	Appropriate statistical methods used and described, and methods for addressing confounders included. Number of participants with missing data reported, and appropriate statistical methods used if data missing.
No	Statistical methods not described, or inappropriate methods used. Missing data not mentioned or accounted for.
Unclear	Description of above unclear or unsatisfactory.
Not Applicable	No statistical testing was undertaken.
ACS NSQIP: American College of Surgeons National Surgical Quality Improvement Program; ***BMI***: Body Mass Index; ***LoS:*** Length of stay; ***QoL*****:** quality of life; ***UTI:*** urinary tract infection; ***VTE*****:** venous thromboembolism.	

Cohort study design: Further explanation of Question 3

A number of included studies collected data from large databases:

- Pearldiver – only provided ICD-9 codes for classification of obesity:
  - ICD-9 did not describe how BMI was measured and, consequently Question 3 was answered 'No'.
  - ICD-9 did not describe how outcomes of interest were measured and, consequently Question 3 was answered 'No'.
- National Inpatient Sample Database – only provided ICD-9 codes for classification of conditions:
  - ICD-9 did not describe how the condition was measured and, consequently Question 3 was answered 'No'.

- American College of Surgeons National Surgical Quality Improvement Program database (ACS NSQIP):
    - Provides a definition and inclusion criteria for the variable 'diabetes', however no information on how it is diagnosed, consequently Question 3 was answered 'No'.
    - Does not provide a definition of BMI or information on what instruments are used to measure height and weight. Consequently Question 3 was answered 'No'.

Cohort study design: Further explanation for Question 7

A number of included studies collected data from large databases. If the study provided a reference to the definition of an outcome measure, the references were checked in order to determine if the outcome was measured in a valid and reliable way. The user-guides of the following database were sought and found to contain descriptions of outcomes measured in a valid and reliable way. The approach was only applicable to the following outcome measures: infection, UTI, pneumonia, VTE, acromial or stem fractures.

- ACS NSQIP: Outcome measures described:
    - UTI
    - VTE (PE and DVT)
    - Superficial infection
    - Deep infection
    - Pneumonia
- PearlDiver Database – Used ICD-9 codes to identify postoperative outcomes. ICD-9 codes did not provide a description of how the outcome was measured; consequently the answer to Question 7 was unclear.
- National Inpatient Sample Database – Used ICD-9 codes to identify postoperative outcomes. ICD-9 codes did not provide a description of how the outcome was measured, consequently the answer to Question 7 was unclear.
- Medicare claims by hospitals and outpatient institutions – Used ICD-9 codes to identify postoperative outcomes. ICD-9 codes did not provide a description of how the outcome was measured, consequently the answer to Question 7 was unclear.

Table 3.2. Case-control study explanatory table

Question 1. Were the groups comparable other than the presence of disease in cases or the absence of disease in controls?	
Yes	Controls were matched on the basis of, at minimum, age, gender, surgical procedure and duration of follow-up.
No	Controls were not matched on the basis of age, gender, surgical procedure and duration of follow-up.
Unclear	Description of above unclear or unsatisfactory.
Not Applicable	
Question 2. Were cases and controls matched appropriately?	
Yes	Data was collected from the same source population, for example the same joint registry or cases from a single surgeon.
No	Data was not collected from the same source population.
Unclear	Description of above unclear or unsatisfactory.
Not Applicable	
Question 3. Were the same criteria used for identification of cases and controls?	
Yes	All cases and controls were identified by any one of the following: - Levels of obesity, identified through the BMI Classification, or similar existing measure. - Presence or absence of diabetes mellitus, with explanations of how the condition was diagnosed. This may include the use of existing definitions or diagnostic criteria.

No	All cases and controls were not identified by any one of the following: - Levels of obesity, identified through the BMI Classification, or similar existing measure. - Presence or absence of diabetes mellitus, with explanations of how the condition was diagnosed. This may include the use of existing definitions or diagnostic criteria.
Unclear	Description of above unclear or unsatisfactory.
Not Applicable	
Question 4. Was exposure measured in a standard, valid and reliable way?	
Yes	<u>Obesity</u> Methods and/or equipment used to measure the height and weight, used to calculate BMI for each patient in the study population is described. Methods described are standard, valid and reliable, for example through repeated measures. <u>Diabetes Mellitus</u> A description of how diabetes mellitus was diagnosed is reported, for example through medical testing or identified through internationally accepted diagnostic references, i.e. International Classification of Diseases, Ninth Revision, Clinical Modification.
No	<u>Obesity</u> Methods and/or equipment used to measure the height and weight, used to calculate BMI for each patient in the study population is not described. Methods described are not standard, valid or reliable. <u>Diabetes Mellitus</u> A description of how Diabetes Mellitus was diagnosed is not provided.
Unclear	Description of above unclear or unsatisfactory.

Not Applicable	
Question 5. Was exposure measured in the same way for cases and controls?	
Yes	Obesity Equivalent methods were employed for the measurement of obesity for all cases and controls. Diabetes Mellitus Equivalent methods are reported for diagnosis of diabetes mellitus for all cases and controls.
No	Equivalent methods were not reported for the measurement of obesity or diabetes mellitus for all cases and controls.
Unclear	Description of above unclear or unsatisfactory.
Not Applicable	
Question 6. Were confounding factors identified?	
Yes	Key confounders (i.e. age, gender or comorbidities) are identified.
No	The presence or absence of confounding factors is not reported.
Unclear	Authors do not specifically report the presence or absence of confounding factors, but purely describe that they would be statistically accounted for, if present. Description of above is unclear or unsatisfactory.
Not Applicable	
Question 7. Were strategies to deal with confounding factors stated?	

Yes	Subgroup analysis or multivariate analysis was conducted to adjust for confounding variables.
No	Strategies to deal with confounding variables are not discussed.
Unclear	Description of above unclear or unsatisfactory.
Not Applicable	No confounding variables reported.
Question 8. Were outcomes assessed in a standard, valid and reliable way for cases?	
Yes	Outcomes are measured using standardised medical testing, methods or instruments for outcomes including infection, UTI, pneumonia, VTE, acromial or stem fractures. Alternatively, authors provide a reference to the description of a standardised method from which the outcome was measured. Authors reference or report on the reliability and/or validity of the measurement tools they use for outcomes including: pain, function and QoL. Outcomes including blood transfusion, unscheduled return to theatre, revision or mortality are reported as simply having occurred. Outcomes, LoS is reported in days, and operative duration is reported in minutes.
No	Outcomes were not measured, referenced or reported as described above.
Unclear	Description of above unclear or unsatisfactory.
Not Applicable	
Question 9. Was the exposure period of interest long enough to be meaningful?	
Yes	Follow-up time period is clearly defined for each outcome measure. Follow-up time period is adequate for each outcome to present:

	- Minimum in-hospital duration for outcomes including infection, UTI, pneumonia, VTE, QoL, function and mortality. - No minimum follow-up time period required for the outcomes including pain, unscheduled return to theatre or revision. Not applicable for the outcomes including blood transfusion, acromial or stem fractures, LoS, operative duration.
No	Follow-up time period is not clearly defined or long enough to be meaningful.
Unclear	Description of above unclear or unsatisfactory.
Not Applicable	
Question 10. Was appropriate statistical analysis used?	
Yes	Appropriate statistical methods used and described, and methods for addressing confounders included. Numbers of participants with missing data reported, and appropriate statistical methods used if data missing.
No	Statistical methods not described, or inappropriate methods used. Missing data not mentioned or accounted for.
Unclear	Description of above unclear or unsatisfactory.
Not Applicable	No statistical testing was undertaken.
BMI: Body Mass Index; ***LoS:*** length of stay; ***QoL*****:** quality of life; **UTI*:*** urinary tract infection; ***VTE*****:** venous thromboembolism.	

Appendix 4: Data Extraction Template

Table 4.1. Summary of included studies data extraction template

Included study	**Methods**	**Exposure, Arthroplasty procedure**	**Participants**	**Setting**	**Complications and postoperative outcomes**	
	Study design: Follow-up: Country of origin: No. of surgeons performing procedure: Surgical technique:	Exposure: Procedure: Indication for procedure:	Sample size: Demographics: *Age:* *Gender: (F: M)* *Ethnicity/Nationality:* *DM/Obesity comorbidity: n (%)*	Setting: Exclusions:		
***DM** = diabetes mellitus; **F** = Female; **M** = Male; **n** = number of arthroplasties.*						

Appendix 5: Meta-analyses Summary Table

Outcome	**Studies (n)**	**Total patients (n)**	**Events**	**Heterogeneity (I^2, %)**	**Statistical method**	**Effect estimate**	**P-Value**
Operative duration Obese class 2 vs normal	2	1732	-	4	MD (I – V, Fixed, 95% CI)	12.48 [8.40, 16.55]	< 0.00001
Operative duration Obese vs normal	3	1955	-	0	MD (I – V, Fixed, 95% CI)	10.00 [6.31, 13.69]	< 0.00001
Operative Duration Obese vs overweight	3	2697	-	0	MD (I – V, Fixed, 95% CI)	4.78 [1.50, 8.07]	0.004
LoS Obese vs normal	2	91	-	14	MD (I – V, Fixed, 95% CI)	0.15 [-0.28, 0.58]	0.48
LoS Morbidly obese vs non-obese	2	30 203	-	0	MD (I – V, Fixed, 95% CI)	0.28 [0.14, 0.43]	0.0001
LoS Obese vs overweight	2	103	-	45	MD (I – V, Fixed, 95% CI)	0.05 [-0.58, 0.68]	0.88

Blood transfusion (ALL) Obese vs non-obese	4	11 937	296	95	OR (M – H, Fixed, 95% CI)	1.47 [1.17, 1.85]	0.0008
Blood transfusion (ALL)# Obese vs non-obese	4	11 937	296	95	OR (M – H, **Random,** 95% CI)	2.06 [0.48, 8.82]	0.33
Blood transfusion (ALL)## Obese vs non-obese (TSA/RTSA Only)	3	4357	164	29	OR (M – H, Fixed, 95% CI)	0.71 [0.52, 0.97]	0.03
Blood transfusion (ALL)## Obese vs non-obese (TSA/RTSA Only)	3	4357	164	29	OR (M – H, **Random,** 95% CI)	1.02 [0.35, 3.01]	0.97
Blood transfusion Obese class 2 vs normal	3	1768	71	59	OR (M – H, Fixed, 95% CI)	0.46; [0.28, 0.74]	0.002
Blood transfusion Obese class 2 vs normal	3	1768	71	59	OR (M – H**, Random,** 95% CI)	1.04; [0.18, 5.94]	0.97
Blood transfusion DM vs no DM	2	80 183	7024	92	OR (M – H, Fixed, 95% CI)	1.49; [1.41, 1.57]	< 0.00001
Blood transfusion# DM vs no DM	2	80 183	7024	92	OR (M – H, **Random**, 95% CI)	1.62; [1.24, 2.11]	0.0004
Infection (ALL)* Obese vs non-obese	11	190 738	4942	61	OR (M – H, **Random**, 95% CI)	2.37; [1.65, 3.41]	< 0.00001

Periprosthetic infection* Obese vs non-obese	2	2404	37	59	OR (M – H, Fixed, 95% CI)	1.31; [0.68, 2.55]	0.42
Infection* Obese vs normal	4	4406	37	25	OR (M – H, Fixed, 95% CI)	1.50; [0.74, 3.05]	0.27
Infection Morbidly obese vs non-obese	5	158 473	3673	52	OR (M – H, Fixed, 95% CI)	5.04; [4.70, 5.39]	< 0.00001
Infection DM vs no DM	3	82 771	331	65	OR (M – H, Fixed, 95% CI)	1.26; [0.97, 1.64]	0.08
Urinary Tract Infection (ALL) Obese vs non-obese	2	4351	43	0	OR (M – H, Fixed, 95% CI)	0.88; [0.48, 1.61]	0.68
Pneumonia DM vs no DM	2	80 183	560	0	OR (M – H, Fixed, 95% CI)	1.38; [1.14, 1.67]	0.001
Venous thromboembolism Obese vs non-obese	5	188 733	2107	72	OR (M – H, Fixed, 95% CI)	3.92; [3.59, 4.28]	< 0.00001
Venous thromboembolism### Obese vs non-obese (removal of heavily weighted study)	4	44 494	179	55	OR (M – H, Fixed, 95% CI)	2.40; [1.72, 3.36]	< 0.00001
Venous thromboembolism# Obese vs non-obese	5	188 733	2107	72	OR (M – H, **Random,** 95% CI)	2.64; [1.66, 4.22]	< 0.00001

Venous thromboembolism** Morbidly obese vs non-obese	3	156944	1494	55	OR (M – H, Fixed, 95% CI)	5.46; [4.91, 6.07]	< 0.00001
Venous thromboembolism** Morbidly obese vs non-obese### (removal of heavily weighted study)	2	36 669	118	57	OR (M – H, Fixed, 95% CI)	3.35; [1.97, 5.71]	< 0.00001
VTE (pulmonary embolism only) DM vs no DM (Meta-analysis of effect estimates)	3	-	-	38	OR (I – V, Fixed, 95% CI)	1.17; [0.94, 1.44]	0.15
Dislocation Obese vs non-obese (ALL)	4	151 909	3610	0	OR (M – H, Fixed, 95% CI)	2.51 [2.35, 2.69]	< 0.00001
Dislocation Morbidly obese (BMI > 40.0) vs non-obese	2	126 925	2673	0	OR (M – H, Fixed, 95% CI)	2.96 [2.26, 3.23]	< 0.00001
Periprosthetic facture Obese vs non-obese	3	153920	2544	52	OR (M – H, Fixed, 95% CI)	1.94; [1.79, 2.10]	< 0.00001
Periprosthetic facture Obese vs non-obese### (removal of heavily weighted study)	2	9681	81	61	OR (M – H, Fixed, 95% CI)	2.49; [1.60, 3.88]	< 0.00001

Fracture** Morbidly obese vs non-obese	4	128 354	1911	42	OR (M – H, Fixed, 95% CI)	2.01; [1.80, 2.25]	<0.0001
Fracture** Morbidly obese vs non-obese### (removal of heavily weighted study)	3	7979	63	0	OR (M – H, Fixed, 95% CI)	3.74 [2.14, 6.55]	<0.0001
Pain scores (VAS – Pain) Obese vs non-obese	2	124	-	0	MD (I – V, Fixed, 95% CI)	1.13; [0.21, 2.06]	0.02
ASES functional score Obese vs non-obese	3	390	-	61	MD (I – V, Fixed, 95% CI)	-0.80; [-4.57, 2.97]	0.68
Abduction functional core Obese vs non-obese	3	379	-	53	MD (I – V, Fixed, 95% CI)	-0.78; [-7.27, 5.71]	0.81
External rotation functional score Obese vs non-obese	3	379	-	0	MD (I – V, Fixed, 95% CI)	-1.41; [-5.11, 2.29]	0.45
Unscheduled return to theatre Obese vs non-obese	3	5066	80	0	OR (M – H, Fixed, 95% CI)	0.74; [0.44,1.24]	0.26
Revision (ALL) Obese vs non-obese	4	151 979	5252	58	OR (M – H, Fixed, 95% CI)	1.52; [1.43, 1.61]	<0.0001
Revision (ALL) Obese vs non-obese###	3	7740	334	0	OR (M – H, Fixed, 95% CI)	1.99; [1.58, 2.50]	<0.0001

(removal of heavily weighted study)							
Revision Morbidly obese vs non-obese	3	127 009	4161	55	OR (M – H, Fixed, 95% CI)	1.62; [1.49, 1.75]	<0.0001
Revision Morbidly obese vs non-obese[###] (removal of heavily weighted study)	2	7979	63	0	OR (M – H, Fixed, 95% CI)	3.74; [2.14, 6.55]	<0.0001
Mortality (ALL) Obese vs non-obese	5	37 004	45	0	OR (M – H, Fixed, 95% CI)	1.79 [0.79, 4.03]	0.16
Mortality DM vs no DM	2	69 669	101	0	OR (M – H, Fixed, 95% CI)	2.93; [1.97, 4.35]	< 0.00001

ASES = American Shoulder and Elbow Score; **CI** = confidence interval; **DM** = diabetes mellitus; **H – M** = Mantel – Haenszel; **I – V** = inverse variance; **LoS** = length of stay; **MD** = mean difference; **OR** = odds ratio; **Random** = random-effects model; **VAS – Pain** = Visual Analogue Scale for Pain; **VTE** = venous thromboembolism; **Vs.** = Versus.

(ALL) = All studies that reported this outcome were combined in the meta-analysis comparing BMI < 30.0 versus ≥ 30.0, despite variations in individual study BMI groupings.

Body Mass Index (kg/m^2) Groups:
Normal: < 25.0, *Overweight:* 25.0 – 29.9, *Obese:* 30.0 – 39.9 (or *Obese class 2:* 35.0 – 39.9), *Morbidly obese:* ≥ 40.0; *Non-obese:* < 30.0

*****Morris et al.[167] BMI group for *obese* = BMI > 30.0 kg/m^2

******Griffin et al.[164] BMI group for *morbidly obese* = BMI > 40.0 kg/m^2

[#] Sensitivity analysis – Random Effects Model when there was substantial or statisically significant hetrogeneity:

- Blood transfusion: Obese vs non-obese (ALL); obese class 2 vs normal.
- Blood transfusion: DM vs no DM
- VTE - Obese Vs. Non-obese

Sensitivity analysis – Excluding TEA site studies

- Blood transfusion - Obese vs non-obese (ALL) (random and fixed-effects models)

Sensitivity analysis – Removal of heavily weighted study

- VTE – Obese vs non-obese
- VTE - Morbidly obese vs non-obese
- Periprosthetic Fracture - Obese vs non-obese
- Fracture - Morbidly obese vs non-obese
- Revision (ALL) - Obese vs non-obese
- Revision - Morbidly obese vs non-obese

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