Should We Avoid Shoulder Surgery In Wheelchair Users?: A Systematic Review of Outcomes and Complications

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Abstract

Introduction

The prevalence of shoulder pathology in wheelchair dependent patients is high. The shoulder joint is critical for maintaining independence but traditionally there has been reluctance to offer surgical intervention in view of perceived poor outcomes. The aim of this study was to provide patients and surgeons with a realistic overview of outcomes following surgical intervention for shoulder pathology.

Methods

A systematic review of the online databases Medline and EMBASE was performed in September 2017. Studies reporting functional outcomes, complications or rate of revision surgery after shoulder surgery in patients' dependent on wheelchair for mobility were included. A narrative synthesis of the studies and appraisal using the MINORS tool was performed.

Results

The search strategy identified 11 eligible studies; 7 assessed rotator cuff repair and 4 shoulder arthroplasty. Six of the seven studies reporting on rotator cuff repairs demonstrated improvement in pain, range of motion and functional outcomes with a re-tear rate between 12% and 39%. Although total shoulder arthroplasty and hemiarthroplasty reportedly improved pain and function, the subsequent risk of rotator cuff failure was reported up to

100%. The two studies assessing reverse arthroplasty demonstrated significant improvement in function and pain with the largest series reporting a 15.8% failure rate.

Conclusion

Rotator cuff repairs and reverse shoulder arthroplasties performed in wheelchair users are associated with significant functional improvement and a slightly higher complication profile to those performed in ambulatory patients. This review provides a resource to aid surgeons and patients in holding realistic expectations following shoulder surgery in wheelchair users.

Keywords

Shoulder

Rotator cuff

Shoulder arthroplasty

Wheelchair user

Wheelchair dependence

Introduction

Shoulder pathology in wheelchair dependent patients is very common. The prevalence of pain and restricted movement in this population is reported to occur in 33% to 62% of individuals [1, 2]. The high prevalence of shoulder complaints is thought to be due to the overuse of the glenohumeral joint [1] especially during propulsion and transfers [3-6]. A biomechanical study demonstrated that the vertical forces acting on the shoulder increase by more than 360% during these movements [3]. This upward force is likely to cause increased strain on the rotator cuff tendons with subsequent risk of degeneration and injury. This may explain the reported four-fold higher incidence of rotator cuff lesions in wheelchair users (63% vs 15%) compared to ambulatory individuals [7]. Akbar et al. reported that rotator cuff tears were present in 49% of wheelchair users of which 70% were full thickness and all involved the supraspinatus [8]. Risk factors for developing tears were found to be patient age and period of wheelchair dependence [8], the prevalence increased from 30% to 50% at five years to 70% at 20 years [9, 10].

Shoulder function is critical for wheelchair users to maintain independence. Even in those who use electric chairs it remains important for weight-bearing during transfers [5]. The loss of shoulder function can lead to decline in mood and social integration [11], even small improvements to range of motion have been found to return patients to key activities of daily living [12]. This reliance on the shoulder may explain the high expectations that wheelchair users have from surgery [13]. However traditionally there has been a reluctance of surgeons to offer intervention in view of the prolonged immobilisation, the perceived poor outcomes and the loss of independence that can occur as a result of prolonged post-operative immobilisation [1, 14, 15]. The aim of this systematic review was to determine whether the traditional reluctance to avoid shoulder surgery in wheelchair users is supported by the available evidence specifically relating to functional outcomes, complications and the rate of revision surgery following common shoulder procedures.

Methods

A systematic review of the literature was conducted in accordance with the PRISMA guidelines (see Table 1) [16] using the online databases Medline and EMBASE. The review was registered on the PROSPERO database on 10th September 2017. The searches were performed independently by two authors on 18th February 2018 and repeated on 20th February 2018 to ensure accuracy. Any discrepancies were resolved through discussion between these two authors, with the senior author resolving any residual differences. The EMBASE search strategy is illustrated in Table 2. Keywords used during the search included; "shoulder", "glenohumeral joint", "acromioclavicular joint", "rotator cuff injury", "arthroscopic surgery", "arthroscopy", "weight bearing shoulder" and "wheelchair." A flow chart of the search strategy is shown in Figure 1.

Only studies that were published in English were considered for eligibility. Both cases series and comparative studies reporting outcomes of any surgical procedure for shoulder pathology in patients' dependent on wheelchair for mobility were included. Studies reporting only the incidence or causes of shoulder pathology in these patients were excluded. The study must have reported functional outcomes, complications or the rate of revision surgery to be eligible for inclusion. In addition, only primary research was considered for review with any abstracts, comments, review articles and technique articles excluded. The search strategy identified 11 studies eligible for inclusion; 7 studies assessed rotator cuff repair and subacromial decompression surgery [13-15, 18-21] and 4 studies assessed shoulder arthroplasty [22-25].

Data from the included studies was extracted and analysed according to surgical intervention; rotator cuff repair and shoulder arthroplasty. Mean improvements in functional scores and rates of complications, re-tears and revision surgery were presented. Only data included in the published articles were included in the review. Due to study heterogeneity only a narrative synthesis was performed; neither sub-group nor a meta-analysis was performed. The studies were appraised independently by two authors using the Methodological index for non-randomised studies (MINORS) tool [17], however formal evaluation of study bias was not undertaken.

Results

The total number of participants in all studies was 170; subacromial decompression and rotator cuff studies (n=138) and shoulder arthroplasty case series (n=32). Concise details of the included studies are given in Tables 3 and 4 which also summarise the outcomes of surgery.

Rotator cuff repair

Kerr et al. performed the largest case series and reported results following arthroscopic rotator cuff repair [20]. Of the 61 patients who underwent surgery 79% were paraplegic secondary to a spinal cord injury. Postoperatively patients were restricted to 6 weeks of passive movement and the use of an electric wheelchair, strengthening exercises commenced at 12 weeks. A mean functional improvement was seen at a mean of 46 months follow up; ASES from 56 to 92 and Constant score 50 to 80. All patients underwent an USS during follow up and a re-tear was demonstrated in 39% of cases, of these 61% were full thickness and 28% required revision surgery. Although the study had some limitations including being a single centre study and having a 24% loss to follow up. It provided the only series to assess solely arthroscopic repair and contained a high volume of patients over the five-year study period.

Jung et al. reported the outcomes of 16 patients undergoing an open rotator cuff repair in addition to either an open or arthroscopic subacromial decompression over a 17-year study period [19]. Patients were restricted to passive motion for four weeks before commencing active motion at 6 weeks. The most common causes of paraplegia were poliomyelitis (60%) and spinal cord injury (27%). The authors reported a significant increase in functional scores at mean of 32 months; ASES 53 to 85 ($p<0.001$) and Constant score 48 to 75 ($p<0.001$). Patients had either an MRI or USS at one year when 2 patients were found to have a re-tear (12%); further imaging at final follow up was not available.

Popowitz et al. studied 8 patients undergoing rotator cuff repair following spinal cord injuries over a six year period, restricting patients to passive motion for the first 6 weeks postoperatively [21]. A mean improvement in ASES (34 to 84) was demonstrated at a mean of 40 months, in addition forward flexion (133 to 167), abduction (147 to 168) and external rotation (62 to 66) all improved. The authors gave further details of only 3 cases, one case suffered a re-tear of the supraspinatus at 12 months but exact details of re-tear rates were not reported.

Hanada et al. reported the outcome from open rotator cuff repair in four shoulders of patients with poliomyelitis using a postoperative regime of passive motion and avoiding transfers for the first 8 weeks [18]. The authors demonstrated improvement in pain and range of motion in 75% of the patients; one patient suffered a re-tear at two years and although underwent a subsequent superior capsular reconstruction remained in severe pain and had reduced motion at final follow up.

Robinson et al. reported six cases of shoulder impingement in patients with spinal cord injuries [15]. All six underwent open subacromial decompression and four patients underwent simultaneous open rotator cuff repair. Rehabilitation varied from 1 to 3 weeks of passive movement. Patients were followed up for between 1 and 2 years in which time the mean range of motion had improved (flexion 40°, abduction 25° and external rotation 60°). The mean time for patients to be pain free was eight weeks, all patients returned to independence but the re-tear rate was not reported.

Fattal et al. performed a prospective case series of 38 shoulders who had various surgical interventions for shoulder pathology after a spinal cord injury and compared them against 25 shoulders who had been managed non-operatively [13]. 87% of procedures were performed arthroscopically and these included 20 rotator cuff repairs, 37 subacromial decompressions and 18 biceps tenodesis. Postoperative rehabilitation varied between cases and the exact details of postoperative restrictions were not given. The authors concluded that postoperative results demonstrated functional stability and satisfaction in terms of pain relief. The mean pain intensity at rest and during daily movements was lower after surgery 0 +/- 1.3 (range 0 to 6) and 2 +/- 2.2 (range 0 to 7) compared to non-operative treatment 1.8 +/- 2 (range 0 to 6) and 5.1 +/- 2.9 (range 0 to 8) respectively. Satisfactory resistance in supraspinatus (100% vs 55%) and infraspinatus (100% vs 77%)) were higher in the operative group, although the definition of what quantified satisfactory resistance is not clearly defined. Those undergoing rotator cuff repair had a mean satisfaction index of 8.5 (range 0 to 10). The decision to perform surgical intervention was made by a multidisciplinary team although further information regarding this process was not supplied. These details are required to know whether only those patients who had failed non-operative treatment were considered for surgery or if certain conditions were more likely to be managed surgically which would risk the introduction of selection bias. Additional limitations included the number of different surgical procedures reported, the undefined rehabilitation regime, the wide variation in follow up and the lack of a validated functional outcome measure.

Goldstein et al. also reported no improvement in pain, ROM and activities of daily living in five patients following open cuff repair but only followed up all of their patients for 10 weeks reporting on only three patients at final follow up [14].

Shoulder arthroplasty

Hattrup et al. retrospectively reported on 6 patients (3 poliomyelitis, 1 transverse myelitis, 1 spinal bifida and 1 familial spastic paraparesis) undergoing shoulder arthroplasty over a 24-year period [23]. Five patients underwent a total shoulder arthroplasty and the final patient had a stemmed hemiarthroplasty. Patients were restricted to passive motion for 6 weeks and transfers allowed from 8 weeks. At a mean of 84 months the pain had improved in 83% and the majority reported either satisfactory or excellent results. However, during follow up all patients' radiographs demonstrated either superior or anterior translation of the humeral head suggesting all had subsequent rotator cuff tears. In addition, one patient suffered a greater tuberosity fracture requiring revision and a second patient suffered a significant brachial plexopathy. De Loubresse et al. reported a case series of five patients (4 osteoarthrosis and 1 avascular necrosis) of whom three had preoperative rotator cuff tears [22]. Four patients underwent a total shoulder arthroplasty and one a hemiarthroplasty, the postoperative rehabilitation regime was not described. Pain and function improved (ASES 28 to 37 and Constant score 30 to 52) but follow up was for only 30 months. Two patients suffered a complication requiring glenoid revision at 2 days and 30 months respectively. In the first case, the postoperative radiographs demonstrated that the glenoid implant locking screws had not been tightened. In the second case, the single cemented glenoid implant migrated at 30 months postoperatively causing a sudden and dramatic deterioration in the pain and function of the shoulder. Patients did not undergo USS or MRI scan during follow up period so the subsequent rotator cuff tear rate is unknown.

Kemp et al. retrospectively reported on 19 shoulders undergoing reverse arthroplasty with a mean age of 72 years (range 59-84) [24]. 75% were suffering from rotator arthropathy and the remainder from osteoarthritis. Neurological impairment was responsible for wheelchair dependence in half (poliomyelitis and spinal cord injury) with the remainder secondary to lower extremity impairment (severe arthritis or amputation). Patients were treated in a sling for the first 3 weeks post-operatively, then passive motion commenced until 6 weeks and weight-bearing from 12 weeks. Final follow up data was available in 12 patients; patients were followed up for a mean of 40 months and functional scores including Constant and ASES significantly improved ($p<0.05$). The failure rate was 15.8% with 2 cases of instability and 1 case of glenoid baseplate loosening. In addition, one patient suffered a peri-prosthetic fracture and the rate of notching was 42%. Ueblacker et al. reported a patient with syringomyelia undergoing bilateral reverse shoulder arthroplasty, postoperatively shoulder movement was restricted for 1 week and then gradually increased [25]. The patient was followed up for 24 months in which time the patients pain resolved, range of motion improved and daily functional score improved from 4/15 to 9/15 on the right and 3/15 to 9/15 on the left. Further details of the functional score used are not provided or referenced in the article. At three months one of the glenoid screws in right shoulder had to be changed for loosening but otherwise no other complications were reported.

Appraisal of the evidence

The eleven studies consisted of 10 case series and one retrospective comparative study thus providing level IV evidence. All studies were appraised using the MINORS criteria (Table 5) which consists of twelve indicators of quality with the mean score for the included studies being 4.7 (range 3 to 6). Aspects of study methodology that were performed consistently well included clear definition of study aim, clear identification of study population, appropriate outcome measures and follow up. These allowed the reviewers to identify relevant studies for inclusion and collate clinically relevant data. However, there were some weaknesses that were consistently identified during the appraisal process. The vast majority of studies lacked a control group which restricted comparison of surgical treatment against results that could be achieved with a non-operative approach. The lack of prospective sample size calculations and adequate statistical testing limited the ability of studies to demonstrate statistically significant results. The failure of the studies to clarify if the assessors were either blinded or independent risks the introduction of assessor bias. These methodological issues need to be considered when interpreting the results.

Discussion

This systematic review did not find any evidence to support the perception [1, 14, 15] that rotator cuff surgery in wheelchair users is associated with a high incidence of poor outcomes. In contrast, rotator cuff repair in wheelchair users has been shown to improve pain, range of motion and functional outcomes in the short [13, 15] and midterm [18-21]. In addition, the re-tear rate at midterm follow up ranges between 12% and 39% [19, 20]. These figures are comparable to previous studies assessing rotator cuff repair in ambulatory individuals which have shown a re-tear rate from 17% to 46% [16, 26] suggesting that wheelchair users may not be at an increased risk of early re-tear. Three patients were reported to undergo revision rotator cuff repair in all studies during follow up (2.2%). However, the follow up of the studies ranged from 18 to 60 months and it is possible that both the re-tear and revision rates would increase with time due to ongoing weight-bearing through the shoulder.

The results of this systematic review also demonstrate that total shoulder arthroplasty and hemiarthroplasty can improve pain and function in wheelchair users [22, 23] but they suggest that the risk of subsequent cuff failure is high. Hattrup et al. [23] reported that all six cases had radiological evidence of cuff failure at follow up. Rotator cuff failure has the potential to reduce function and increases the need for re-intervention although the reviewed studies to do not explore the effects of these subsequent cuff failures. Reverse shoulder arthroplasty has been successful in rheumatoid patients who have a similarly high risk of subsequent rotator cuff failure [27]. The concern regarding subsequent rotator cuff failure in wheelchair users makes reverse shoulder arthroplasty an attractive option particularly because the re-operation rate does not appear to be excessive. Kemp et al. reported a 15.8% failure rate in the largest case series at a mean follow-up of 40 months (range 22-66) [24]; this included one baseplate dislocation and two cases of glenohumeral instability although none required revision surgery. This failure rate was comparable to the 15% reported by Farshad et al. in 441 reverse shoulder arthroplasties performed in an ambulatory population [28]. In addition the two studies reporting reverse shoulder arthroplasty in wheelchair dependent patients demonstrated significant improvement in function and pain [24, 25].

Previous authors have suggested that there is a traditional reluctance to offer surgical interventions for wheelchair users with shoulder pathologies [1, 14, 15] as significant restriction in shoulder use will limit patient's independence making them reliant on carers postoperatively. The evidence analysed in this review suggests that wheelchair users can benefit in terms of functional improvement and pain relief with slightly higher complication profiles following rotator cuff repair and reverse shoulder arthroplasty. Therefore, after adequate counselling, patients deemed appropriate should be considered for surgical intervention. This conclusion is in consensus with Fattal et al. who stated that given increasing prevalence of rotator cuff lesions in this population, it is paradoxical to be reluctant to perform shoulder surgery [13]. The period of immobilisation and rehabilitation is an important factor when counselling patients regarding surgical intervention, Fattal et al. reported 28% of patients initially refused surgical intervention with one of the commonest reasons being this fear of increased postoperative dependence [13]. In the studies reviewed the period of passive range of motion varied from 1 to 8 weeks after rotator cuff repair but was more uniform at around 6 weeks after arthroplasty. However, the optimal period of time in which transfers or manual propulsion in wheelchair users should be avoided after surgery has not been studied and remains unknown.

The limitations of this systematic review include the overall quality of the included studies. The case series provide only low quality evidence with variation in methodology as demonstrated by the MINOR criteria in Table 5. The numbers of patients included in the reviewed studies is low which is likely to be a result of this being a rare presentation. This is reflected in the long study periods (up to 24 years) and the low numbers reported even in multicentre studies, which risks significant changes to other aspects of practice over time. Given these limitations further high quality studies are required to confirm the conclusions drawn in this systematic review. Future direction for research should compare the outcomes of rotator cuff repair against non-operative treatment, define the optimal period of immobilisation postoperatively for the different surgical interventions and analyse the long-term survival data of reverse shoulder arthroplasty in this cohort of patients.

Conclusion

Rotator cuff repair in wheelchair users is associated with high satisfaction with pain relief, significant functional improvement and broadly comparable re-tear rates in the midterm to those performed in ambulatory individuals. Total shoulder arthroplasty can improve symptoms but is associated with a high risk of subsequent cuff failure. Reverse shoulder arthroplasty seems to have comparable outcomes and a similar complication profile to those performed for cuff arthropathy in ambulatory patients but long-term follow up data is lacking.

This review demonstrates that rotator cuff repair and reverse shoulder arthroplasty in wheelchair dependent patients is associated with good pain relief and improved function without a high complication or re-operation rate. This suggests that the general reluctance to offer wheelchair dependent patients shoulder surgery is unfounded.

Conflict of Interest and Source of Funding

Professor A Saithna is currently a consultant for Arthrex.

Neither author has any additional financial, consultant, institutional and other relationships that might lead to bias or a conflict of interest.

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Figure 1: Flow diagram of review process

Table 1: PRISMA Checklist

Table 2: Search strategy for EMBASE

Table 3 – Summary of studies reporting rotator cuff repairs in wheelchair dependent patients

Table 4 – Summary of studies reporting shoulder arthroplasty in wheelchair dependent patients

Table 5: Methodological items for non-randomized studies (MINORS) Scores for transtendinous repair case series

Figure 1: Flow diagram of review process

MEDLINE search

N = 158

EMBASE search

Searches combined

59 Duplications

After title review

N = 24

296 Incorrect population

145 Incorrect intervention

88 Secondary article

58 abstract only

After abstract review

8 Incorrect population

5 Secondary article

Table 2: Search strategy for EMBASE

Number	**Search term**	**Results**
1	shoulder/ or shoulder.mp	93486
2	glenohumeral joint.mp.	2842
3	acromioclavicular joint/	2202
4	rotator cuff injury/ or rotator cuff/	6883
5	shoulder arthroscopy/ or arthroscopy/	18607
6	manual wheelchair/ or wheelchair/	8754
7	weight-bearing shoulder.mp.	8
8	1 or 2 or 3 or 4 or 5	109353
9	6 or 7	8761
10	1 and 4	522
11	limit 10 to english language	512

Table 3 – Summary of studies reporting rotator cuff repairs in wheelchair dependent patients

ly	Population	Intervention (s)	Post-op therapy	Follow up	Outcome Measures	Results	Complications
r et al. **rospective series**	N = 61 Age 55 (27 – 89)	Arthroscopic RCR ◻ 25% single tendon ◻ 52% 2 tendons ◻ 23% 3 tendons 84% biceps tenotomy	6 weeks electric wheelchair and passive 12 weeks strengthening	46 months (24-82)	ASES Constant SSV USS	ASES 56 to 92 Constant 50 to 80 Mean postop SSV score 84%	39% retear ◻ 11% FT requiring surgery ◻ 13% FT non-operatively treated ◻ 15% partial tear
g et al. **rospective series**	N = 16 Age 61 (44-78) 11 massive, 3 large and 2 medium tears	14 open SAD and RCR 2 arthroscopic SAD and open RCR	8 weeks abduction brace 4 weeks passive 4- 6 weeks active assisted 6 weeks active	32 months (13-71)	ASES Constant VAS pain ROM MRI and USS	Improvement ◻ ASES 53 to 85 ◻ Constant 48 to 75 ◻ Flexion 115° to 148° ◻ ER 21° to 41°	12% re-tear at 12 months, but none required re-intervention
al et 3] **spective series**	N = 38 Age 54 (28 to 69)	Surgery (20 RCR, 37 SAD, 17 tenodesis) Comparative group non-operatively treated	Varied depending on procedure	18 months (2 to 35)	Pain ROM Functional independenc e measure (FIM)	Operative vs non-operative groups ◻ Pain at rest 0 (0-6) vs 1.8 (0 to 6) ◻ Max pain 1.8 (0-6) vs 5.1 (0-8) ◻ Supraspinatus strength (100% vs 55%0 ◻ Infraspinatus strength (100% vs 77%) Satisfaction of cuff repair 8.8 (0-10)	Not reported
owitz et 21] **rospective series**	N = 8 Age 48.6 (41-57)	Arthroscopic SAD and mini open RCR	6 weeks passive Active movement from 8 weeks	40 months (12-72)	ASES ROM	ASES 34.1 to 84.3 FF 133° to 167° Abduct 147° to 168° ER 62° to 66°	1 (12.5%) re-tear (3cm) at 12 months managed non-operatively
dstein et 14] **rospective series**	N = 5 46-72	Open RCR and SAD	6 weeks passive From 6 weeks active ROM	Up to 5 years	ROM Pain Function in ADLs	No improvement in any patient at 10 weeks 3 seen at 5 years no improvement	Not reported
ıada et al.	N = 4 Age 52.8 (47-	Open RCR and SAD 2 large tear	8 weeks passive and avoiding	4.7 yrs (2.5 – 11)	Pain ROM	All had improvement in pain and ROM initially	1 revision at 2 years for re-tear requiring superior capsular

Table 4 – Summary of studies reporting shoulder arthroplasty in wheelchair dependent patients

Study	Population	Diagnosis and intervention (s)	Post-op therapy	Follow up	Outcome Measures	Results	Complications
Kemp et al. [24] Retrospective case series	N = 19 Age 72 (59-84)	Reverse arthroplasty	3 weeks sling Passive 3-6 weeks Active from 6 weeks Strengthening and WB 12 weeks	40 months (22-66)	SPADI score Constant score ASES UCLA SST SF12 ROM VAS pain Complications	Significant improvement ($p<0.05$) ➢ SPADI 58 ➢ Constant 42 ➢ ASES 45 ➢ UCLA 18 ➢ SST 5 ➢ Flexion 44° ➢ ER 29°	15.8% failure rate ◻ 1 baseplate loosening ◻ 2 instability ◻ None required reintervention Notching 42% 1 periprosthetic fracture 33 months
Hattrup et al. [23] Retrospective case series	N = 6 Age 69 (54-87)	5 Total shoulder arthroplasty (2 partial, 2 small and 1 large cuff tear) 1 hemiarthroplasty (massive cuff tear)	6 weeks passive 6-8 weeks active assisted From 8 weeks transfers	84 months (24-200)	Complications ROM Neer classification	Pain 67% good relief Flexion 30° and ER 21°	Complications ➢ All had evidence of cuff failure during follow up ➢ 1 greater tuberosity fracture requiring revision ➢ 1 brachial plexopathy
De Loubresse et al. [22]	N = 5 Age 70	4 total shoulder arthroplasty	Not described	30 months (24-31)	Constant score ASES	Improvement ➢ Constant 30 to	2 complications ➢ 1 loose glenoid

Table 5: Methodological items for non-randomized studies (MINORS) Scores

	Kerr [20]	Jung [19]	Popowitz [21]	Hanada [18]	Robinson [15]	Fattal [13]	Goldstein [14]	Hattrup [23]	De Loubresse [22]	Kemp [24]	Ueblacker [25]
clearly stated aim	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No
clusion of consecutive tients	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
dpoints appropriate to aim of the study	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
biased assessment of study endpoint	Yes	No	No	No	No	No	No	No	No	Yes	No
llow-up period propriate to the aim of study	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
ss to follow up less in 5%	No	Yes	No	Yes	Yes	Yes	No	Yes	Yes	No	Yes
ospective calculation of study size	No	No	No	No	No	No	No	No	No	No	No

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4-5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Table 2
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5-6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5-6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5-6
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	5-6

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