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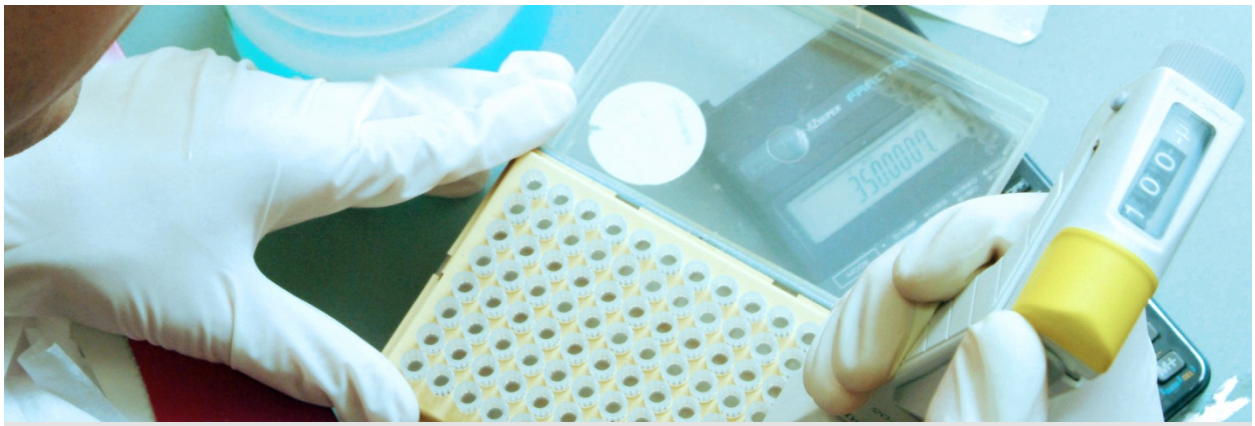
Comparative effectiveness, safety, and costs of surgical versus non-surgical treatment in patients with full-thickness rotator cuff tears: a systematic review and health economic assessment



Final Report

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Abbreviations

ASES	American shoulder and elbow surgeons score (0 – 100 points, 100 = best outcome)
BIA	Budget impact analysis
CHF	Swiss franc
CHOP	Swiss operation classification (schweizerische Operationsklassifikation)
CI	Confidence interval
CMS	Constant-Murley score (0 – 100 points, 100 = best outcome); subscores for: pain (0 – 15 points, 15 = best outcome), range of motion (0 – 40 points, 40 = best outcome), strength (0 – 25 points, 25 = best outcome)
CONSORT	Consolidated standards of reporting trials
COPACABANA	Conservative vs. operative treatment of atraumatic rotator cuff rupture, anatomically and radiology after one year study
DSST	Dutch simple shoulder test (0 – 12 points, 12 = best outcome)
EQ-5D	European quality of life - 5 dimensions
EUR	Euro
GBP	British pound sterling
GP	General practitioner
GRADE	Grading of Recommendations, Assessment, Development and Evaluation
HTA	Health technology assessment
ICD	International classification of diseases
ICER	Incremental cost-effectiveness ratio
ICTRP	International Clinical Trials Registry Platform
ITT	Intention-to-treat
JOA	Japanese orthopaedic association score (0 – 100 points, 100 = best outcome)
LYG	Life years gained
MCID	Minimal clinically important difference
MD	Mean difference
MRA	Magnetic resonance arthrography
MRI	Magnet resonance imaging
NRS	Non-randomised controlled study
NSAID	Non-steroidal anti-inflammatory drugs
OR	Odds ratio
PICO	Patients/Population, intervention, comparator, outcome
PRISMA	Transparent reporting of systematic reviews and meta-analyses
PROSPERO	Prospective register of systematic reviews
QALY	Quality-adjusted life year
QoL	Quality of life
RC-QoL	Rotator cuff quality-of-life
RCT	Randomised controlled trial
RD	Risk difference
RevMan	Review manager

ROBINS-I	Risk of bias in non-randomised studies of interventions
ROM	Range of motion
RR	Risk ratio
SD	Standard deviation
SF-36	Short-form 36
SFSO	Swiss federal statistical office
SHS	Swiss hospital statistic
SMB	Swiss medical board
STROBE	Strengthening the reporting of observational studies in epidemiology
SwissDRG	Swiss diagnosis related group
UCLA	University of California at Los Angeles
UK	United Kingdom
US	Ultrasonography
USA	United States of America
USD	United States dollar
VAS	Visual analogue scale
vs.	Versus
WHO	World Health Organisation

1 Executive summary

1.1 Summary

Objective
The aim of the current evidence synthesis and analysis was to systematically review the comparative effectiveness, safety, and health economic properties of surgical versus non-surgical treatment in patients with full-thickness rotator cuff tears.

Clinical effectiveness and safety
Literature search
Electronic searches for published clinical studies were conducted in five databases (Medline, Science Citation Index Expanded, Cochrane Library, Embase and Sportdiscus) from inception to May 2018. Furthermore, we used relevant studies and systematic reviews to search for additional references, and searches for unpublished and ongoing studies were conducted in ClinicalTrials.gov and the World Health Organisation (WHO) International Clinical Trials Registry Platform (ICTRP).

Study selection
Two reviewers independently screened the titles and abstracts of the 7,908 references identified by the literature search. Full text copies of 154 potentially relevant articles were obtained, and two reviewers independently assessed these articles for inclusion. Patients with traumatic or degenerative full-thickness rotator cuff tears who were treated surgically within randomised controlled trials (RCTs) or non-randomised controlled studies (NRSs) were included. Eligible comparison treatments included no treatment, 'watchful waiting' or any conservative treatment.

Data extraction and synthesis
One reviewer extracted data on study, patient and intervention characteristics, and a second reviewer checked the extracted data. Data from RCTs and NRSs were, due to different mechanisms of bias, analysed separately. The treatment effect for each continuous outcome was expressed as the mean difference (MD) with its 95% confidence interval (95%-CI) and the treatment effect for dichotomous outcomes was expressed as risk ratio with 95%-CI. The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach was used to assess the certainty of evidence.

Results
In total, three RCTs (332 patients) and seven NRSs (667 patients) met the inclusion criteria. (i) In RCTs, the effect estimates for shoulder function measured with the 100-points Constant-Murley Score (CMS) and pain measured with a 10-cm visual analogue scale (VAS) showed statistical significance in favour of surgery when compared to conservative treatment: **Outcome shoulder function** *at 12 months:* MD 6.9 points higher with surgery; 95%-CI 1.6, 12.3 (3 RCTs; moderate certainty of evidence); *at 24 months:* MD 4.4 points higher with surgery; 95%-CI 0.04, 8.8 (2 RCTs; moderate certainty of evidence); *at 60 months:* MD 8.7 points higher with surgery; 95%-CI 1.3, 16.1 (1 RCT; moderate certainty of evidence). Applying a published estimate for the

minimal clinically important difference (MCID) of 10.4 points[1], the observed MDs are below this threshold of clinical relevance, and their 95%-CIs include both values below and above it. **Outcome pain** *at 12 months:* MD 1.1 cm lower with surgery; 95%-CI 0.4, 1.8 (3 RCTs; low certainty of evidence); *at 24 months:* MD 0.9 cm lower with surgery; 95%-CI 0.3, 1.5 (2 RCTs; low certainty of evidence); *at 60 months:* MD 1.3 cm lower with surgery; 95%-CI 0.5, 2.1 (1 RCT; low certainty of evidence). Applying a published estimate for the MCID of 1.4 cm,[2] the observed MDs are below this threshold of clinical relevance, and their 95%-CIs include both values below and above it. (ii) For other patient-relevant outcomes such as shoulder range of motion, muscle strength, quality of life (QoL) and adverse events only very limited data were available, showing no differences between the groups. (iii) Structural outcomes were reported in relation to fatty degeneration, muscle atrophy, tendon retraction, and tear progression. Where data were compared between the surgical and non-surgical groups, the observed differences mostly favoured surgery.

Although the effect estimates of the RCTs and NRSs were similar, the certainty of evidence varied by study type: whereas in RCTs the certainty of evidence was judged to be *moderate to low*, it was judged to be *very low* in NRSs. Overall, the certainty of evidence was hampered by serious imprecision for both bodies of evidence. However, the risk for bias was judged as more serious in the NRSs, because the observed differences between the interventions could be attributable to critical confounding rather than to the effects of the interventions.

Health economic assessment

The health economic assessment consisted of a systematic review of the currently published health economic literature, a *de novo* cost analysis with supplemental cost-effectiveness considerations, and a budget impact analysis (BIA) from a Swiss health insurance law perspective.

Systematic literature review and implications

The results of the systematic review indicated absence of published cost-effectiveness analyses assessing costs per quality-adjusted life year (QALY) or costs per life year gained (LYG). Therefore, it was not possible to extrapolate international cost-effectiveness results and adapt them for Switzerland. In addition, due to a lack of suitable data and information on quality of life of patients undergoing surgery or conservative treatment, it was not possible to perform a proper *de novo* cost-effectiveness analysis.

De novo cost model and results

The model was built on data from the three RCTs identified in the clinical part and reflecting populations of symptomatic full-thickness rotator cuff tears patients, either with degenerative tears (single or multiple tendon tears) or of small to medium sized traumatic tears, with a previous symptom duration of approximately one or 2.5 years, and mostly pre-treated with conservative treatment. The *de novo* cost model assumptions were chosen based on the settings and outcomes of the three available RCTs assessed in the clinical systematic review part, feedback from a group of medical experts involved in this Health Technology Assessment (HTA), feedback from the medical controlling departments of two University hospitals, outpatient costs from the Swiss Tarmed system, inpatient surgery costs from the Swiss Diagnosis Related Group (SwissDRG) system, drug prices from the list of drugs reimbursable by the Swiss statutory health insurance, and information from the international literature.[3-7]

The results of the *de novo* cost analysis suggested that the 6-month costs per person for the initial repair surgery of a full-thickness rotator cuff tear plus subsequent physiotherapy were approximately 10 times higher than for conservative (physiotherapy) treatment alone, in the Swiss setting (CHF 10,458 vs. CHF 1,018), leading to a cost difference of CHF 9,440. Surgery costs of CHF 9,379 constituted the highest cost factor, followed by the costs for physiotherapy (CHF 773 for 18 sessions). Over a time horizon of five years, costs per person for the initial surgery strategy amounted to CHF 10,662, whereas costs for the conservative treatment strategy reached CHF 3,599. The cost difference between the treatment strategies of CHF 9,440 at 6 months decreased to CHF 7,063 at five years. Deterministic sensitivity analysis of the model with a time horizon of five years showed these results to be most strongly influenced by surgery costs, followed by the overall crossover rate at 24 months (crossover from conservative treatment to surgery). All other variables only had a minor impact.

Cost-effectiveness considerations

Since a proper cost-effectiveness analysis was not possible, we determined in supplementary calculations what differences in utilities and QALYs (between the initial surgery strategy and the conservative treatment strategy) over periods of two and five years would be necessary to achieve an incremental cost-effectiveness ratio (ICER) of CHF 50,000 or 100,000 per QALY gained. For an estimated cost difference of CHF 6,992 at two years, a QALY difference of 0.140 and 0.070 would be needed in order to obtain an ICER of CHF 50,000 and CHF 100,000, respectively. At five years, the estimated cost difference of CHF 7,063 would require similar QALY differences (0.141 and 0.071). Based on a simplifying assumption of constant utility differences across the 2-year or 5-year time horizons, a utility difference of 0.070 and 0.035 would be required over a 2-year time horizon to meet an ICER threshold of CHF 50,000 and CHF 100,000, respectively. For a 5-year time horizon, utility differences of 0.028 and 0.014 would be necessary.

Budget impact analysis and results

The aim of the BIA was to investigate the overall costs of full-thickness rotator cuff tear surgeries in comparison with conservative treatment in Switzerland. Estimation of the number of full-thickness rotator cuff tear surgeries in Switzerland was based on the Swiss Hospital Statistics (SHS) 2016.[8] The unit costs for the budget impact calculation were based on data from the *de novo* cost analysis. Assuming 5-year treatment costs per patient, we estimated the number of cases undergoing surgery between 2018 and 2022, and the number of cases who underwent surgery up to four years prior to 2018 but who would still require follow-up treatment between 2018 and 2022. It was not possible to estimate the number of patients undergoing conservative treatment in Switzerland, due to lack of suitable data. Considering this, the same number of cases were applied to both the initial surgery and conservative treatment strategies. The resulting costs for the initial surgery strategy would represent the actual costs of full-thickness rotator cuff tear surgery and subsequent physiotherapy in Switzerland. In contrast, the costs for the conservative treatment strategy would represent the potential cost for the same patients in case of initial conservative treatment and a secondary repair surgery for a certain percentage of patients.

The results suggested that total costs for the initial surgery strategy between 2018 and 2022 would reach CHF 659.4 million when only considering 6-month treatment costs for each patient. In case of use of an initially conservative treatment strategy, the total costs would be CHF 64.2

million (i.e. approximatively one tenth compared to surgery). When considering 5-year treatment costs for each patient, total costs for the initial surgery strategy between 2018 and 2022 would reach CHF 672.4 million. The initially conservative treatment strategy for the same number of cases would cost CHF 227.2 million (i.e. approximatively one third if compared to surgery).

Conclusion

In terms of clinical effectiveness and safety, our findings suggest that surgery may be more effective than conservative treatment to improve shoulder function and reduce pain. However, the clinical relevance of the differences is questionable. For other patient-relevant outcomes such as shoulder range of motion, muscle strength, quality of life and adverse events only very limited data were available, which showed no differences between the groups.

The systematic review of the economic literature suggested that there is currently no published cost-effectiveness study addressing the current question (Patients/Population, Intervention, Comparator, Outcomes, PICO).

The *de novo* cost analysis suggested that in the management of full-thickness rotator cuff tears, an initial surgery strategy is much more expensive than an initially conservative treatment strategy, in the short-term and mid-term. Assuming 5-year treatment costs per patient, the BIA results indicated that the current use of full-thickness rotator cuff tear surgery in Switzerland may lead to additional costs in the range of CHF 90 million per year, in comparison with an initially conservative treatment strategy. It was not possible to estimate the total costs of conservative treatment in Switzerland since there is currently no information concerning the utilisation of conservative full-thickness rotator cuff tear treatment. Given the paucity of high-quality and long-term data on clinical outcomes and health related quality of life, it remains unclear whether an analysis over a longer time horizon or including indirect costs related to productivity losses might lead to different health economic results.

Ultimately, it is not possible to judge based on currently available data if the initial surgery strategy might meet frequently assumed cost-effectiveness thresholds (e.g. CHF 50,000 or CHF 100,000 per QALY gained). In this optic, long-term studies investigating treatment effectiveness and the quality of life of full-thickness rotator cuff tear patients after surgery or conservative treatment, are needed. Long-term studies investigating the difference in outcomes for patients with traumatic vs. atraumatic full-thickness rotator cuff tears as well as for single vs. multiple tendon tears would also be important for refined analyses.

1.2 Zusammenfassung

Zielsetzung
Das Ziel der vorliegenden Evidenzsynthese und Analyse war, die relative Wirksamkeit und Sicherheit sowie die gesundheitsökonomischen Charakteristika chirurgischer versus nicht-chirurgischer Behandlung bei Patienten mit kompletten Rotatorenmanschettenrupturen systematisch zu reviewen.

Klinische Wirksamkeit und Sicherheit
Literatursuche
Elektronische Suchen nach publizierten klinischen Studien wurden in fünf Datenbanken durchgeführt (Medline, Science Citation Index Expanded, Cochrane Library, Embase und Sportdiscus), für den Zeitraum von Beginn der Aufzeichnungen bis Mai 2018. Weiterhin verwendeten wir relevante Studien und systematische Übersichtsarbeiten für die Suche nach weiteren Literaturreferenzen. Zusätzlich wurden auf ClinicalTrials.gov and auf der International Clinical Trials Registry Platform (ICTRP) der Weltgesundheitsorganisation (World Health Organisation, WHO) Suchen nach nicht publizierten und nicht abgeschlossenen Studien durchgeführt.

Studienauswahl
Zwei Reviewer sichteten unabhängig voneinander die Titel und Abstracts der 7,908 durch die Literatursuche identifizierten Referenzen. Von 154 potentiell relevanten Artikeln wurden die Volltexte herangezogen. Zwei Reviewer beurteilten diese Artikel unabhängig voneinander auf Erfüllen der Einschlusskriterien. Es wurden Patienten mit kompletten Rotatorenmanschettenrupturen traumatischer oder degenerativer Genese eingeschlossen, die im Rahmen randomisierter, kontrollierter Studien (randomised controlled trials, RCTs) oder nicht-randomsierter, kontrollierter Studien (non-randomised controlled studies, NRSs) chirurgisch behandelt wurden. Zulässige Vergleichsbehandlungen umfassten keine Behandlung, 'beobachtendes Abwarten' und jegliche konservative Behandlung.

Datenextraktion und Synthese
Ein Reviewer extrahierte Daten zu Studien-, Patienten- und Behandlungscharakteristika; ein zweiter Reviewer überprüfte die extrahierten Daten. Daten von RCTs und NRSs wurden - aufgrund unterschiedlicher Mechanismen, die zu Verzerrungen führen können – separat analysiert. Der Behandlungseffekt für jeden kontinuierlichen Ergebnisparameter wurde als mittlere Differenz (MD) mit 95%-Konfidenzintervall (95%-KI) ausgedrückt. Der Behandlungseffekt für dichotome Ergebnisparameter wurde als Risikoverhältnis mit 95%-KI ausgedrückt. Der Grading of Recommendations, Assessment, Development and Evaluation (GRADE)-Ansatz wurde verwendet, um die Sicherheit der verfügbaren Evidenz zu bestimmen.

Ergebnisse
Insgesamt erfüllten drei RCTs (332 Patienten) und sieben NRSs (667 Patienten) die Einschlusskriterien. (i) In RCTs zeigten die Effektschätzungen für Schulterfunktion, gemessen mit dem 100 Punkte Constant-Murley Score (CMS), und Schmerz, gemessen auf einer 10 cm visuellen Analogskala (VAS), statistische Signifikanz zugunsten des chirurgischen Vorgehens im

Vergleich zu konservativer Behandlung: **Ergebisparameter Schulterfunktion** *nach 12 Monaten:* MD 6.9 Punkte höher mit Chirurgie; 95%-KI 1.6, 12.3 (3 RCTs; mittlere Sicherheit der verfügbaren Evidenz); *nach 24 Monaten:* MD 4.4 Punkte höher mit Chirurgie; 95%-KI 0.04, 8.8 (2 RCTs; mittlere Sicherheit der verfügbaren Evidenz); *nach 60 Monaten:* MD 8.7 Punkte höher mit Chirurgie; 95%-KI 1.3, 16.1 (1 RCT; mittlere Sicherheit der Evidenz). Ausgehend von einer publizierten Schätzung für die minimale klinisch relevante Differenz (minimal clinically important difference, MCID) von 10.4 Punkten[1] waren die beobachteten MDs unterhalb des Schwellenwerts für klinische Relevanz, und ihre 95%-KIs schlossen sowohl Werte darunter als auch darüber ein. **Ergebnisparameter Schmerz** *nach 12 Monaten*: MD 1.1 cm niedriger mit Chirurgie; 95%-KI 0.4, 1.8 (3 RCTs; niedrige Sicherheit der verfügbaren Evidenz); *nach 24 Monaten:* MD 0.9 cm niedriger mit Chirurgie; 95%-KI 0.3, 1.5 (2 RCTs; niedrige Sicherheit der verfügbaren Evidenz); *nach 60 Monaten:* MD 1.3 cm niedriger mit Chirurgie; 95%-KI 0.5, 2.1 (1 RCT; niedrige Sicherheit der verfügbaren Evidenz). Ausgehend von einer publizierten Schätzung für die MCID von 1.4 cm² waren die beobachteten MDs unterhalb des Schwellenwerts für klinische Relevanz, und ihre 95%-KIs schlossen sowohl Werte darunter als auch darüber ein. (ii) Für andere patientenrelevante Ergebnisparameter wie Bewegungsbereich der Schulter, Muskelstärke, Lebensqualität (quality of life, QoL) und Behandlungsnebenwirkungen waren nur sehr limitierte Daten verfügbar, die keine Unterschiede zwischen den Behandlungsgruppen zeigten. (iii) Strukturelle Ergebnisparameter wurden hinsichtlich degenerativer Verfettung, Muskelatrophie, Sehnenretraktion und Fortschreiten des Risses berichtet. Soweit chirurgische und nichtchirurgische Behandlungsgruppen verglichen wurden, favorisierten die beobachteten Differenzen meist das chirurgische Vorgehen.
Obwohl die Effektschätzungen für RCTs und NRSs ähnlich waren, variierte die Sicherheit der verfügbaren Evidenz nach Studientyp: während sie bei den RCTs als *mittel bis niedrig* beurteilt wurde, wurde sie bei den NRSs als *sehr niedrig* beurteilt. Insgesamt wurde die Sicherheit der verfügbaren Evidenz bei beiden Evidenzquellen durch schwerwiegende Ungenauigkeit beeinträchtigt. Das Risiko für Verzerrungen wurde jedoch bei den NRSs als schwerwiegender eingestuft, da die beobachteten Unterschiede zwischen den Interventionen mehr auf kritische Konfundierung als auf die Effekte der Interventionen zurückzuführen sein könnten.

Gesundheitsökonomisches Assessment

Das gesundheitsökonomische Assessment bestand aus einer systematischen Review der publizierten gesundheitsökonomischen Literatur, einer *de novo*-Kostenanalyse mit ergänzenden Betrachtungen zur Kosteneffektivität, und einer Budget impact-Analyse (BIA) aus der Perspektive des Schweizerischen Krankenversicherungsgesetzes.

Systematische Literaturreview und Implikationen

Die systematische Review ergab das Fehlen publizierter Kosteneffektivitätsanalysen mit Bestimmung der Kosten pro qualitätsadjustiertem Lebensjahr (quality-adjusted life year, QALY) oder der Kosten pro gewonnenem Lebensjahr (life year gained, LYG). Es war deshalb nicht möglich, internationale Kosteneffektivitätsresultate zu extrapolieren und sie für die Schweiz anzupassen. Ausserdem war es, aufgrund eines Mangels an geeigneten Daten und Informationen zur Lebensqualität chirurgisch oder konservativ behandelter Patienten, nicht möglich, eine adäquate *de novo*-Kosteneffektivitätsanalyse durchzuführen.

De novo-Kostenmodell und Resultate

Das Modell wurde auf Daten der drei RCTs aufgebaut, die im klinischen Teil identifiziert wurden und Population von Patienten mit symptomatischen, kompletten Rotatorenmanschettenrupturen repräsentierten. Die Patienten hatten entweder degenerative Rupturen (Rupturen einzelner oder multipler Bänder) oder kleine bis mittelgrosse traumatische Rupturen, mit einer Symptomdauer von etwa einem oder 2.5 Jahren. Die meisten Patienten waren konservativ vorbehandelt. Die Annahmen des *de novo*-Kostenmodells basierten auf den Settings und Ergebnisparametern der drei verfügbaren, im Rahmen der klinischen systematischen Review untersuchten RCTs, auf Rückmeldungen einer Gruppe medizinischer Experten, die in dieses Health Technology Assessment (HTA) involviert waren, auf Rückmeldungen der Abteilungen für medizinisches Controlling zweier Universitätsspitäler, auf ambulanten Kosten aus dem Schweizerischen Tarmed-Tarifsystem, auf Kosten für stationäre chirurgische Behandlungen aus dem Swiss Diagnosis Related Group (SwissDRG)-System, auf Medikamentenpreisen aus der Liste der durch die Schweizerische obligatorische Krankenpflegeversicherung vergütungsfähigen Medikamente, und auf Informationen aus der internationalen Literatur.[3-7]

Die Ergebnisse der *de novo*-Kostenanalyse legten nahe, dass die Sechsmonats-Kosten einer initialen chirurgischen Behandlung einer kompletten Rotatorenmanschettenruptur mit nachfolgender Physiotherapie im Schweizerischen Setting pro Person etwa zehnmal höher sind als für eine konservative (physiotherapeutische) Behandlung alleine (CHF 10,458 vs. CHF 1,018), was zu einer Kostendifferenz von CHF 9,440 führt. Kosten der chirurgischen Behandlung von CHF 9,379 stellten den höchsten Kostenfaktor dar, gefolgt von den Physiotherapiekosten (CHF 773 für 18 Sitzungen). Über einen Zeithorizont von fünf Jahren beliefen sich die Kosten der initial chirurgischen Strategie auf CHF 10,662, während die Kosten für die konservative Behandlungsstrategie CHF 3,599 erreichten. Die Kostendifferenz zwischen den Behandlungsstrategien von CHF 9,440 nach sechs Monaten reduzierte sich auf CHF 7,063 nach fünf Jahren. Deterministische Sensitivitätsanalysen des Modells mit einem Zeithorizont von fünf Jahren zeigten, dass diese Ergebnisse am stärksten durch die Kosten der chirurgischen Behandlung beeinflusst wurden. Am zweitstärksten wirkte sich die gesamthafte Übergangsrate nach 24 Monaten zwischen den Behandlungsstrategien aus (Übergang von konservativer zu chirurgischer Behandlung). Alle anderen Variablen hatten nur geringen Einfluss.

Überlegungen zur Kosteneffektivität

Da eine eigentliche Kosteneffektivitätsanalyse nicht möglich war, ermittelten wir in ergänzenden Berechnungen, was für Nutzwert- und QALY-Unterschiede (zwischen der initial chirurgischen Strategie und der konservativen Behandlungsstrategie) über Zeiträume von zwei und fünf Jahren nötig wären, um ein inkrementales Kosteneffektivitätsverhältnis (incremental cost-effectiveness ratio, ICER) von CHF 50,000 oder CHF 100,000 pro gewonnenem QALY zu erreichen. Bei einer geschätzten Kostendifferenz von CHF 6,992 nach zwei Jahren wäre eine QALY-Differenz von 0.140 bzw. 0.070 erforderlich, um ein ICER von CHF 50,000 bzw. CHF 100,000 zu erreichen. Nach fünf Jahren würde die geschätzte Kostendifferenz von CHF 7,063 ähnliche QALY-Differenzen (0.141 und 0.071) erfordern. Ausgehend von der vereinfachenden Annahme konstanter Nutzwertdifferenzen über die Zweijahres- oder Fünfjahres-Zeithorizonte wären Nutzwertdifferenzen von 0.070 bzw. 0.035 über den Zweijahres-Zeithorizont erforderlich, um einen ICER-Schwellenwert von CHF 50,000 bzw. CHF 100,000 zu erreichen. Für den Fünfjahres-Zeithorizont wären Nutzwertdifferenzen von 0.028 bzw. 0.014 nötig.

Budget impact-Analyse und Ergebnisse

Das Ziel der BIA war, die gesamthaften Kosten chirurgischer Behandlungen von kompletten Rotatorenmanschettenrupturen im Vergleich zu konservativer Behandlung in der Schweiz zu untersuchen. Die Schätzung der Anzahl chirurgischer Behandlungen von kompletten Rotatorenmanschettenrupturen in der Schweiz basierte auf der Schweizerischen Spitalstatistik 2016.[8] Die Kosten pro Einheit für die Budget Impact-Berechnung basierten auf den Daten der *de novo*-Kostenanalyse. Unter der Annahme, dass pro Patient über fünf Jahre Behandlungskosten anfallen, schätzten wir die Anzahl der Fälle mit einer chirurgischen Behandlung zwischen 2018 und 2022 sowie ausserdem die Anzahl der Fälle, die sich in den vier Jahren vor 2018 einer chirurgischen Behandlung unterzogen und die zwischen 2018-2022 noch Folgebehandlungen brauchen würden. Es war mangels geeigneter Daten nicht möglich, die Anzahl der Patienten zu schätzen, die in der Schweiz konservativ behandelt werden. In Anbetracht dessen wurde die gleiche Fallzahl auf die primär chirurgische und auf die konservative Behandlungsstrategie angewandt. Die sich ergebenden Kosten für die initial chirurgische Strategie repräsentieren die tatsächlichen Kosten der chirurgischen Behandlung kompletter Rotatorenmanschettenrupturen und darauffolgender Physiotherapie in der Schweiz. Die Kosten der konservativen Behandlungsstrategie repräsentieren dagegen die potentiellen Kosten derselben Patienten im Falle einer primär konservativen Strategie und einer sekundären chirurgischen Behandlung bei einem bestimmten Prozentsatz der Patienten.

Es ergab sich, dass die totalen Kosten der initial chirurgischen Strategie zwischen 2018 und 2022 CHF 659.4 Millionen erreichen würden, wenn für jeden Patienten nur die Sechsmonats-Behandlungskosten berücksichtigt würden. Im Falle des Einsatzes einer initial konservativen Behandlungsstrategie wären die totalen Kosten CHF 64.2 Millionen (also etwa ein Zehntel im Vergleich zur Chirurgie). Bei Berücksichtigung der Fünfjahres-Behandlungskosten für jeden Patienten würden die Kosten der initial chirurgischen Strategie zwischen 2018 und 2022 CHF 672.4 Millionen erreichen. Die initial konservative Behandlungsstrategie für die gleiche Anzahl von Fällen würde CHF 227.2 Millionen kosten (also etwa ein Drittel im Vergleich zur Chirurgie).

Schlussfolgerung

Hinsichtlich der klinischen Wirksamkeit und Sicherheit legen unsere Ergebnisse nahe, dass die chirurgische Behandlung bezüglich Verbesserung der Schulterfunktion und Schmerzreduktion möglichweise effektiver ist als die konservative Behandlung. Die klinische Relevanz der Unterschiede ist jedoch fraglich. Für andere patientenrelevante Ergebnisparameter wie Bewegungsbereich der Schulter, Muskelstärke, Lebensqualität und Behandlungsnebenwirkungen waren nur sehr begrenzte Daten verfügbar, die keine Unterschiede zwischen den Behandlungsgruppen zeigten.

Die systematische Review der ökonomischen Literatur ergab, dass es derzeit keine publizierte Kosteneffektivitätsstudie gibt, die die vorliegende Fragestellung (Patients/Population, Intervention, Comparator, Outcomes, PICO) adressiert.

Die *de novo*-Kostenanalyse ergab, dass bei der Behandlung von kompletten Rotatorenmanschettenrupturen eine initial chirurgische Therapie viel teurer ist als eine initial konservative Therapie. Dies gilt kurz- und mittelfristig. Ausgehend von Fünfjahres-Behandlungskosten pro Patient zeigten die BIA-Resultate, dass der gegenwärtige Einsatz der Rotatorenmanschetten-Chirurgie in der Schweiz möglicherweise zu Zusatzkosten in einer Grössenordnung von CHF 90 Millionen pro Jahr führt, im Vergleich mit einer initial

konservativen Behandlungsstrategie. Es war nicht möglich, die totalen Kosten der konservativen Therapie in der Schweiz zu schätzen, da es derzeit keine Informationen zur Verwendungshäufigkeit konservativer Behandlungen von kompletten Rotatorenmanschettenrupturen gibt. Angesichts des Mangels an qualitativ hochwertigen und langfristigen Daten zu klinischen Ergebnissen und zur Lebensqualität bleibt unklar, ob eine Analyse über einen längeren Zeithorizont, oder unter Berücksichtigung indirekter Kosten aus Produktivitätsverlusten, zu anderen ökonomischen Ergebnissen führen würde.
Letztlich ist es nicht möglich, anhand der derzeit verfügbaren Daten zu beurteilen, ob die initial chirurgische Strategie häufig angenommene Schwellenwerte für Kosteneffektivität (z.B. CHF 50,000 oder CHF 100,000 pro gewonnenem QALY) einhalten könnte. Aus dieser Perspektive sind langfristige Studien erforderlich, die die Behandlungswirksamkeit und die Lebensqualität von Patienten mit kompletten Rotatorenmanschettenrupturen nach chirurgischer oder konservativer Behandlung untersuchen. Langfristige Studien, die für Patienten mit traumatischen versus atraumatischen kompletten Rotatorenmanschettenrupturen sowie für Rupturen einzelner versus multipler Bänder die Unterschiede in den Ergebnisparametern untersuchen, wären für feinere Analysen ebenfalls wichtig.

1.3 Résumé

Objectif
Le but de la synthèse et de l'analyse des données probantes actuelles était d'examiner systématiquement l'efficacité comparative, la sécurité, ainsi que les propriétés économiques pour la santé du traitement chirurgical par rapport au traitement non chirurgical pour les patients atteints d'une rupture complète de la coiffe des rotateurs.

Efficacité et sécurité clinique
Recherche de littérature
Cinq bases de données électroniques (Medline, Science Citation Index Expanded, Cochrane Library, Embase et Sportdiscus) ont été utilisées pour rechercher des études cliniques depuis le début jusqu'à Mai 2018. Par ailleurs, nous avons utilisé des études et revues systématiques considérées pertinentes afin de rechercher des références supplémentaires, et nous avons recherché des études non-publiées ou en cours sur ClinicalTrials.gov et le Système d'enregistrement international des essais cliniques (International Clinical Trials Registry Platform, ICTRP) de l'Organisation Mondiale de la Santé (World Health Organisation, WHO).

Sélection des études
Les titres et les résumés de 7,908 références identifiées par la recherche de littérature ont été analysés par deux examinateurs indépendants. Une fois les copies de l'intégralité des textes de 154 articles considérés potentiellement pertinents ont été obtenues, deux examinateurs indépendants ont évalué l'inclusion des articles. Les patients avec une rupture complète de la coiffe des rotateurs traumatique ou dégénérative ayant été traité chirurgicalement dans le cadre d'essais contrôlés randomisés (randomised controlled trials, RCTs) ou lors d'essais contrôlés non-randomisés (non-randomised controlled studies, NRSs) ont été inclus. Les traitements éligibles comme comparateurs comprenaient l'absence de traitement, "l'attente sous surveillance" ou tout traitements conservateurs.

Extraction des données et synthèse
Les caractéristiques de l'étude, des patients et de l'intervention ont été extraites par un examinateur, et un deuxième examinateur a vérifié les données extraites. Les données des RCTs et des NRSs ont été analysé séparément en raison de différents mécanismes de biais. L'effet du traitement pour chaque résultat continu a été exprimé comme une différence moyenne (mean difference, MD) avec un intervalle de confiance de 95% (95%-CI) et l'effet du traitement sur des résultats dichotomiques a été exprimé comme rapport de risque avec 95%-CI. Le GRADE ("Grading of Recommendations, Assessment, Development and Evaluation") a été utilisé pour évaluer la certitude des données probantes.

Résultats
Au total, trois RCTs (332 patients) et sept NRSs (667 patients) répondaient aux critères d'inclusion. (i) Dans les RCTs, les estimations de l'effet de la fonction de l'épaule mesurées à l'aide du score d'évaluation scapulaire de Constant-Murley (Constant-Murley Score, CMS) ainsi que la mesure de la douleur avec l'échelle visuelle analogique (visual analogue scale, VAS) ont montré un résultat statistiquement significatif en faveur de la chirurgie, en comparaison avec les traitements conservateurs: **Résultats sur la fonction de l'épaule** *à 12 mois*: MD de 6.9 points

plus élevée avec la chirurgie; 95%-CI 1.6, 12.3 (3 RCTs; certitude modérée des preuves); *à 24 mois*: MD de 4.4 points plus élevée avec la chirurgie; 95%-CI 0.04, 8.8 (2 RCTs; certitude modérée des preuves); *à 60 mois*: MD de 8.7 point plus élevée avec la chirurgie; 95%-CI 1.3, 16.1 (1 RCT; certitude modérée des preuves). Si on applique une estimation publiée de la différence minimale d'importance clinique (minimal clinically important difference, MCID) de 10,4 points[1], les MD observées sont inférieures à la limite de l'importance clinique, et leurs 95%-CIs incluent des valeurs inférieures et supérieures à cette limite. **Résultats sur la douleur**: *à 12 mois*: MD d'1.1 cm inférieure avec la chirurgie; 95%-CI 0.4, 1.8 (3 RCTs; faible certitude des preuves); *à 24 mois*: MD de 0.9 cm inférieure avec la chirurgie; 95%-CI 0.3 (2 RCTs; faible certitude des preuves) ; *à 60 mois*: MD d'1.3 cm inférieure avec la chirurgie; 95%-CI 0.5, 2.1 (1 RCT; faible certitude des preuves). En appliquant une estimation publiée de 1.4 cm pour la MCID[2] , les MDs observées sont inférieures à la limite d'importance clinique, et les 95%-CIs incluent des valeurs inférieures et supérieures à cette limite. (ii) Pour les autres résultats, concernant des paramètres importants pour le patient tel que l'amplitude du mouvement, la force musculaire, la qualité de vie (quality of life, QoL), ainsi que les effets indésirables, les données disponibles étaient très limitées, ne montrant aucune différence entre les groupes. (iii) Les résultats structurels ont été reporté en relation avec la dégénérescence graisseuse, l'atrophie musculaire, la rétraction tendineuse, ainsi que la progression des lésions. En comparant ces données entre le groupe recevant une chirurgie et le groupe sans chirurgie, les différences observées allaient majoritairement en faveur de la chirurgie.
Même si les estimation des effets des RCTs et NRSs étaient similaires, la certitude des données probantes variait selon le type d'étude: alors que dans les RCTs, la certitude des données probantes était jugée *modérée à faible*, elle était *très faible* dans les NRSs. Cependant, le risque de biais était jugé plus important dans les NRSs, car les différences observées entre les interventions pourraient être attribuables à des facteurs de confusion critiques plutôt qu'aux effets des interventions.

Évaluation économique de la santé

L'évaluation économique de la santé a été réalisée en effectuant une revue systématique de la littérature économique actuellement publiée, une analyse des coûts *de novo* avec des considérations supplémentaires de coûts-efficacité, et une analyse d'impact budgétaire (BIA) du point de vue des lois sur les assurances maladie suisses.

Revue systématique de la littérature, et implications

Les résultats de la revue systématique ont indiqué une absence d'analyses coûts-efficacité publiées qui évaluent les coûts par année de vie pondérée par la qualité (quality-adjusted life year, QALY) ou les coûts par année de vie gagnée (life year gained, LYG). Il a donc été impossible d'extrapoler les résultats des analyses coûts-efficacité au niveau international afin de les adapter pour la Suisse. De plus, en raison d'un manque de données nécessaires et d'information appropriées sur la qualité de vie des patients ayant subi une chirurgie ou un traitement conservateur, il a été impossible d'effectuer une analyse coûts-efficacité *de novo* exacte.

Model des coûts de novo et résultats

Le modèle a été construit à partir des données de trois RCTs identifiés dans la partie Clinique de l'étude, et représentant une population de patients avec une rupture complète de la coiffe des rotateurs symptomatique, soit avec des ruptures dégénératives (lésions des tendons simple ou

multiples) ou des ruptures traumatiques petites ou moyennes, avec des symptômes ayant duré environ un ou 2.5 ans et principalement traité jusque-là avec un traitement conservateur. Les hypothèses du modèle *de novo* ont été choisies en fonction des paramètres et des résultats des trois RCTs identifiés dans la revue clinique systématique, des commentaires d'un groupe d'experts médicaux impliqués dans cet Health Technology Assessment (HTA), des commentaires des services de control médical de deux hôpitaux universitaires, des coûts des consultations externes du système de facturation Suisse TARMED, des coûts des interventions pour les patients hospitalisés du Swiss Diagnostic Related Group (SwissDRG), des prix des médicaments tirés de la liste des médicaments remboursé par l'assurance maladie obligatoire en Suisse, et des informations provenant des publications internationales. [3-7]

Dans un contexte Suisse, les résultats de l'analyse des coûts *de novo* suggèrent que les coûts à six mois par personne pour la réparation chirurgicale initiale d'une rupture complète de la coiffe des rotateurs, plus la physiothérapie subséquente, étaient environ 10 fois plus élevé que pour le traitement conservateur (physiothérapie) (CHF 10,458 vs. CHF 1,018), correspondant à une différence de coûts de CHF 9,440. Les coûts de l'opération de CHF 9,379 ont constitué le facteur de coût le plus important, suivi par les coûts des séances de physiothérapie (CHF 773 pour 18 séances). Sur un horizon de cinq ans, les coûts par personne de la stratégie chirurgicale initiale se sont élevés à CHF 10,662, tandis que les coûts de la stratégie de traitement conservateur ont atteint CHF 3,599. La différence de coût entre les deux stratégies de traitement de CHF 9,440 à six mois a diminué à une différence de CHF 7,063 à cinq ans. L'analyse de sensibilité déterministe du modèle avec un horizon temporel de cinq ans a montré que ces résultats étaient principalement influencés par les coûts de l'opération, suivi par le taux global de crossover à 24 mois (passage du traitement conservateur au traitement chirurgical). Toutes les autres variables ont montré un impact mineur.

Considérations relatives au rapport coût efficacité

Comme une analyse coûts-efficacité appropriée n'était pas possible, nous avons déterminé dans des calculs supplémentaires quelles différences dans les utilités et QALYs (entre la stratégie chirurgicale initiale et la stratégie de traitement conservatrice) sur des périodes de deux à cinq ans seraient nécessaires pour atteindre un rapport coût-efficacité différentiel (incremental cost-effectiveness ratio, ICER) de CHF 50,000 et 100,000 par QALY gagné. Pour une différence de coût estimé à CHF 6,992 à deux ans, une différence en QALY de 0.140 et 0.070 serait nécessaire pour obtenir un ICER de CHF 50,000 et CHF 100,000, respectivement. À cinq ans, la différence de coût estimé à CHF 7,063 nécessiterait des différences en QALY similaire (0.141 et 0.071). En se basant sur une hypothèse simplificatrice de différences d'utilités constantes sur les horizons de deux ou de cinq ans, une différence d'utilité de 0.070 et 0.035 seraient nécessaire sur un horizon de deux ans pour atteindre un seuil ICER de CHF 50,000 et CHF 100,000, respectivement. Pour un horizon temporel de cinq ans, des différences d'utilité de 0.028 et 0.014 seraient nécessaires.

Analyse de l'impact budgétaire et résultats

L'objectif du BIA était d'évaluer les coûts globaux du traitement chirurgical de la rupture complète de la coiffe des rotateurs en comparaison avec le traitement conservateur en Suisse. L'estimation du nombre d'opérations de la coiffe des rotateurs avec rupture complète a été basée sur la statistique hospitalière suisse (SHS) de 2016. Les coûts unitaires pour le calcul de l'impact budgétaire sont basés sur les données de l'analyse des coûts *de novo*. En supposant des coûts de traitement sur 5 ans par patient, nous avons estimé le nombre de cas ayant subi une

opération entre 2018 et 2022, ainsi que le nombre de cas ayant subi une opération jusqu'à quatre ans avant 2018 mais qui auraient encore besoin d'un traitement de suivi entre 2018 et 2022. Il n'a pas été possible d'estimer le nombre de patients sous traitement conservateur en Suisse, dû à un manque de données adéquates. Par conséquent, le même nombre de cas a été appliqué pour la stratégie chirurgicale initiale tandis que pour la stratégie de traitement conservateur. Les coûts résultants pour la stratégie chirurgicale initial représenteraient alors les coûts réels de l'opération de la coiffe de rotateur avec rupture complète en Suisse. En revanche, les couts de la stratégie de traitement conservateur représenteraient le cout potentiel pour les mêmes patients dans le cas d'un traitement conservateur initial, suivi pour un certain pourcentage de patients d'une opération secondaire de réparation de la coiffe.
Les résultats suggèrent que le coût total de la stratégie chirurgicale initiale entre 2018 et 2022 atteindraient CHF 659.4 millions en considérant les coûts du traitement sur six mois par patient. En cas d'utilisation d'une stratégie de traitement initialement conservatrice, le coût total serait de CHF 64.2 millions (soit environ un dixième par rapport à la chirurgie). En considérant les coûts de traitement sur cinq pour chaque patient, le coût total de la stratégie chirurgicale initiale entre 2018 et 2022 s'élèverait à CHF 672.4 millions. La stratégie de traitement initialement conservatrice pour le même nombre de cas coûterait CHF 227,2 millions (soit environ un tiers par rapport à la chirurgie).

Conclusion
En termes d'efficacité clinique et de sécurité, nos résultats suggèrent que le traitement chirurgical pourrait être plus efficace que le traitement conservateur pour améliorer la fonction de l'épaule ainsi que réduire la douleur. Cependant, la pertinence clinique des différences est discutable. Pour d'autres résultats importants pour le patient, tel que l'amplitude des mouvements de l'épaule, la force musculaire, la qualité de vie, ainsi que les effets indésirables, les données disponibles étaient très limités et ne montrerai aucune différence entre les groupes.

La revue systématique de la littérature économique indique qu'il n'existe actuellement aucune étude de coût efficacité publiée qui aborde la question actuelle (Patients/Population, Intervention, Comparator, Outcomes, PICO).
L'analyse des coûts *de novo* suggère que dans la prise en charge des ruptures complètes de la coiffe des rotateurs, une stratégie chirurgicale initiale est beaucoup plus coûteuse qu'une stratégie de traitement initialement conservatrice, à court et à moyen terme. En considérant les coûts de traitement sur cinq ans par patient, les résultats du BIA indiquent que l'utilisation actuelle du traitement chirurgicale pour les ruptures complètes de la coiffe des rotateurs en Suisse pourrait entraîner des coûts supplémentaires de l'ordre de CHF 90 millions par an, par rapport à une stratégie du traitement initialement conservatrice. Il n'a pas été possible d'estimer le coût total du traitement conservateur en Suisse car il n'existe actuellement aucune information concernant l'utilisation du traitement conservateur pour le traitement de ruptures complètes de la coiffe des rotateurs. Étant donné la rareté de données de haute qualité et à long terme sur les résultats cliniques ainsi que sur la qualité de vie liée à la santé, il est incertain si une analyse à plus long terme ou incluant les coûts indirects liés aux pertes de productivité puisse mener à des résultats économiques différents. Finalement, il n'est pas possible de juger, sur la base des données actuellement disponibles, si la stratégie chirurgicale initiale pourrait atteindre les seuils de coûts efficacité fréquemment supposés (par exemple CHF 50,000 ou CHF 100,000 par QALY gagné). Dans cette optique, des études à long terme sur l'efficacité du

traitement et la qualité de vie des patients avec une rupture complète de la coiffe des rotateurs sont nécessaires. Des études sur le long terme enquêtant sur la différence entre les résultats chez les patients présentant des ruptures complètes de la coiffe des rotateurs de façon traumatique versus non traumatique, ainsi que la lésion des tendons simple versus multiples seraient également importantes pour des analyses plus précises.

2 Introduction

2.1 Medical background

The rotator cuff is a group of four deep shoulder muscles (supraspinatus, infraspinatus, teres minor, and subscapularis) that acts to stabilise the shoulder and aids in moving the upper extremity. A rotator cuff tear involves the partial (incomplete) or full discontinuation of the tendon(s) of one or more of these muscles and is accordingly termed either a partial-thickness or full-thickness tear. Rotator cuff tears can be either traumatic or atraumatic (i.e., degenerative); however, most (>90%) are considered to be non-traumatic.[9] Rotator cuff tears are diagnosed in both symptomatic populations (i.e., in people with shoulder symptoms) and symptom-free (asymptomatic) populations. Prevalence rates vary across the literature. Amongst the general population, the overall prevalence of rotator cuff tears has been reported to be over 20% and to increase with age.[10] In a systematic review of prevalence studies, the prevalence of full-thickness rotator cuff tears was found to be 35% (assessed with ultrasonography [US]) and 41% (assessed with magnetic resonance imaging [MRI]) in symptomatic populations whereas, in asymptomatic populations, a rate of 22% (assessed with US) and 10% (assessed with MRI) was reported.[11]

The diagnosis of a rotator cuff tear is usually made by clinical history, physical examination and diagnostic imaging, with US and MRI representing the most commonly used diagnostic imaging modalities.[12] Full-thickness tears, the condition of interest for this review, can be classified in various ways including (i) their size (small, medium, large), (ii) the number of affected tendons, (iii) the degree of tendon retraction (i.e., retraction of the torn ends from their bony insertion) or (iv) the extent of sequelas such as fatty degeneration or atrophy of the affected muscle(s) on tissue quality.[13]

Rotator cuff tears can have a considerable impact on individuals' lives by impairing shoulder function, activities of daily living, and quality of life.[14,15] Moreover, shoulder disorders may also result in substantial utilisation of healthcare resources, absenteeism from work and disability. Therefore, knowledge about the optimal treatment of rotator cuff-related shoulder complaints is important for both the individual and for society.

Treatment options for rotator cuff tears, i.e., for rotator cuff tear-related shoulder complaints, include conservative and surgical options. The primary aim of both approaches is to alleviate symptoms and restore shoulder function. Conservative treatment commonly includes physiotherapy (e.g., exercises or manual therapy), 'activity' advice (e.g., on temporary activity modifications), oral pain medication (e.g., non-steroidal anti-inflammatory drugs [NSAIDs]) and/or steroid injections.[16] Surgical treatment includes a variety of techniques (arthroscopic, open or mini-open surgery) and methods (e.g., suture, reconstruction, reinsertion or refixation with or without augmentation and/or acromioplasty through to tendon transfer). Both conservative and surgical treatment options have been shown to be effective in improving clinical outcomes, but definite recommendations regarding the precise indications for either treatment are lacking.[17-20]

2.2 Incidence and prevalence of (full-thickness) rotator cuff tears and surgeries

The published literature on the prevalence and incidence of rotator cuff tears is sparse internationally with information on numbers of surgeries performed somewhat more accessible.

Rotator cuff tears

Rotator cuff problems account for up to 70% of shoulder pain problems and are the third most prevalent musculoskeletal disorder after those occurring in the lower back and neck.[21]

Rotator cuff tear may lead to major reductions in quality of life and is one of the most common reasons for orthopaedic clinic visits.[22] The incidence of rotator cuff tears increases with age.[23] It is therefore expected to increase further in absolute terms, given an aging population who has in addition a growing desire to stay in good functional shape.

Rotator cuff tear surgeries

Rotator cuff tear treatment – including rotator cuff repair - is frequently performed in various countries. For example, Dornan et al. reported that 275,000 rotator cuff repairs of symptomatic rotator cuff tears are being performed every year in the USA and that the frequency is increasing.[24,25] The number of surgeries carried out per year in the USA increased by 141% between 1996 and 2006 (i.e., from 41 per 100,000 population to 98 per 100,000 population).[26] In a recent retrospective survey analysis published by Longo et al., the authors reported that the incidence of rotator cuff repair in Italy increased from 28.6 per 100,000 inhabitants over 25 years of age in 2001 to 73.5 per 100,000 inhabitants in 2014.[27] Using hospital records between 2001 and 2014, the authors reported that "approximately 65% of rotator cuff repairs were performed annually in patients under 65 years of age, thus affecting the working population."[27]

Full-thickness rotator cuff tear prevalence

Most of the studies mentioning or estimating the number of rotator cuff tear in a general population refer to two studies published by Minagawa et al. and Yamamoto et al.[24,28,29] Both studies were conducted in Japan and included residents from an unknown village. Yamamoto et al. reported that rotator cuff tears were present in 20.7% of the population older than 20 years.[29] Minagawa et al. did a health check-up of all residents in one village in Japan, reporting that *"One hundred and forty seven out of 664 subjects (22.1%) had full-thickness rotator cuff tears. The prevalence of tear in each decade was 0% in the 20s to 40s, 10.7% in the 50s, 15.2% in the 60s, 26.5% in the 70s, and 36.6% in the 80s. Symptomatic rotator cuff tears accounted for 34.7% of all tears and asymptomatic tears for 65.3%. The prevalence of asymptomatic rotator cuff tears was one-half of all tears in the 50s, whereas it accounted for two-thirds of those over the age of 60. The prevalence of tear was significantly greater in male than in female in the 50s and 60s, but not in the 70s and 80s."*[28]

Dornan et al. reported that the prevalence of full-thickness rotator cuff tears in the general population is about 20%, with one-third being symptomatic.[24] He based his assumption on the above-cited articles by Minagawa et al. and Yamamoto et al.[28,29]

Whether the frequency of rotator cuff tears in Japan may be comparable to the frequency in Switzerland is unclear.

Full-thickness rotator cuff tear incidence

In Sweden, in 2015, the estimated population-based annual incidence of acute traumatic full-thickness rotator cuff tears was 16 (confidence interval (CI): 11–23) per 100.000 inhabitants and year for the age group 18–75 years.[30] However, the underlying prospective study was restricted to patients with traumatic tears aged 18-75 years (acute onset of pain after shoulder trauma, with limited active abduction, and with normal conventional radiographs). The authors further reported that the annual incidence of full-thickness rotator cuff tear for the population at risk (aged 40–75 years) was 25 (CI: 18–36) per 100.000 inhabitants.

3 Objective

In view of the existing uncertainties regarding the best treatment of full-thickness rotator cuff tears, the aim of this report was to address the comparative effectiveness, safety, and costs of any surgical repair intervention in comparison to either conservative treatment or no treatment in patients with full-thickness rotator cuff tears.

4 PICO

In short, following Patients/Population-Intervention-Control-Outcome (PICO) question was posed: are surgical repair interventions compared with no treatment or conservative treatment in patients with full-thickness rotator cuff tears associated with better patient-relevant outcomes?

In this section we describe more in detail the PICO for the current Health Technology Assessment (HTA).

4.1 Population

Eligible patients were children and adults with traumatic or degenerative full-thickness rotator cuff tears. We defined a rotator cuff tear as the complete discontinuation of the tendon(s) of any (one or more) of the rotator cuff muscles (supraspinatus, infraspinatus, teres minor, subscapularis), irrespective of the aetiology of the tear (degenerative or traumatic), time of diagnosis, patient age and co-morbidities. To be eligible, a full-thickness tear had to be confirmed by an appropriate diagnostic imaging modality such as MRI, US or magnetic resonance arthrography (MRA). Studies including a mixed patient population (i.e., patients with a variety of rotator cuff diseases) were considered only (i) if the proportion of patients with a full-thickness rotator cuff tear exceeded 80%, or (ii) if the study included subgroup results for patients with full-thickness rotator cuff tears.
Studies focusing on populations of patients with rotator cuff tendinopathy, partial-thickness rotator cuff tears, biceps injuries or calcific tendinitis in the absence of a full-thickness tear were excluded. We further excluded studies in which the full-thickness tear had not been confirmed by diagnostic imaging.
In the health economic assessment patients with full-thickness rotator cuff tears irrespective of tear size.

4.2 Intervention

Any surgical technique (i.e., arthroscopic cuff repair, open or mini-open surgery) using any repair method (e.g., suture, reinsertion or refixation with or without debridement, augmentation and/or acromioplasty, reconstruction by tendon transfer and/or capsular reconstruction) were considered (provided the intervention was applied in the patient population defined above).
Studies in which the surgical repair intervention was supplemented by a biological intervention (e.g., platelet-rich plasma, growth factors, stem cell or other cell-based therapies) were excluded. Shoulder joint replacements were also not considered as an intervention.

4.3 Comparison treatment

Eligible comparison treatments included placebo, sham, no treatment, ‘watchful waiting’ or any conservative treatment such as physiotherapy or pharmacological treatment including injection therapies.

Studies comparing different surgical repair interventions were not considered as well as studies in which the surgical intervention was compared with extracorporeal shockwave therapy, magnetic field therapy, biological interventions (e.g., platelet-rich plasma, growth factors, stem cell or other cell-based therapies), laser treatment, thermotherapy (heat or cold) or hyperbaric oxygen therapy.

4.4 Outcome measures

The following patient-relevant outcome measures, which were selected in collaboration with the stakeholders, were considered:

- Shoulder function, measured by a standardised outcome measure, e.g., Constant-Murley Score (CMS), American Shoulder and Elbow Surgeons (ASES) score, University of California at Los Angeles (UCLA) score or Dutch Simple Shoulder Test (DSST)
- Shoulder pain, e.g., pain intensity, measured by a standardised instrument such as a visual analogue scale (VAS)
- Shoulder range of motion
- Shoulder muscle strength
- Health-related Quality of Life (QoL), measured by a standardised instrument, e.g., the 36-Item Short Form Health Survey (SF-36)
- Occupational impairment defined as (i) the length of time until re-entry into working life and/or (ii) the rates of individuals who changed their occupation because of their shoulder problem
- Length of hospital stay
- Any treatment-related adverse events (except for surgical complications; see below) as defined by the study authors[31-33]
- Any surgical complication, e.g., peripheral neurologic injuries, infections
- Failed surgery (i.e., re-tear of the repaired tendon[s]) as defined by the study authors
- Re-operation rates
- Structural findings, e.g., muscle atrophy, measured by an appropriate imaging modality (as suggested by the stakeholders)

In studies in which outcomes were measured at multiple time points, we intended to capture the time-dependent 'variability' of outcomes by extracting all numerical data reported for each individual time point considered.

Relevant (but not necessarily achievable) outcomes for the health economic assessment were:

- Costs (total and by category)
- Medical resource use
- Utilities
- Quality-adjusted life years (QALYs), life years gained (LYG)
- Incremental cost-effectiveness ratio (ICER; expressed as cost per QALY gained or cost per LYG)

5 Clinical assessment - Methods

This systematic review was registered in the international prospective register of systematic reviews (PROSPERO; https://www.crd.york.ac.uk/prospero/) on 14/08/2018 (PROSPERO ID CRD42018100343) and is reported in accordance with the Transparent Reporting of Systematic Reviews and Meta-Analyses Statement (PRISMA; http://prisma-statement.org/PRISMAStatement/).[34]

5.1 Study types

(i) Randomised controlled trials (RCTs) and (ii) non-randomised studies (NRSs) including prospective and retrospective controlled cohort studies, case-control studies, and controlled before-after studies fulfilling the abovementioned inclusion criteria were considered.
For RCTs, we considered study results reported in full text publications, study registers or in abstract form (provided sufficient data were available). For NRSs, we considered study results reported only in full text publications and study registers. We did not consider study results of NRSs reported exclusively in abstract form. The reason for this restriction was that the limited information on study methods generally precludes a thorough risk of bias assessment, which, however, is particularly important for this study type (NRSs).

5.2 Literature search

The searches for this review were conducted in May 2018. We did not use any date or language restrictions in the electronic searches for trials. Furthermore, the search strategies for all databases were adapted from our Medline strategy (Appendix D). This search strategy was peer-reviewed by a second information specialist and was validated by checking whether the strategy identified studies already known, including those cited in the systematic reviews by Ryösä et al.[35] and Coghlan et al.[36]. For each database, the date of the search and the search strategy as well as the number of search results was documented.

5.2.1 Bibliographic database searches

Systematic literature searches for relevant published studies were conducted by an information specialist (IK) in the following electronic databases:

- Medline, Medline Daily Update, Medline In-Process & Other Non-Indexed Citations and Medline Epub Ahead of Print (via Ovid)
- Science Citation Index Expanded, Conference Proceedings Citation Index-Science and BIOSIS Citation Index (via Web of Science)
- Cochrane Library (via Wiley)
- Embase (via Embase.com/Elsevier)
- SPORTDiscus (via Ebsco)

5.2.2 Searches in study registers

Searches for ongoing trials or unpublished completed trials were conducted in ClinicalTrials.gov (www.clinicaltrials.gov) and the the World Health Organisation (WHO) International Clinical Trials Registry Platform (ICTRP, http://www.who.int/ictrp/search/en).

5.2.3 Supplementary searches

We used relevant studies and systematic reviews to search for additional references via the PubMed similar articles function (https://www.nlm.nih.gov/bsd/disted/pubmedtutorial/020_190.html) and forward citation tracking using the Web of Science Core Collection. Reference lists of relevant studies and reviews were searched, and experts in the field were contacted to inquire about any further relevant studies that may not have been retrieved by the electronic searches.

5.3 Identification of relevant studies

Titles and abstracts of the citations identified by the searches were independently screened by two reviewers (title and abstract screening; CB, VT, or AD), and the full texts of all potentially relevant articles were obtained. The full texts were also independently checked for eligibility by two reviewers (CB and VT or AD or BNS), and the reasons for exclusion were documented (full text screening). Any disagreement was resolved by consensus, moderated by a third reviewer (CS).

To standardise the screening process, two purpose-designed forms were used: an 'abstract screening form' and a 'full text screening form'. Both included the inclusion and exclusion criteria for the review. The 'abstract screening form' was used as a guidance document to assist the title and abstract screening. The 'full text screening form' was used to extract and document the key criteria that were relevant for the ultimate decision of whether a study was included or excluded as well as the key justification for each reviewer's decision. The title and abstract screening was first piloted in abstrackr (http://abstrackr.cebm.brown.edu/) on a random subset of 50 search results. The 'full text screening form' was also piloted on three exemplary RCTs using the same software. Finally, the complete screening process (title and abstract screening and full text screening) was conducted in Covidence (https://www.covidence.org/home).

5.4 Data extraction

One review author (CB or CS) extracted the following data, and a second reviewer (VT) checked the extracted data:

- Study characteristics: including year of publication, study type, setting, start and end of study, sample size, follow-up time and inclusion and exclusion criteria.
- Missing patient data: including numbers and reasons for each treatment arm.
- Patient characteristics: including patient age, number of patients with re-operations, number of patients with co-morbidities, numbers of females and males, aetiology of the full-thickness rotator cuff tear (traumatic, degenerative), extent of the full-thickness rotator cuff tear (e.g., minor, major, single tendon or combined/multiple tendon rupture), extent of shoulder-related functional disability and the diagnostic imaging modality used to establish the diagnosis (e.g., MRI, US).
- Characteristics of the intervention: including the definition of the surgical technique (arthroscopic cuff repair, open or mini-open surgery) as well as the method (e.g., suture, reinsertion or refixation with or without augmentation, and/or acromioplasty), professional experience of the surgeon, time between the diagnosis and surgical intervention and information regarding postoperative treatment.

- Characteristics of the comparator treatment: including the type of conservative treatment as well as the duration and information on additional pharmacological treatment.
- Outcome measures: including the description of the measurement tools used, the unit of measurement, upper and lower scale limits and the reported time points of the measurements; where adjusted analyses were available in primary studies, these adjusted estimates of the treatment effects were used; where adjusted analyses were not available, we extracted the data as reported in the study. Of note, in cases where the outcome data were only presented graphically in the primary study (which was often the case, indicated in grey in the outcome tables), a graphical analysis with a web-based plot digitiser software (WebPlotDigitizer V4.1, https://automeris.io/WebPlotDigitizer/) was done to extract the outcome data from the graphs. All outcome data were entered into the Review Manager software (RevMan 5.3)[37] by one reviewer (CS) and checked by a second (AD, BNS, or VT).

5.5 Risk of bias assessment

Risk of bias in RCTs was assessed separately for each study outcome according to the methodology described in the Cochrane Handbook for Systematic Reviews of Interventions,[38] addressing the following domains: (i) randomised sequence generation, (ii) allocation concealment, (iii) the blinding of patients, trial personnel, and outcome assessors, (iv) incomplete outcome data, (v) selective outcome reporting (e.g., the absence of data for outcomes measured) and (vi) other sources of bias (bias due to problems not covered elsewhere). Each domain was judged as either 'low', 'high' or 'unclear' risk of bias.
Bias in NRSs was evaluated separately with the 'Risk of Bias in Non-randomised Studies of Interventions' (ROBINS-I) tool,[39] addressing the following domains: (i) bias due to confounding (e.g., the etiology or extent of the full-thickness rotator cuff tear, age, gender, co-morbidity, patients with re-operations, cointervention), (ii) bias in the selection of patients into the study (e.g., inception bias), (iii) bias in the measurement of the intervention, (iv) bias due to departures from intended interventions, (v) bias due to missing data, (vi) bias in the measurement of outcomes, (vii) bias in the selection of the reported results and (viii) overall bias. Each domain was judged as either 'low', 'moderate', 'serious', 'critical' or 'unclear' risk of bias. The ratings for the individual domains form the basis for the overall risk of bias judgement for each study, with possible ratings being low risk, moderate risk, serious risk, critical risk or no information.
All risk of bias assessments were conducted by two reviewers (CB and CS). Any disagreement was resolved by discussion and consensus involving a third person (JJM) as needed. The ratings for the individual domains for each RCT and NRS were documented separately (Figure 2 and Figure 3 [RCTs] and Table 21 [NRSs]).

5.6 GRADE assessment

The certainty of evidence of the predefined patient-relevant outcomes (shoulder function, shoulder pain, range of motion, muscle strength and adverse events) was assessed using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach.[40,41]
In brief, this assessment addresses study limitations (risk of bias), imprecision (when 95% confidence intervals [95%-CI] are wide and/or close to the null effect around the point estimate), inconsistency (i.e., differences in the estimates of effect across studies that assessed

the same comparison), indirectness (i.e., differences in patient characteristics, differing (co-)intervention, a differing extent to which the intervention of interest is optimally conducted, a differing comparator, and differences in the measurement of outcome), dissemination bias and potential criteria (e.g., large effect estimates) that can increase certainty. Based on these criteria, the certainty of the evidence for each comparison and outcome can be categorised as high, moderate, low or very low. The results of this assessment were presented in GRADE evidence profiles separated by RCTs (best available evidence, Table 30) and NRSs (Table 31), as suggested by the GRADE Working Group.[42] The GRADE assessments were conducted by two reviewers (CS and JJM).

5.7 Assessment of dissemination bias

Our intention was to minimise the impact of dissemination bias by ensuring a comprehensive search for eligible studies including searches of trial registries (see 'literature' search above). We intended to construct funnel plots and conduct appropriate statistical tests for small-study effects provided that at least ten studies were available for an outcome.[43] Since none of the meta-analyses included ten or more studies, a thorough assessment of dissemination bias was not feasible.

5.8 Data synthesis and analysis

5.8.1 Data from different study types

Data from RCTs and NRSs were—due to different mechanisms of bias—analysed separately.[44]

5.8.2 Measures of effect sizes

We analysed outcomes measured with a scale as continuous outcomes (e.g., patient-reported shoulder function, shoulder pain). The treatment effect for each continuous outcome was expressed as the mean difference (MD) with its 95%-CI, considering the change between the baseline and follow-up measurement of each treatment arm. Where continuous outcomes measured with different scales were pooled, the treatment effect was expressed as the standardised MD with its 95%-CI. The treatment effect for dichotomous outcomes was expressed as the risk ratio (RR) with 95%-CI.

5.8.3 Meta-analyses

We conducted meta-analyses of all outcomes depending on the availability of data. Meta-analyses of data from NRSs were only considered among studies with sufficiently comparable designs. Meta-analyses were conducted using RevMan Version 5.3, and all treatment effects were calculated based on a random effects model (DerSimonian & Laird).[45]

5.8.4 Assessment of heterogeneity

Heterogeneity was evaluated and quantified based on I^2 and the statistical test Chi-square. Thereby, a Chi-square p value <0.10 or an I^2 ≥75% was considered as 'significant' heterogeneity.[46]

5.8.5 Sensitivity and subgroup analyses

Sensitivity analyses were planned (irrespective of the presence of 'significant' heterogeneity, see above) to determine the impact of bias through the exclusion of studies with a high risk of bias, and subgroup analyses were planned to examine whether effect estimates were affected by patients' age, the etiology and/or extent of the complete rotator cuff tear, the extent of shoulder-related functional disability, the surgical repair intervention or the type of conservative treatment. However, the limited available study data precluded such analyses.

5.8.6 Unit of analysis

The unit of analysis was the individual participant including cases (studies) in which the number of participants and shoulders differed (this was the case only in one RCT including 180 patients representing 173 shoulders).[47,48]

5.8.7 Dealing with missing data

We intended to analyse all outcome data on an intention-to-treat (ITT) basis and/or according to recently developed recommendations for systematic reviewers for addressing missing data in clinical trials.[49,50] In cases where missing data could not be 'reliably' replaced, we referred to the number of patient data reported for the corresponding time points in the studies. Furthermore, in cases where the results were exclusively reported in graphs, we estimated the corresponding values based on these graphs using a web-based plot digitiser software (section 5.4 Data extraction).

6 Clinical assessment - Results

6.1 Literature search

The results of the database searches and supplementary searches are displayed in Table 1. The searches identified 15,717 citations, including 7,810 duplicates. Among the 7,908 unique records (references, publications) screened, 154 were considered for the full text screening. Of these, 16 studies corresponding to 19 publications were eligible for inclusion in this systematic review (Appendix A):

- three RCTs (corresponding to five publications): Kukkonen et al.,[47 48] Lambers Heerspink et al.,[51] Moosmayer et al.[52 53]
- seven NRSs (corresponding to eight publications): Boorman et al.,[54 55] De Carli et al.,[56] Fabbri et al.,[57], Lee et al.,[58] Vad et al.,[59] Yamada et al.,[60]Yoo et al.[61]
- six ongoing studies: five RCTs and one NRS

Figure 1 outlines the screening and selection process of the identified references; excluded references with reasons for exclusions are presented in Appendix C.

Table 1: Literature search

Data source	N records
Medline, Medline Daily Update, Medline In-Process & Other Non-Indexed Citations, Medline Epub Ahead of Print (via Ovid) Search date: 29 May 2018	4,468
Embase (via Embase.com/Elsevier) Search date: 29 May 2018	4,590
Science Citation Index Expanded, Conference Proceedings Citation Index-Science, BIOSIS Citation Index (via Web of Science) Search date: 29 May 2018	4,452
Cochrane Library (via Wiley) Search date: 29 May 2018	388
SPORTDiscus (via Ebsco) Search date: 7 June 2018	1,070
Searches in study registers (www.clinicaltrials.gov and (http://www.who.int/ictrp/search/en) Search date: 29 May 2018	440
Supplementary searches (PubMed similar articles function https://www.nlm.nih.gov/bsd/disted/pubmedtutorial/020_190.html and forward citation tracking using the Web of Science Core Collection) Search date: 29 May 2018	309
Records with duplicates	**15,717**
Records without duplicates	**7,907**

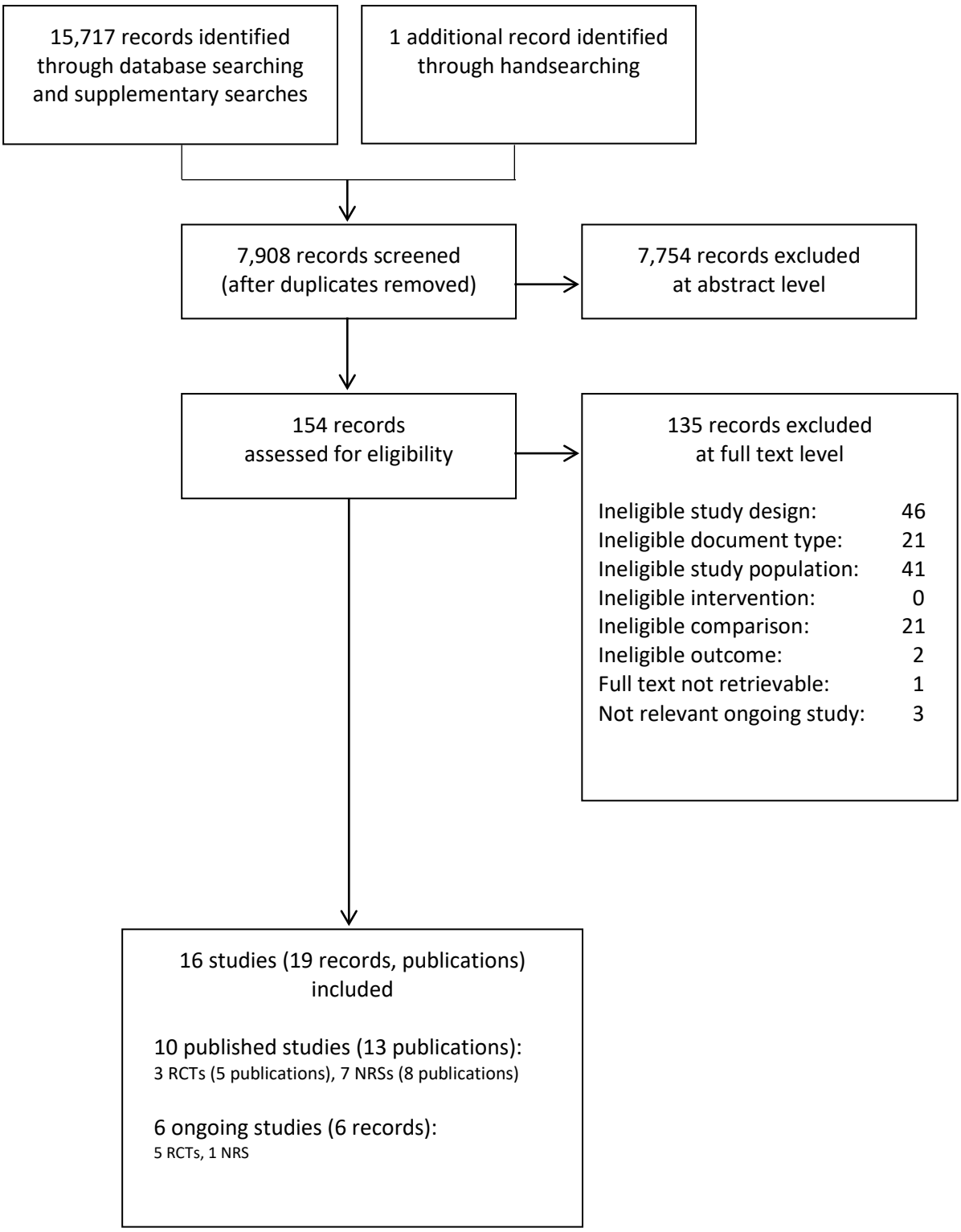

Figure 1: PRISMA Flow chart
RCTs = Randomised controlled trials; NRS = Non-randomised study

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6.2 Randomised controlled trials (RCTs)

6.2.1 Study characteristics (RCTs)

The characteristics of the three identified RCTs (five publications)[47,48,51-53] are shown in Table 2 to Table 6.

Setting and key characteristics

The studies were conducted in Northern Europe (Finland [173 participants],[47,48] the Netherlands [56 participants][51] and Norway [103 participants][52,53]), and were published between 2010[52] and 2015.[48,51] In total, 332 patients (representing 339 shoulders) were investigated; 197 shoulders were assigned to surgical treatment and 142 to conservative treatment. Except for one study (two publications),[52,53] the RCTs were conducted as multicentre studies (i.e., surgery took place in six different hospitals). Outcomes were assessed at three,[47,48] six, [47,48,52,53], 12[47,48,51-53], 24[47,48,52,53] and 60 months.[52,53]

Participants

Across the RCTs, the mean patient age ranged between 59[52,53] and 65[47,48] years, and the proportion of female patients ranged from 29%[52,53] to 50%.[47,48] Two studies[47,48,51] used MRI as the imaging method for diagnosing the tears, whereas Moosmayer et al.[52,53] used MRI and US. Two studies included exclusively patients with degenerative (atraumatic) full-thickness rotator cuff tears.[47,48,51] Furthermore, Kukkonen et al.[47,48] specified that only patients with supraspinatus tendon tears were considered, whereas the other two RCTs also included shoulders with more than one affected tendon. However, the proportion of shoulders with more than one affected tendon did not exceed 30%. Previous surgery of the effected shoulder was an exclusion criterion in all three studies.

Surgical and conservative treatment

Surgery was done arthroscopically,[47,48] using a mini-open[51-53] or open technique[52,53] and included acromioplasty. Kukkonen et al.[47,48] also reported on a group treated with subacromial acromioplasty only (without repair). The characteristics and outcome data of this acromioplasty only group are included in the characteristics and outcome tables but are not reported in the review text because the intervention did not comply with the intervention of interest for this review. All three RCTs reported that the surgical repair interventions were carried out by 'experienced surgeons' and followed by some postoperative rehabilitation. Patients in the conservative treatment group underwent physiotherapy (exercise-based rehabilitation), which was supervised by physiotherapists in all studies. Lambers Heerspink et al. reported that the patients additionally received subacromial steroid injections and analgetics.[51] The overall duration of the conservative treatment was at least 12 weeks.

Table 2: Key study characteristics (RCTs)

Study	Design	Setting	Total N randomised	Intervention and comparison (N randomised)	Recruitment (start-end)	Follow-up	Losses to follow-up
Kukkonen 2014 & 2015[47,48]	RCT (parallel-group, patient randomised)	Finland multicentre (3 hospitals)	173 patients* 'patients with isolated atraumatic full-thickness SSP tendon tear'	I1 (60 shoulders): surgery (repair+acromioplasty) I2 (60 shoulders): surgery (acromioplasty) C (60 shoulders): conservative treatment	02/09-11/13	at 3, 6, 12, 24 months after baseline assessment	Total: 13/180 (7%)[$] I1: 6/60 (10%) patient withdrawal (3), partial tear in second-look MRI and operation (2), missed data (1) I2: 2/60 (3%) patient withdrawal (1), missed data (1) C: 5/60 (8%) withdrawal (1), malignant disease (1), death (1), missed data (2)
COPACABANA Lambers Heerspink 2015[51]	RCT (parallel-group, patient randomised)	Netherlands multicentre (3 hospitals)	56 patients 'patients with atraumatic full-thickness rotator cuff tears'	I (25 patients): surgery (repair+acromioplasty) C (n = 31 patients): conservative treatment	01/09-12/12	at 1.5, 3, 6, 12 months[+] after surgery or inclusion	Total: 11/56 (20%) I: 5/25 (20%) moved (1), rotator cuff repair not done (intact cuff or irreparable tear) (4) C: 6/31 (19%) intervention discontinued (3), death (1), moved (2)
Moosmayer 2010 & 2014[52,53]	RCT (parallel-group, patient randomised)	Norway single-centre (1 hospital)	103 patients 'patients with traumatic and atraumatic full-thickness rotator cuff tears'	I (52 patients): surgery (repair+acromioplasty) C (51 patients): conservative treatment	09/04-10/07	at 6, 12, 24, 60 months after intervention[#]	Total: 5/103 (5%)[§] I: 3/52 (6%) death (1), patients refused to meet (2) C: 2/51 (4%) death (1), due to medical reasons (1)

C = Control; COPACABANA: Conservative vs. Operative Treatment of Atraumatic Rotator Cuff Rupture; Anatomically and Radiology After One Year Study; I = Intervention; MRI = Magnetic Resonance Imaging; N = Number of patients; RCT(s) = Randomised Controlled Trial(s); SSP = Supraspinatus.
* Kukkonen: 173 patients randomised, and 180 shoulders were operated on, i.e., from seven patients, both shoulders were included. The study authors, however, did not report how these seven patients were distributed between the groups.
+ Lambers Heerspink: outcome data were presented only for the 12-month follow-up.
$ Kukkonen: Data extracted from 2015 report; the report from 2015 refers to data from the longest follow-up (of note, there were minor data discrepancies between the reports).
# Moosmayer: Not further specified.
§ Moosmayer: Data extracted from 2014 report; there were minor discrepancies between the data reported in the different publications.

Table 3: Inclusion and exclusion criteria (RCTs)

Study	Study population
Kukkonen 2014 & 2015[47,48]	Inclusion: - patients (age > 55 years) with a symptomatic, isolated degenerative full-thickness supraspinatus tendon tear (comprising < 75% of the tendon insertion) - full shoulder ROM -diagnosis by MRI Exclusion: - age < 55 years - massive tendon tears and/or combined tears - glenohumeral joint stiffness and glenohumeral osteoarthritis with osteophytes - systemic corticosteroid or antimetabolite medication - significant malignant, haematological, endocrine, metabolic, rheumatoid or gastrointestinal disease - history of trauma relating to the onset of symptoms - previous surgery of the same shoulder
Lambers Heerspink 2015[51]	Inclusion: - patients with degenerative full-thickness rotator cuff tears - diagnosis by MRI Exclusion: - frozen shoulder - glenohumeral or acromioclavicular joint osteoarthritis - arthritis/rheumatoid arthritis, diabetes mellitus - cognitive disorders - neurologic disease affecting the function of the upper extremity - previous surgical treatment of the same shoulder
Moosmayer 2010 & 2014[52,53]	Inclusion: - patients with symptomatic traumatic and degenerative (atraumatic) full-thickness rotator cuff tears (size ≤ 3 cm, muscle atrophy ≤ stage 2) - ROM shoulder abduction and flexion ≥ 140° - diagnosis by US and MRI Exclusion: - age < 18 years - presence of other local or systemic diseases affecting shoulder function - tears with an absolute indication for surgery - medical co-morbidities - previous tendon surgery on the relevant shoulder

MRI = Magnetic Resonance Imaging; ROM = Range of Motion; US = Ultrasonography.

Table 4: Patient characteristics (RCTs)

Study	Age (years) mean (SD)		Sex N (%) females		Def. of patient population Symptom duration (months) mean (SD) or median (IQR)		Shoulder-related functional disability; CMS at baseline (points) mean (SD) or mean (95%-CI)		Affected tendon(s) N (%)		Affected shoulder and/or dominant arm N (%)	
	I	C	I	C	I	C	I	C	I	C	I	C
Kukkonen 2014 & 2015[47,48]	I1: 65 (5.8)* I2: 65 (5.1)	64 (5.6)	I1: 25 (46) I2: 29 (50)	33 (60)	atraumatic full-thickness tears I1: 27 (9.5) I2: 28 (9.7)	27 (10.0)	I1: 58.0 (54.1; 61.9) I2: 59.6 (55.8; 63.4)	57.8 (53.9; 61.7)	SSP: 60 (100)	SSP: 60 (100)	side: right shoulder I1: 36 (67) I2: 34 (59)	41 (75)
Lambers Heerspink 2015[51]	60.8 (7.2)	60.5 (7.0)	10 (40)	11 (35)	atraumatic full-thickness tears 12.5 (4.8; 25.6)	12.0 (7.8; 24.0)	55.6 (18.4)	56.9 (15.0)	SSP: 24 (96) SSP+SSC: 1 (4)	SSP: 26 (84) SSP+ISP: 1 (3) SSP+SSC: 4 (13)	side: right shoulder 12 (48) dominant arm: right 20 (80)	20 (65) 26 (84)
Moosmayer 2010 & 2014[52,53]	59 (7.5)	61 (7.6)	15 (29)	15 (29)	traumatic and atraumatic full-thickness tears 12.3 (18.7)#	9.8 (9.8)	35.3 (13.2)	38.4 (14.2)	SSP: 37 (71) SSP+ISP: 14 (27) SSP+SSC: 1 (2)	SSP: 40 (78) SSP+ISP: 10 (20) SSP+SSC: 1 (2)	side: right shoulder 31 (60)	29 (57)

CI = Confidence Interval; CMS = Constant-Murley Score; C = Control; I1 = Repair + Acromioplasty; I2 = Acromioplasty; IQR = Interquartile range; I = Intervention; ISP = Infraspinatus; MRI = Magnetic Resonance Imaging; N = Number of patients; SD = Standard deviation; SSC = Subscapularis; SSP = Supraspinatus; US = Ultrasonography.
* Kukkonen: Data extracted from 2015 report, because it reports data from longer follow-up (some discrepancies between the reports).
In general: Table data in grey are based on own calculations.
Moosmayer: The "high" SD of 18.7 months can be explained by one patient showing a symptom duration of 120 months (information provided by Dr. Moosmayer by having E-mail contact on the 5th of April 2019).

Table 5: Characteristics of the surgical treatment (RCTs)

Study	Surgery (intervention group)			Postoperative treatment
	N randomised	Surgical technique and methods	Provision of treatment	
Kukkonen 2014 & 2015[47,48]	I1: 60 shoulders*	Surgical technique: - arthroscopic Repair method: - supraspinatus tendon was repaired anatomically with standard titanium bone anchors and non-absorbable sutures - biceps tenotomy and/or acromioclavicular joint resection where indicated - acromioplasty and subacromial debridement	Surgeon's experience: '[…] 4 experienced shoulder surgeons' Timing: '[…] treatment started within 1 month' (after randomisation)	- after the operation: immobilisation in a sling for 3 weeks - after 3 weeks: referral for physiotherapy following a standardised protocol
	I2: 60 shoulders*	Surgical technique: - arthroscopic Repair method: - acromioplasty and subacromial debridement - biceps tenotomy and/or acromioclavicular joint resection where indicated		
Lambers Heerspink 2015[51]	25 patients (25 shoulders)	Surgical technique: -mini-open Repair method: - side-to-side repair or repair augmented with bone anchors - acromioplasty with bursectomy (subacromial bursa) and subacromial debridement	Surgeons' experience: '[…] two qualified and experienced surgeons' Timing: '[…] surgery was scheduled within 6 weeks of inclusion'	- after the operation: immobilisation in a sling for 6 weeks - after 6 weeks: referral for physiotherapy following a standardised protocol
Moosmayer 2010 & 2014[52,53]	52 patients* (52 shoulders)	Surgical technique: -mini-open (n = 9) or open (n = 43) Repair method: - tendon-to-tendon and tendon-to-bone technique - acromioplasty (open repair) or arthroscopic acromioplasty (mini-open repair)	Surgeons' experience: '[…] 1 of 3 experienced orthopaedic surgeons' Timing: No information	- after the operation: immobilisation in a sling for 6 weeks and passive ROM exercises - after 6 weeks: active-assisted movements - after 12 weeks: supplementation with strengthening exercises

I1 = Repair + Acromioplasty; I2 = Acromioplasty; N = Number of patients; ROM = Range of Motion.
* Kukkonen: 60 shoulders randomised, 59 shoulders received the corresponding intervention (I1 and I2); Lambers Heerspink: 25 patients randomised; however, in 2 patients, the tear could not be repaired, and no rotator cuff rupture was found in 2 patients despite MRI diagnosis; Moosmayer: 52 patients randomised, 51 patients received intervention.

Table 6: Characteristics of the conservative treatment (RCTs)

Study	Conservative treatment group		
	N randomised	Treatment characteristics	Provision of treatment
Kukkonen 2014 & 2015[47,48]	60 shoulders	Conservative treatment (with exercise-based rehabilitation): - written information and guidance on how to perform a standardised training exercise protocol at home - week 0 to 6: improvement of glenohumeral motion and active scapular retraction - week 6 to 12: gradual increase of static and dynamic exercises - week 12 to 24: increased resistance and strength training	Provision: - by a physiotherapist trained in shoulder rehabilitation Duration: - referral for 10 sessions of outpatient physiotherapy (monitoring of progress); home-based training up to 24 weeks
Lambers Heerspink 2015[51]	31 patients (31 shoulders)	Conservative treatment (with exercise-based rehabilitation): - subacromial steroid injections - pain medication (NSAIDs, paracetamol, or tramadol) - physiotherapy based on a standardised protocol including information, advice on activities of daily living, passive movements and static and dynamic exercises - week 4 to 6: gradual progression and deltoid training - week 6 to 12: further progression, mobility and strength training (rotator cuff and deltoid)	Provision: - by physiotherapists Duration: - 12 weeks, but '[…] was continued until patients reached an optimum range of motion, and an improvement in strength was achieved'.
Moosmayer 2010 & 2014[52,53]	51 patients (51 shoulders)	Conservative treatment (with exercise-based rehabilitation): - exercises to restore scapulothoracic and glenohumeral muscular control and stability - postural correction - isometric and dynamic (resisted concentric and eccentric) exercises - progression through increasing loads and more challenging positions - exercises addressing specific demands in work, sports, and leisure activities	Provision: - by 4 experienced physiotherapists Duration: - treatment sessions of 40 minutes, on average 2x/week for 12 weeks, with increasing intervals after 6 and up to 12 weeks Of note: patients who did not improve after at least 15 sessions of physiotherapy were reassessed and re-examined by an orthopaedic surgeon (with consideration of secondary surgery)*

N = Number of patients; NSAID = Non-Steroidal Anti-Inflammatory Drug(s);
* Moosmayer: 'The decision to offer secondary surgery after a minimum of fifteen physiotherapeutic treatment sessions was based on the non-acceptance of the achieved result by the patient and the persistence of clinical findings at examination.'

6.2.2 Risk of Bias (RCTs)

The risk of bias summary for each study is presented in Figure 2, and the review authors' judgements for each risk of bias item are presented as percentages across all included studies (risk of bias graph) in Figure 3.

Overall, the studies reported sufficient details about the randomisation process, with allocation concealment being guaranteed in all three trials. However, blinding was a critical issue. Due to the nature of these studies comparing a surgical intervention with a non-surgical treatment, the risk for performance bias is generally and inevitably high in all studies making such comparisons. Although two studies (four publications)[47,48,52,53] described that the study personnel and/or the outcome assessors were blinded, all patients were inevitably aware of the intervention they received. Hence, the three trials were rated with a high risk of detection bias for all subjectively measured outcomes, such as pain and QoL. The observed differences may, therefore, be attributable to the influence of patients' perception and preferences rather than to the effects of the intervention. Of note, outcomes based on the CMS (e.g., shoulder function) were judged with an 'unclear' risk of bias in the two studies reporting a blinded outcome assessment.[47,48,52,53] The reason for this 'in-between' judgement was that approximately a third of the total CMS is based on a subjective patient self-assessment and two-thirds are based on the assessment of the examiner. Therefore, we judged that the outcome assessment should not be considered as 'fully blinded'. One study[51] had an unclear risk of bias concerning missing data for almost all reported outcomes. The reason for this judgement was a considerable loss of approximately 20% to the follow-up rate in both groups. Although reasons for the dropouts were provided, these participants were excluded from the analysis (except for the outcome shoulder function). Therefore, attrition bias cannot be fully excluded. In the remaining studies, the risk for attrition bias was low. Selective reporting could only be assessed in one study.[51] The remaining two studies did not provide enough information, i.e., no protocol was pre-published. No other sources of bias were identified in the three RCTs.

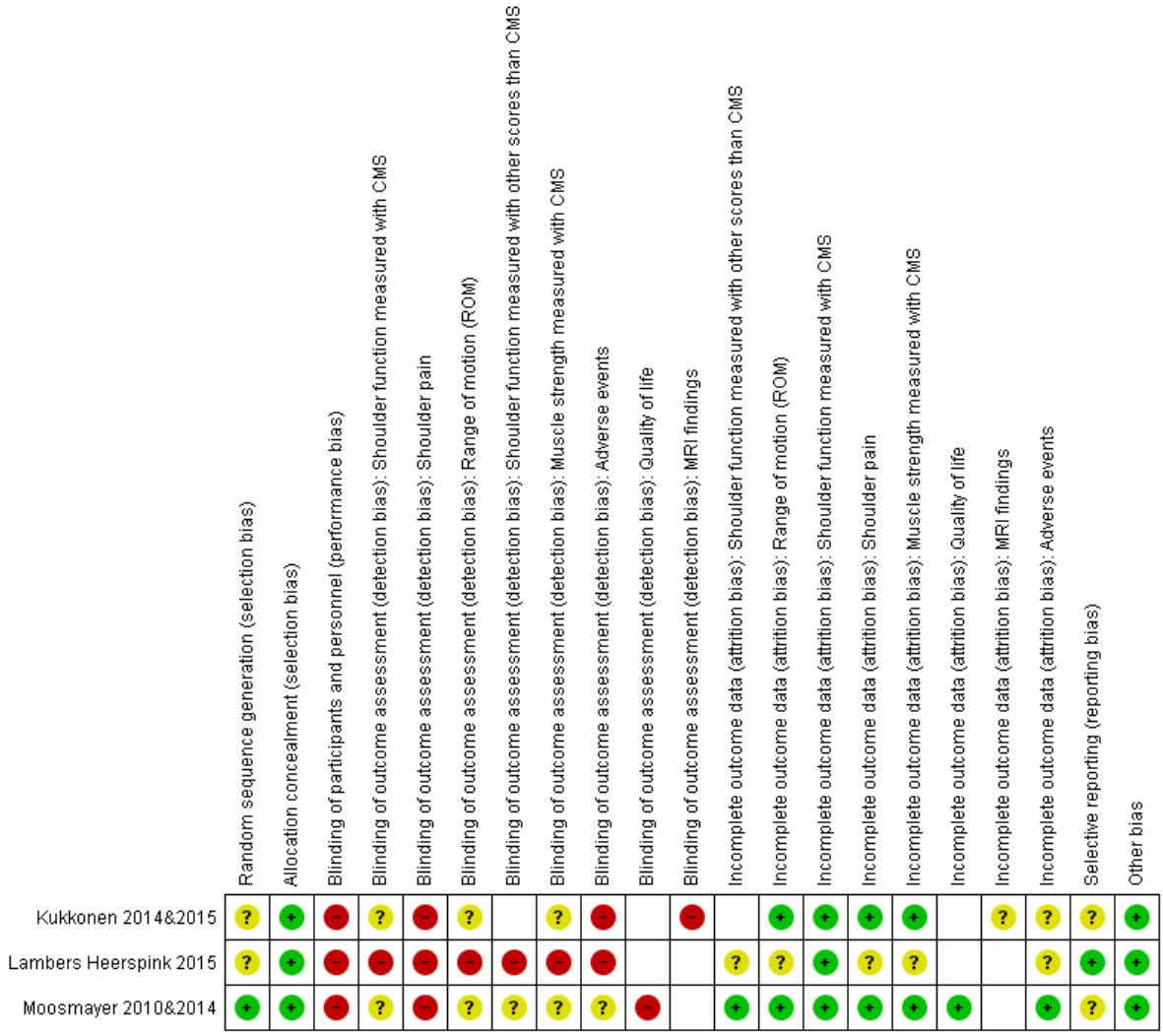


Figure 2: Risk of bias summary
Of note: White fields mean that this item was not evaluated by the corresponding study

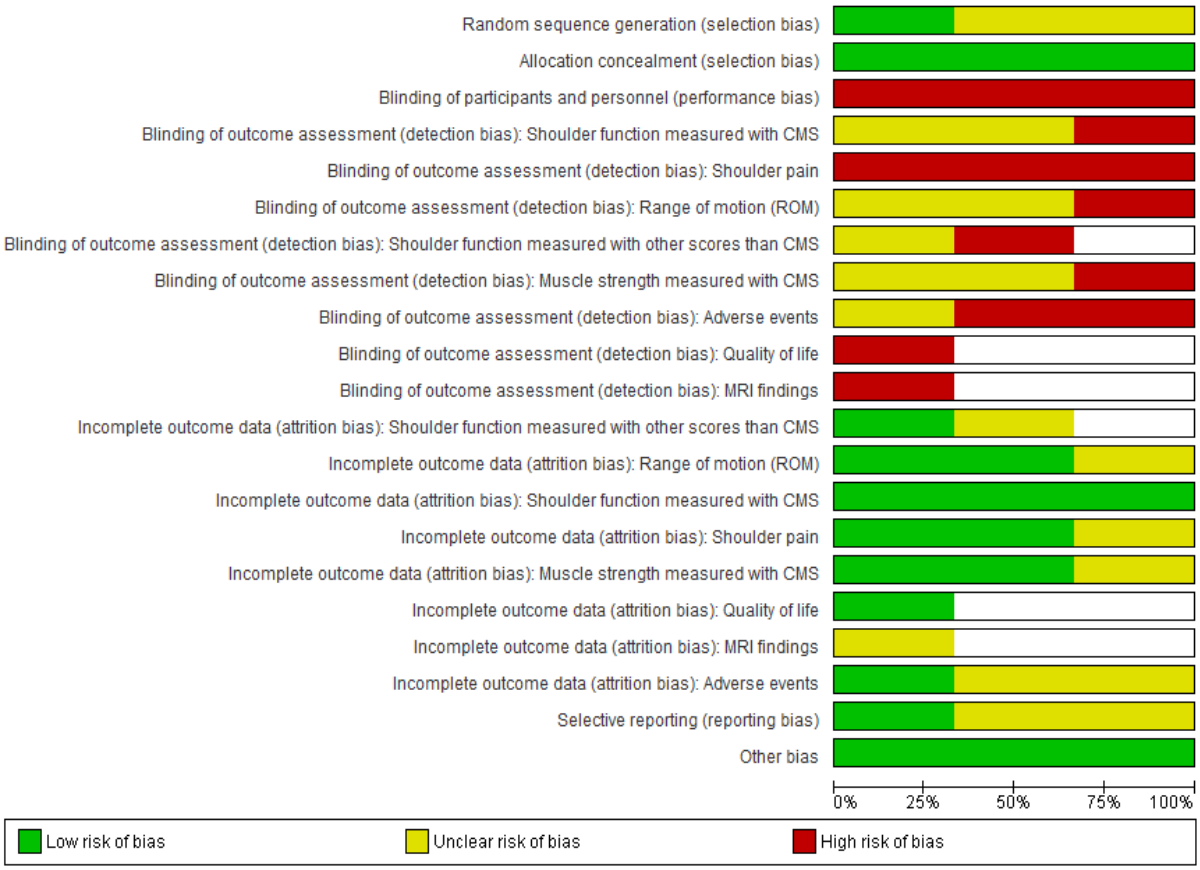


Figure 3: Risk of bias graph
Of note: White areas in the graphs mean that this percentage of studies did not evaluate the corresponding outcome

6.2.3 Outcomes (tabular view, RCTs)

The outcomes reported in the identified studies, including the corresponding results, are displayed in Table 7 to Table 16. These data provide the basis for the forest plots (graphical view of the outcome data), quantitative results (pooled estimates) (section 6.2.4), and the GRADE evidence profile for selected outcomes (Table 30; section 6.4.1).

In brief, all but one (occupational impairment and/or hospital length of stay) of the predefined outcomes in section 4.4 were reported in the published RCTs. Shoulder function was measured with four different scales: (i) CMS (0 – 100, 100 = best outcome);[47,48,51-53] (ii) ASES score (0 – 100, 100 = best outcome);[52,53] (iii) DSST (0 – 12, 12 = best outcome)[51] and (iv) VAS for function (0 – 10, 10 = worst outcome).[51] Shoulder pain was measured with the (i) VAS for pain (0 – 10, 10 = worst outcome)[47,48,51-53] and the (ii) CMS pain subscore (0 – 15, 15 = best outcome).[47,48] Range of motion and muscle strength were measured with the corresponding CMS subscore either for range of motion[47,48] (including the assessment of abduction, flexion, internal rotation and external rotation, score 0 – 40, 40 = best outcome) or strength[47,48,52,53] (0 – 25, 25 = best outcome). Besides the CMS subscore, shoulder range of motion was also measured by a goniometer, assessing pain-free active flexion and abduction in degrees.[52,53] Health-related QoL was reported by one study and measured with the Short Form (36) Health Survey (SF–36) (0 – 100, 100 = best outcome).[52,53] Adverse event data including treatment-related adverse events and structural findings, including failed surgery defined as the re-tear of the repaired tendon, were derivable from all studies.[47,48,51-53]

Table 7: Shoulder function (RCTs)

Study	Definition of outcome measurement	Follow-up	Surgical group		Conservative treatment group	
			N	Mean (SD)	N	Mean (SD)
Kukkonen 2014 & 2015[47,48] I1*	CMS (0–100 points) 0 = worst; 100 = best outcome	**baseline**	**59**	**58.1 (13.2)**	**58**	**57.1 (16.7)**
		3	55	62.5 (15.9) mean change: 4.4 (17.4)	57	67.7 (14.8) mean change: 10.6 (18.7)
		6	47	72.5 (13.8) mean change: 14.4 (16.0)	57	73.0 (13.3) mean change: 15.9 (18.0)
		12	55	77.9 (12.1) mean change: 19.8 (15.0)	55	74.1 (14.2) mean change: 17.0 (18.4)
		24	54	80.7 (11.0) mean change: 22.6 (14.4)	55	75.5 (12.0) mean change: 18.4 (17.4)
Kukkonen 2014 & 2015[47,48] I2*		**baseline**	**59**	**59.6 (13.3)**	**58**	**57.1 (16.7)**
		3	58	69.1 (12.3) mean change: 9.5 (15.2)	57	67.7 (14.8) mean change: 10.6 (18.7)
		6	54	74.9 (11.4) mean change: 15.3 (14.7)	57	73.0 (13.3) mean change: 15.9 (18.0)
		12	57	77.2 (13.0) mean change: 17.6 (15.6)	55	74.1 (14.2) mean change: 17.0 (18.4)
		24	58	80.1 (13.3) mean change: 20.5 (15.7)	55	75.5 (12.0) mean change: 18.4 (17.4)
Lambers Heerspink 2015[51]*	**CMS (0–100 points)**	**baseline**	**25**	**55.6 (18.4)**	**31**	**56.9 (15.0)**
		12	20#	81.9 (15.6) mean change: 26.3 (20.2)	25#	73.7 (18.4) mean change: 16.8 (19.9)
	DSST (0–12 points) 0 = worst; 12 = best outcome	**baseline**	**25**	**5.5 (2.3)**	**31**	**6.1 (2.7)**
		12	20	11.0 (2.8) mean change: 5.5 (3.0)	25	9.7 (3.6) mean change: 3.6 (3.8)
	VAS (0-10 cm) 0 = best; 10 = worst outcome	**baseline**	**25**	**6.2 (1.7)**	**31**	**5.8 (2.1)**
		12	20	2.1 (1.7) mean change: -4.2 (2.01)	25	3.5 (2.3) mean change: -2.3 (2.6)
Moosmayer 2010 & 2014[52,53]*	**CMS (0–100 points)**$	**baseline**	**52**	**35.3 (13.2)**	**51**	**38.4 (14.2)**
		6	51	65.6 (16.3) mean change: 30.3 (17.6)	51	63.9 (20.2) mean change: 25.5 (20.9)
		12	51	77.7 (13.4) mean change: 42.4 (15.7)	51	70.3 (19.1) mean change: 31.9 (20.1)
		24	51	79.3 (13.6) mean change: 44.0 (15.9)	50	77.7 (14.9) mean change: 39.3 (17.2)
		60	51	79.8 (15.0) mean change: 44.5 (16.7)	50	74.2 (20.3) mean change: 35.8 (21.0)
	ASES score (0–100 points)$ 0 = worst; 100 = best outcome	**baseline**	**52**	**45.5 (14.5)**	**51**	**48.2 (14.4)**
		6	51	85.3 (13.7) mean change: 39.8 (16.7)	51	75.4 (20.2) mean change: 27.2 (21.0)
		12	51	93.6 (12.5)§ mean change: 48.1 (16.1)	51	83.6 (18.3)§ mean change: 35.4 (19.6)
		24	51	93.1 (13.9)§ mean change: 47.6 (16.8)	50	88.0 (14.9)§ mean change: 39.8 (17.3)
		60	51	92.8 (13.3)§ mean change: 47.3 (16.5)	50	85.4 (21.0)§ mean change: 37.2 (21.6)

ASES = American Society of Shoulder and Elbow Surgeons; CMS = Constant Murley Score; DSST = Dutch Simple Shoulder Test; I1 = Repair + Acromioplasty; I2 = Acromioplasty; N = Number of patients; SD = Standard deviation; VAS = Visual Analogue Scale.

* The studies did not provide sufficient information to directly calculate the SD for the mean changes from baseline; therefore, they have been imputed as described in the Cochrane Handbook.[1]

Lambers Heerspink: Presented data refer to a per protocol analyses. When data were calculated after intention-to-treat, the study authors reported '[…] an intention-to-treat analysis was performed in which the last observation of these patients was carried forward. The mean CMS at the 1-year follow-up decreased in the conservative group by including the patients who were lost to follow-up, resulting in a significant difference between surgery and conservative treatment (mean CMS: 81.6 [SD, 14.9] vs 71.5 [SD, 18.1], P = 0.02)'.

$ Moosmayer: The reported data for the CMS and ASES score differ slightly between Moosmayer 2010 and 2014. In our report, we refer to the data reported in Moosmayer 2014.

§ Moosmayer: Outcome data refer to the ASES score ranging from 0-100 points. The study authors, however, report SDs that would exceed the upper limit of the score.

In general: Data in grey colour are based on own calculations; Kukkonen: study arm I2 (acromioplasty): data are displayed but not further considered because intervention does not fulfil inclusion criteria.

Table 8: Shoulder pain (RCTs)

Study	Definition of outcome measurement	Follow-up	Surgical group		Conservative group	
			N	Mean (SD)	N	Mean (SD)
Kukkonen 2014 & 2015[47,48] I1*	**Subscore of CMS (0-15 points)** 0 = worst; 15 = no pain	**baseline**	**59**	**10.2 (3.8)**	**58**	**10.2 (4.5)**
		3	55	12.7 (3.5) mean change: 2.4 (4.3)	57	11.1 (3.7) mean change: 0.9 (4.9)
		6	47	13.4 (2.8) mean change: 3.2 (4.0)	57	12.1 (3.4) mean change: 1.9 (4.8)
		12	55	13.4 (2.9) mean change: 3.2 (4.0)	55	12.2 (3.3) mean change: 1.9 (4.7)
		24	54	13.9 (2.1) mean change: 3.6 (3.7)	55	12.2 (3.5) mean change: 2.0 (4.8)
Kukkonen 2014 & 2015[47,48] I2*		**baseline**	**59**	**10.6 (4.2)**	**58**	**10.2 (4.5)**
		3	58	12.6 (3.0) mean change: 2.0 (4.4)	57	11.1 (3.7) mean change: 0.9 (4.9)
		6	54	13.5 (2.0) mean change: 2.9 (4.1)	57	12.1 (3.4) mean change: 1.9 (4.8)
		12	57	13.4 (2.8) mean change: 2.8 (4.3)	55	12.2 (3.3) mean change: 1.9 (4.7)
		24	58	13.6 (2.7) mean change: 3.0 (4.3)	55	12.2 (3.5) mean change: 2.0 (4.8)
Kukkonen 2014 & 2015[47,48] I1*	**VAS (0-10 cm)** 0 = no; 10 = worst pain	**baseline**	**59**	**2.6 (2.4)**	**58**	**2.7 (2.9)**
		3	55	1.2 (1.9) mean change: -1.3 (2.6)	57	2.0 (2.2) mean change: -0.7 (3.1)
		6	47	0.9 (1.6) mean change: -1.7 (2.5)	57	1.5 (2.1) mean change: -1.2 (3.0)
		12	55	0.9 (2.1) mean change: -1.7 (2.7)	55	1.3 (2.0) mean change: -1.4 (3.0)
		24	54	0.6 (1.7) mean change: -2.0 (2.5)	55	1.4 (2.1) mean change: -1.3 (3.0)
Kukkonen 2014 & 2015[47,48] I2*		**baseline**	**59**	**2.5 (2.8)**	**58**	**2.7 (2.9)**
		3	58	1.2 (2.2) mean change: -1.3 (3.0)	57	2.0 (2.2) mean change: -0.7 (3.1)
		6	54	0.6 (0.9) mean change: -1.9 (2.7)	57	1.5 (2.1) mean change: -1.2 (3.0)
		12	57	1.1 (2.2) mean change: -1.5 (3.0)	55	1.3 (2.0) mean change: -1.4 (3.0)
		24	58	0.8 (1.8) mean change: -1.7§ (2.8)	55	1.4 (2.1) mean change: -1.3 (3.0)
Lambers Heerspink 2015[51]*	**VAS (0-10 cm)**	**baseline**	**25**	**6.7 (1.7)**	**31**	**6.3 (1.3)**
		12	20	2.2 (1.9) mean change: -4.5 (2.1)	25	3.2 (2.1) mean change: -3.1 (2.1)
Moosmayer 2010 & 2014[52,53]*	**VAS (0-10 cm)$**	**baseline**	**52**	**5.6 (2.0)**	**51**	**5.3 (1.9)**
		6	51	1.1 (1.3) mean change: -4.5 (2.0)	51	2.7 (2.2) mean change: -2.6 (2.4)
		12	51	0.5 (1.2) mean change: -5.1 (2.0)	51	1.6 (1.6) mean change: -3.7 (2.1)
		24	51	0.7 (1.5) mean change: -4.9 (2.1)	50	1.4 (1.4) mean change: -3.9 (2.0)
		60	51	0.6 (1.4) mean change: -5.0 (2.1)	50	1.6 (1.6) mean change: -3.7 (2.1)

CMS = Constant Murley Score; I1 = Repair + Acromioplasty; I2 = Acromioplasty; N = Number of patients; SD = Standard deviation; VAS = Visual Analogue Scale.

* The included studies did not provide sufficient information to directly calculate the SD for the mean changes from baseline; therefore, they have been imputed as described in the Cochrane Handbook.[1]

§ Kukkonen: The change in the VAS at 24 months reported in text (mean change: -1.8), does not exactly match the change in the VAS that was calculated using baseline and end-of-study values from Fig. 4 in the original study (-1.7).

$ Moosmayer: The VAS and SD refer to those reported in Moosmayer 2014 (which differ slightly from the values reported in Moosmayer 2010 for 6 and 12 months).

In general: Data in grey are based on own calculations; Kukkonen: study arm I2 (acromioplasty): data are displayed but not further considered because intervention does not fulfil inclusion criteria.

Table 9: Shoulder range of motion (RCTs)

Study	Definition of outcome measurement	Follow-up (months)	Surgical group		Conservative group	
			N total	Mean (SD)	N total	Mean (SD)
Kukkonen 2014 & 2015[47,48] I1*	**Subscore of CMS (0-40 points)** 0 = worst; 40 = best outcome	**baseline**	**59**	**29.9 (8.7)**	**58**	**29.3 (8.7)**
		3	55	30.3 (8.0) mean change: 0.4 (9.9)	57	34.5 (6.3) mean change: 5.2 (9.1)
		6	47	34.4 (6.5) mean change: 4.5 (9.2)	57	36.4 (4.6) mean change: 7.2 (8.5)
		12	55	36.1 (5.0) mean change: 6.2 (8.6)	55	36.4 (5.1) mean change: 7.1 (8.7)
		24	54	36.3 (4.6) mean change: 6.4 (8.5)	55	37.0 (3.4) mean change: 7.7 (8.3)
Kukkonen 2014 & 2015[47,48] I2*		**baseline**	**59**	**31.4 (7.3)**	**58**	**29.3 (8.7)**
		3	58	33.7 (5.9) mean change: 2.3 (7.9)	57	34.5 (6.3) mean change: 5.2 (9.1)
		6	54	35.1 (5.5) mean change: 3.8 (7.7)	57	36.4 (4.6) mean change: 7.2 (8.5)
		12	57	36.0 (5.2) mean change: 4.6 (7.6)	55	36.4 (5.1) mean change: 7.1 (8.7)
		24	58	36.7 (4.3) mean change: 5.3 (7.3)	55	37.0 (3.4) mean change: 7.7 (8.3)
Lambers Heerspink 2015[51]	outcome not reported					
Moosmayer 2010 & 2014[52,53]*	**Pain-free active abduction (degrees)** goniometer based[$]	**baseline**	**52**	**73.3 (28.0)**	**51**	**81.9 (29.8)**
		6	51	135.4 (41.7) mean change: 62.1 (42.7)	51	135.4 (47.9) mean change: 53.5 (48.2)
		12	51	158.4 (33.7) mean change: 85.1 (36.8)	51	143.8 (43.9) mean change: 61.9 (45.1)
		24	51	161.7 (30.8) mean change: 88.4 (34.9)	50	163.6 (32.6) mean change: 81.7 (37.0)
		60	51	167.3 (30.6) mean change: 94.0 (34.7)	50	155.1 (41.2) mean change: 73.2 (43.0)
	Pain-free active flexion (degrees) goniometer based (degrees)[$]	**baseline**	**52**	**86.8 (41.3)**	**51**	**88.6 (32.1)**
		6	51	147.3 (34.5) mean change: 60.5 (45.2)	51	146.6 (46.3) mean change: 58.0 (47.8)
		12	51	166.1 (27.5) mean change: 79.3 (42.2)	51	155.6 (38.4) mean change: 67.0 (42.0)
		24	51	168.5 (26.1) mean change: 81.7 (41.7)	50	170.5 (23.0) mean change: 81.9 (33.4)
		60	51	170.6 (27.9) mean change: 83.8 (42.3)	50	163.5 (35.4) mean change: 74.9 (40.0)

CMS = Constant Murley Score; I1 = Repair + Acromioplasty; I2 = Acromioplasty; N = Number of patients; SD = Standard deviation.
* The included studies did not provide sufficient information to directly calculate the SD for the mean changes from baseline; therefore, they have been imputed as described in the Cochrane Handbook.[1]
$ Moosmayer: ROM (in degrees) and SD refer to those reported in Moosmayer 2014 (which differ slightly from the values reported in Moosmayer 2010 for 6 and 12 months).
In general: Data in grey are based on own calculations; Kukkonen: study arm I2 (acromioplasty): data are displayed but not further considered because intervention does not fulfil inclusion criteria.

Table 10: Muscle strength (RCTs)

Study	Definition of outcome measurement	Follow-up (month)	Surgical group		Conservative group	
			N total	Mean (SD)	N total	Mean (SD)
Kukkonen 2014 & 2015[47,48] I1*	**Subscore of CMS (0-25 points)** 0 = worst; 25 = best outcome	**baseline**	**59**	**8.3 (5.2)**	**58**	**8.4 (5.4)**
		3	55	5.9 (4.9) mean change: -2.3 (6.0)	57	10.3 (5.9) mean change: 1.9 (6.7)
		6	47	8.9 (4.8) mean change: 0.7 (5.9)	57	11.3 (5.7) mean change: 2.9 (6.6)
		12	55	10.8 (5.1) mean change: 2.5 (6.1)	55	11.5 (5.6)mean change: 3.0 (6.5)
		24	54	12.1 (5.6) mean change: 3.8 (6.4)	55	11.7 (5.9) mean change: 3.3 (6.7)
Kukkonen 2014 & 2015[47,48] I2*		**baseline**	**59**	**8.4 (5.7)**	**58**	**8.4 (5.4)**
		3	58	8.6 (5.0) mean change: 0.1 (6.4)	57	10.3 (5.9) mean change: 1.9 (6.7)
		6	54	10.3 (5.1) mean change: 1.8 (6.4)	57	11.3 (5.7) mean change: 2.9 (6.6)
		12	57	10.9 (5.7) mean change: 2.5 (6.7)	55	11.5 (5.6) mean change: 3.0 (6.5)
		24	58	12.2 (6.2) mean change: 3.8 (7.1)	55	11.7 (5.9) mean change: 3.3 (6.7)
Lambers Heerspink 2015[51]	outcome not reported					
Moosmayer 2010 & 2014[52,53]*	**Subscore of CMS (0-25 points)**$	**baseline**	**52**	**7.5 (5.5)**	**51**	**8.1 (5.8)**
		6	51	8.0 (4.6) mean change: 0.5 (6.0)	51	10.6 (5.4) mean change: 2.5 (6.6)
		12	51	11.1 (4.0) mean change: 3.6 (5.7)	51	11.9 (5.1) mean change: 3.8 (6.5)
		24	51	11.9 (4.3) mean change: 4.4 (5.9)	50	12.8 (5.3) mean change: 4.7 (6.6)
		60	51	12.1 (4.7) mean change: 4.6 (6.1)	50	11.4 (5.4) mean change: 3.3 (6.6)

CMS = Constant Murley Score; I1 = Repair + Acromioplasty; I2 = Acromioplasty; N = Number of patients; SD = Standard deviation.
* The included studies did not provide sufficient information to directly calculate the SD for the mean changes from baseline; therefore, they have been imputed as described in the Cochrane Handbook.[1]
$ Moosmayer: Shoulder muscle strength and SD refer to those reported in Moosmayer 2014 (which differ slightly from the values reported in Moosmayer 2010 for 6 and 12 months).
In general: Data in grey are based on own calculations; Kukkonen: study arm I2 (acromioplasty): data are displayed, but not further considered, because intervention does not fulfil inclusion criteria.

Table 11: Health-related Quality of Life (RCTs)

Study	Definition of outcome measurement	Follow-up (month)	Surgical group		Conservative group	
			N total	Mean (SD)	N total	Mean (SD)
Kukkonen 2014 & 2015[47,48]	outcome not reported					
Lambers Heerspink 2015[51]	outcome not reported					
Moosmayer 2010 & 2014[52,53]*	**SF-36 (physical component; 0-100 points)**[$] 0 = worst, 100 = best possible health condition	**baseline**	**52**	**38.2 (6.0)**	**51**	**38.6 (8.7)**
		6	51	48.3 (8.7) mean change: 10.1 (9.0)	51	47.3 (9.5) mean change: 8.6 (10.8)
		12	51	51.2 (10.0) mean change: 13.0 (10.0)	51	50.3 (8.7) mean change: 11.7 (10.3)
		24	51	51.0 (9.7) mean change: 12.8 (9.8)	50	50.4 (9.2) mean change: 11.8 (10.6)
		60	51	50.1 (10.6) mean change: 11.9 (10.5)	50	48.4 (11.2) mean change: 9.8 (11.9)
	SF-36 (mental component; 0-100 points)	**baseline**	**52**	**54.1 (11.8)**	**51**	**57.3 (9.5)**
		6	51	57.5 (9.2) mean change: 3.4 (12.6)	51	57.6 (7.7) mean change: 0.3 (10.3)
		12	51	56.2 (9.4) mean change: 2.1 (12.7)	51	57.5 (7.5) mean change: 0.2 (10.2)
		24	51	data not reported	50	data not reported
		60	51		50	

N = Number of patients; SD = Standard deviation; SF-36 = Short Form (36) Health Survey.
* The included studies did not provide sufficient information to directly calculate the SD for the mean changes from baseline; therefore, they have been imputed as described in the Cochrane Handbook.[1]
$ Moosmayer: The SF-36 (physical) score and SD refer to those reported in Moosmayer 2014 (which differ slightly from the values reported in Moosmayer 2010 for 6 and 12 months).
In general: Data in grey are based on own calculations.

Table 12: Occupational impairment and/or hospital length of stay (RCTs)

Study	Definition of outcome measurement	Follow-up (month)	Surgical group		Conservative group	
			N total	Mean (SD)	N total	Mean (SD)
Kukkonen 2014 & 2015[47,48]	outcome not reported					
Lambers Heerspink 2015[51]						
Moosmayer 2010 & 2014[52,53]*						

N = Number of patients; SD = Standard deviation.

Table 13: Any adverse events (RCTs)

Study	Follow-up (months)	Surgical group		Conservative group	
		N total	N with events (%)	N total	N with events (%)
Kukkonen 2014 & 2015[47,48] I1	24	54	0	55	0
Kukkonen 2014 & 2015[47,48] I2	24	58	0	55	0
Lambers Heerspink 2015[51]	12	20	0	25	1 (4) 'One patient in the group treated conservatively developed a frozen shoulder 9 months after conservative treatment.'
Moosmayer 2010 & 2014[52,53]*	12	51	1 (2) 'Three months post-op, 1 patient in the surgery group sustained a traumatic fracture of the proximal humerus. This was treated in a sling, and routine MRI at 12 months' follow-up showed an intact tendon.'	51	1 (2) 'One patient from the physiotherapy group was diagnosed with polymyalgia rheumatica four months after inclusion and was treated with steroids.'
	60	51	7 (13.7) 'One case of polymyalgia rheumatica prior to 2-year follow-up; 1 case of cerebral apoplexia, 1 case of operatively treated abdominal aortic aneurysm after 2 years; 1 case of lateral humeral epicondylitis and 1 case of cervical radiculopathy prior to 2-year follow-up; 1 case of low back pain and 1 case of cervical radiculopathy after 2-year follow-up.'	50	4 (8) 'One case of polymyalgia rheumatic, 1 case of herpes zoster, 1 case of lymphoma prior to 2-year follow-up; 1 case of cervical radiculopathy prior to 2-year follow-up.'

I1 = Repair + Acromioplasty; I2 = Acromioplasty; MRI = Magnet Resonance Imaging; N = Number of patients.
In general: Kukkonen: study arm I2 (acromioplasty): data are displayed but not further considered because intervention does not fulfil inclusion criteria.

Table 14: Treatment-related adverse events (RCTs)

Study	Follow-up (months)	Surgical group		Conservative group	
		N total	N with events (%)	N total	N with events (%)
Kukkonen 2014 & 2015[47,48] I1	24	54	0 '[…] no treatment-related complications in any of the groups'.	55	0 '[…] no treatment-related complications in any of the groups'.
Kukkonen 2014 & 2015[47,48] I2	24	58	0 '[…] no treatment-related complications in any of the groups'.	55	0 '[…] no treatment-related complications in any of the groups'.
Lambers Heerspink 2015[51]	12	20	0	25	0
Moosmayer 2010 & 2014[52,53]*	60	51	0	50	0

I1 = Repair + Acromioplasty; I2 = Acromioplasty; N = Number of patients.
In general: Kukkonen: study arm I2 (acromioplasty): data are displayed but not further considered because intervention does not fulfil inclusion criteria.

Table 15: Failed surgery (re-tear; RCTs)

Study	Definition of outcome measurement	Follow-up (months)	Surgical group		Conservative group	
			N total	N with events (%)	N total	N with events (%)
Kukkonen 2014 & 2015[47,48] I1	outcome not reported				outcome not applicable for patients treated conservatively	
Kukkonen 2014 & 2015[47,48] I2						
Lambers Heerspink 2015[51]	re-tear (not further defined) (MRI)	baseline	25	-		
		12	19	14 (74)		
Moosmayer 2010 & 2014[52,53]*	partial-thickness re-tear (MRI at 12 months, US at 60 months)	baseline	52	-		
		12	50	6 (12)		
		60	60§	7 (12)		
	full-thickness re-tear (MRI at 12 months, US at 60 months)	baseline	52	-		
		12	50	4 (8)		
		60	60§	8 (13)		

I1 = Repair + Acromioplasty; I2 = Acromioplasty; MRI = Magnetic Resonance Imaging; N = Number of patients; US = Ultrasonography.
* Moosmayer: Results are reported for patients randomised to surgery (n=48 [of 52]) and patients with 'secondary surgery' (n=12 [of 12]), total 60 patients at 60 months follow-up. At 60 months, the study authors did not separate between these two groups and reported 'that the percentage of patients with *partial-thickness re-tear* was identical to the percentage of patients with re-tears diagnosed at 12-month follow-up, and all these re-tears had been diagnosed after one year (by MRI)'. For *full-thickness re-tears* the authors stated that 'five of these re-tears had been diagnosed after one year (by MRI); all were either smaller (n = 5) or the same size (n = 3) compared to the pre-operative assessment'.
In general: Kukkonen: study arm I2 (acromioplasty): data are displayed but not further considered in interpretation because this intervention does not fulfil inclusion criteria.

Table 16: Structural findings (RCTs)

Study	Definition of outcome measurement	Follow-up (months)	Surgical group		Conservative group	
			N total	N with events (%)	N total	N with events (%)
Kukkonen 2014 & 2015[47,48] I1	MRI: fatty degeneration, Goutallier grade 2 (yes, no)	baseline 24	57 49	30 (53) 26 (53)	60 51	32 (53) 34 (67)
Kukkonen 2014 & 2015[47,48] I2*		baseline 24	60 48	29 (48) 25 (52)	60 51	32 (53) 34 (67)
Kukkonen 2014 & 2015[47,48] I1	MRI: fatty degeneration, Goutallier grade 3 (yes, no)	baseline 24	57 49	2 (4) 6 (12)	60 51	1 (2) 3 (6)
Kukkonen 2014 & 2015[47,48] I2*		baseline 24	60 48	5 (8) 5 (10)	60 51	1 (2) 3 (6)
Kukkonen 2014 & 2015[47,48] I1	MRI: muscle atrophy (present, absent)	baseline 24	57 49	18 (32) 17 (35)	60 51	16 (27) 20 (39)
Kukkonen 2014 & 2015[47,48] I2*		baseline 24	60 48	23 (38) 21 (44)	60 51	16 (27) 20 (39)
Kukkonen 2014 & 2015[47,48] I1	MRI: sagittal tear size§ in mm	baseline 24	57 49	8.4 (3.9) mean (SD) 4.2 (7.3) mean change: -4.2 (7.2)	60 51	9.6 (5.4) mean (SD) 10.4 (8.2) mean change: 0.8 (8.4)
Kukkonen 2014 & 2015[47,48] I2*		baseline 24	60 48	9.1 (5.3) mean (SD) 11.7 (10.6) mean change: 2.6 (10.3)	60 51	9.6 (5.4) mean (SD) 10.4 (8.2) mean change: 0.8 (8.4)
Moosmayer 2010 & 2014[52,53]*	US: tear size increase >5 mm	60	outcome not applicable		38	14 (37)
	US: tear size increase ≤ 5 mm				38	24 (63)

I1 = Repair + Acromioplasty; I2 = Acromioplasty; MRI = Magnetic Resonance Imaging; N = Number of patients; SD = Standard deviation; US = Ultrasonography.
* Kukkonen: The publications did not provide sufficient information to directly calculate the SD for the mean changes from baseline; therefore, they have been imputed as described in the Cochrane Handbook.[1]
§ Kukkonen: 'anterior to posterior dimension of the perforating footprint defect'.
In general: Data in grey are based on own calculations; Kukkonen: study arm I2 (acromioplasty): data are displayed but not further considered because intervention does not fulfil inclusion criteria.

6.2.4 Outcomes (forest plots, RCTs)

The outcomes stated in section 6.2.3 are displayed in forest plots either as single-study results or as pooled effect sizes (quantitative analyses), given that more than one study reported the same outcome using a comparable scale at a given time point (Figure 4 to Figure 12).

Shoulder function (based on the CMS [0 – 100 points])

When surgery was compared to conservative treatment, effect estimates (expressed as MD) at 12, 24 and 60 months favoured the surgical intervention (Figure 4A). The largest effect was observed at 60 months: MD 8.7; 95%-CI 1.3, 16.1; 101 patients; 1 study.[53] Of note, at three and six months, no statistically significant difference was observed between the interventions: MD -6.2; 95%-CI -12.9, 0.5; 112 patients; 1 study[47,48] and MD 1.4; 95%-CI -4.8, 7.5; 206 patients; 2 studies,[47,48,52] respectively.

Shoulder function (based on the ASES score [0 – 100 points], DSST [0 – 12 points] or VAS [0 – 10 cm])

In general, improvement of shoulder function (expressed as MD) was in favour of surgery when compared with conservative treatment (Figure 4B). Except for the measurement with the DSST at 12 months, these differences reached statistical significance.

Shoulder pain (based on the VAS [0 – 10 cm])

Similar to the outcome shoulder function (based on the CMS), effect estimates at 12, 24, and 60 months favoured the surgical intervention (Figure 5A). The largest effect was observed at 60 months: MD 1.3; 95%-CI 0.5, 2.1; 101 participants; 1 study.[53] Of note, at three and six months, pain improvement was also in favour of surgery but did not (always) reach statistical significance.

Shoulder pain (based on the CMS subscore [0 – 15 points])

Changes in shoulder pain based on the CMS subscore were assessed in one study (Figure 5B).[47,48] Effect estimates at three, six, 12 and 24 months were in favour of surgery but did not reach statistical significance.

Shoulder range of motion (based on the CMS subscore [0 – 40 points] or goniometer [degrees])

Effect estimates for this outcome were inconsistent: whereas the estimates for range of motion measured with the CMS subscore were in favour of conservative treatment at each time point, the goniometer measurements favoured surgical treatment (Figure 6). However, statistical significance was generally not reached (i.e., most of the 95%-CIs included the possibilities of either worsening or improving symptoms).

Muscle strength (based on the CMS subscore [0 – 25 points])

At three and six months, changes in muscle strength were in favour of the comparison group undergoing conservative treatment: MD -4.2; 95%-CI -6.6, -1.9; 112 patients; 1 study[47,48] and MD -2.10; 95%-CI -3.8, -0.4; 206 patients; 2 studies,[47,48,52] respectively (Figure 7). From 12 months on, no differences in the change in muscle strength were observed between the interventions.

Health-related quality of life (SF-36 [0 – 100 points])

Data from the only study reporting on QoL showed no significant differences between the interventions when surgical treatment was compared with conservative treatment at six, 12, 24 and 60 months (Figure 8).[52,53] Effect estimates (MDs) ranged between 1.0 and 3.1 (102 patients; 1 study),[52,53] but all corresponding 95%-CI included both the possibility of worsening and improving QoL.

Adverse events

The risk of any adverse events was not found to differ, either statistically or clinically, when surgical treatment was compared with conservative treatment (RR 1.5; 95%-CI 0.5, 4.3; 255 patients; 3 studies; Figure 9). [47,48,51-53] Furthermore, no treatment-related complications were reported in any of

the groups (i.e., three zero-event studies). Therefore, no effect estimate could be calculated for this outcome (treatment-related complications).

Failed surgery defined as re-tear of the repaired tendon

Lambers Heerspink et al.[51] reported a high re-tear rate of 74% (14/19 patients) at 12 months, whereas Moosmayer et al.[52,53] reported lower rates of 12% (for partial-thickness re-tears at 12 and 60 months) and between 8% and 13% (for full-thickness re-tears at 12 and 60 months, respectively) (Table 15). For this outcome, no comparative analysis was possible because it relates only to the surgery group.

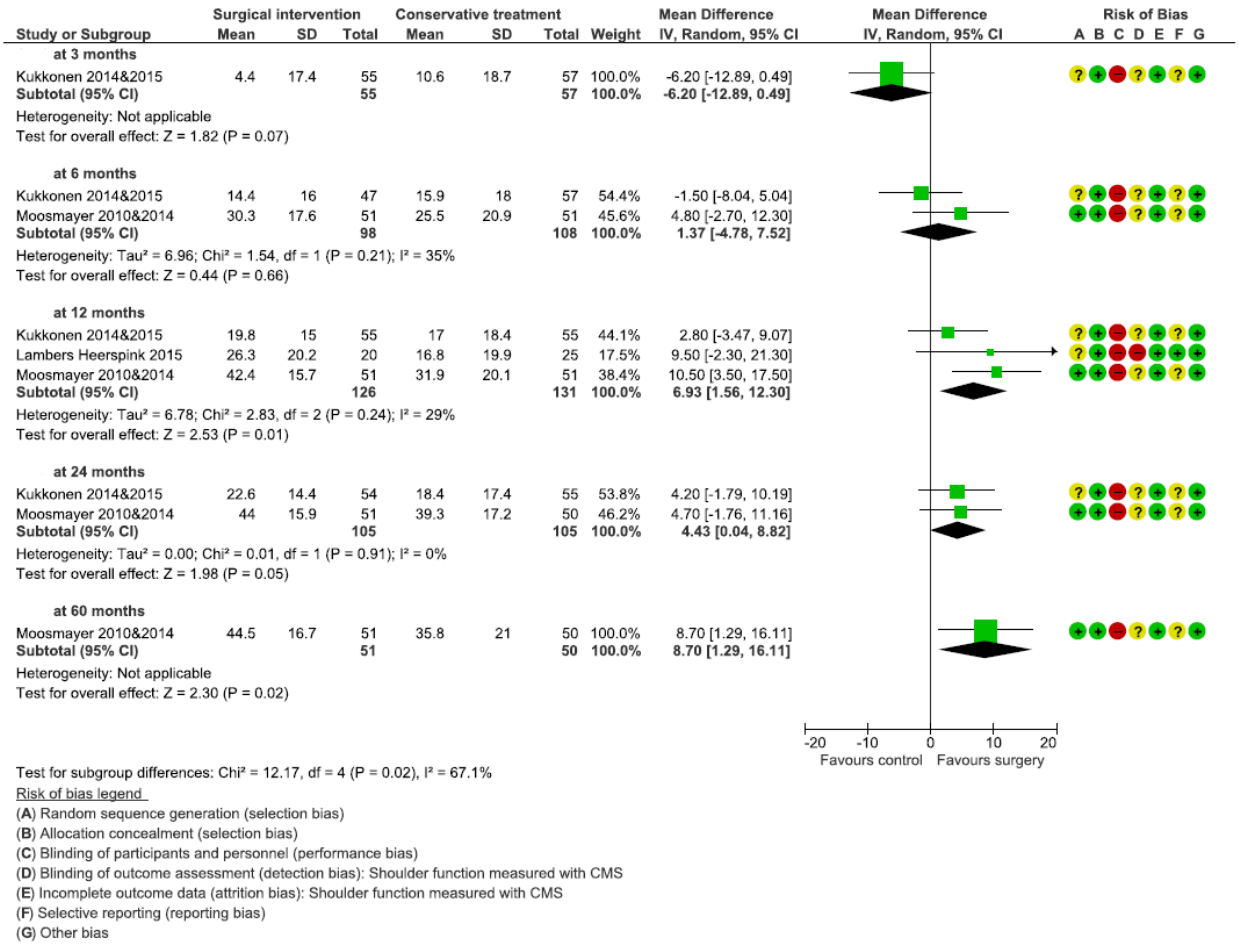
Structural findings, supraspinatus tear characteristics (other than re-tear)

Risk ratios for fatty degeneration and muscle atrophy did not differ between the interventions at 24 months: fatty degeneration (grade 3): RR 2.1; 95%-CI 0.6, 7.9; 100 patients; 1 study[47,48] (Figure 11) and muscle atrophy: RR 0.9; 95%-CI 0.5, 1.5; 100 patients; 1 study[47,48] (Figure 12). However, the sagittal tear size was in favour of the surgical intervention at 24 months: MD -5.0 mm; 95%-CI -8.1, -1.9; 100 patients; 1 study (Figure 13).

Figure 4: Shoulder function (RCTs)

A. Shoulder function measured with the CMS: means refer to the mean change from baseline.

CMS: 0 – 100 points; 0 = worst, 100 = best outcome.

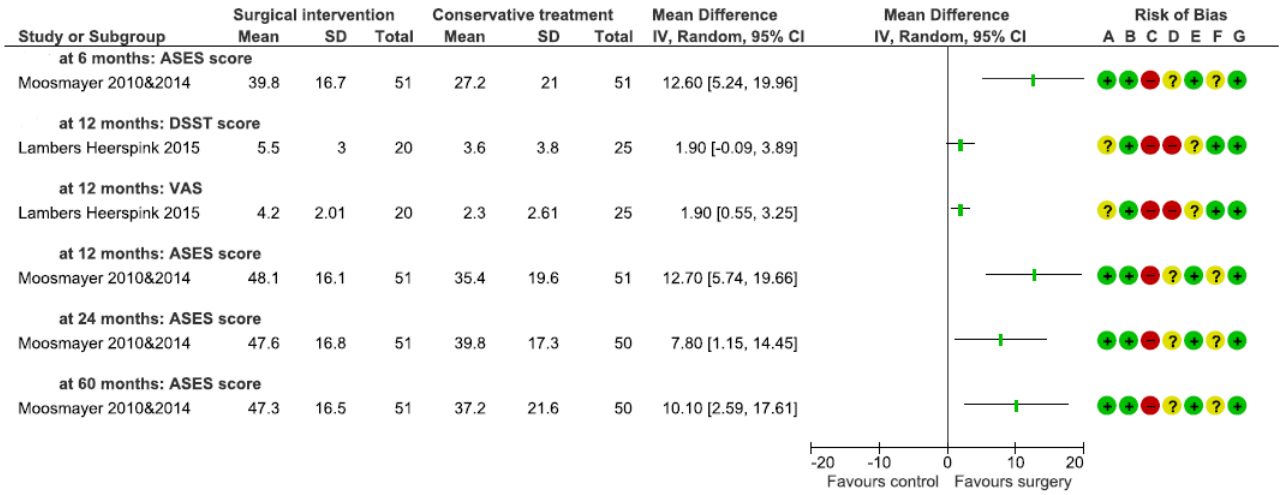


B. Shoulder function measured with different scores: means refer to the mean change from baseline.

ASES: 0 – 100 points; 0 = worst, 100 = best outcome.

DSST: 0 – 12 points; 0 = worst, 12 = best outcome.

VAS: 0 – 10 cm; NOTE: The algebraic sign of the mean changes from baseline measured with the VAS for function were inverted to be in alignment with the other scores (ASES and DSST) reporting better outcomes with increasing scores (compare data with Table 7).



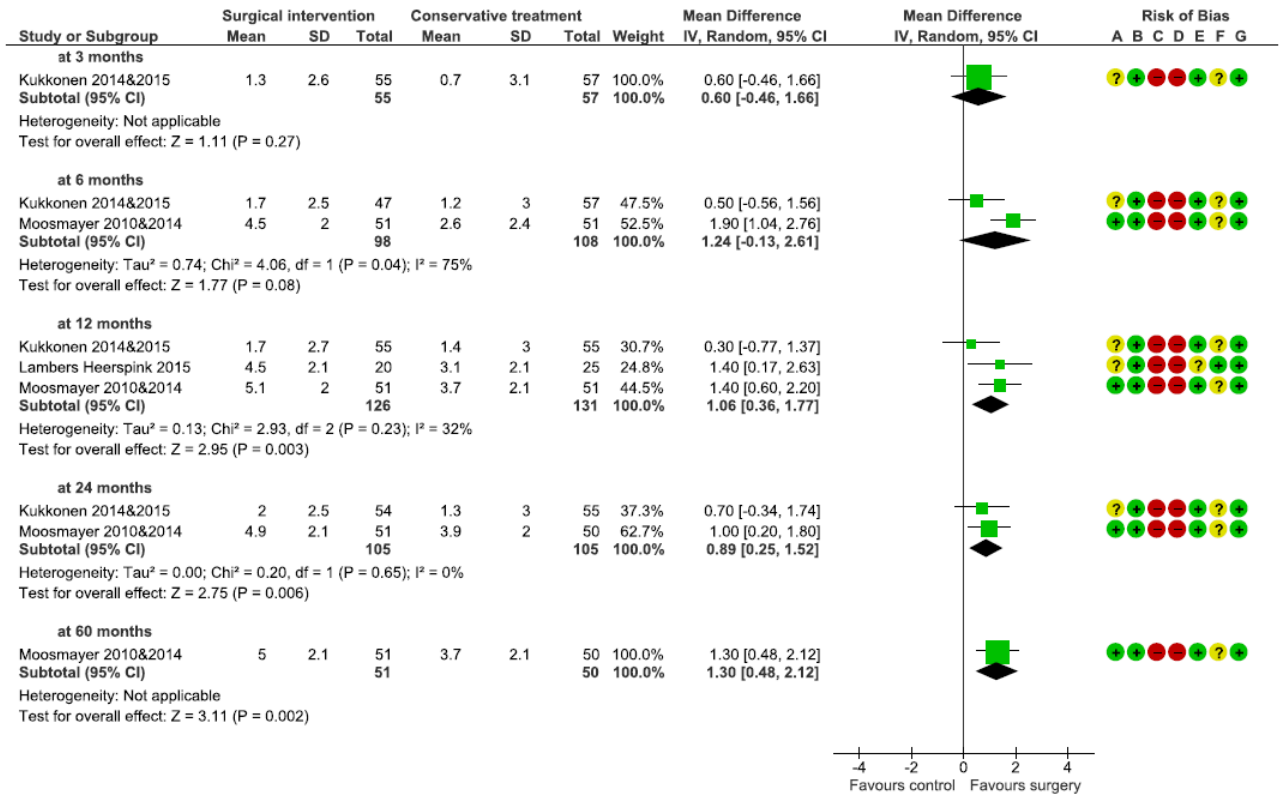
Risk of bias legend
(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
(**C**) Blinding of participants and personnel (performance bias)
(**D**) Blinding of outcome assessment (detection bias): Shoulder function measured with other scores than CMS
(**E**) Incomplete outcome data (attrition bias): Shoulder function measured with other scores than CMS
(**F**) Selective reporting (reporting bias)
(**G**) Other bias

ASES = American Shoulder and Elbow Surgeons Score; Chi^2 = Statistical Test Chi-square; CI = Confidence Interval; CMS: Constant Murley Score; DSST = Dutch Simple Shoulder Test; P = P value; SD = Standard Deviation; VAS Visual Analogue Scale.

Figure 5: Shoulder pain (RCTs)

A. Shoulder pain measured with the VAS: means refer to the mean change from baseline.

VAS: 0 – 10 cm; NOTE: The algebraic sign of the mean changes from baseline measured with the VAS for pain were inverted to be in alignment with the other scores (e.g., CMS, ASES and DSST) reporting better outcomes with increasing scores (compare data with Table 8).

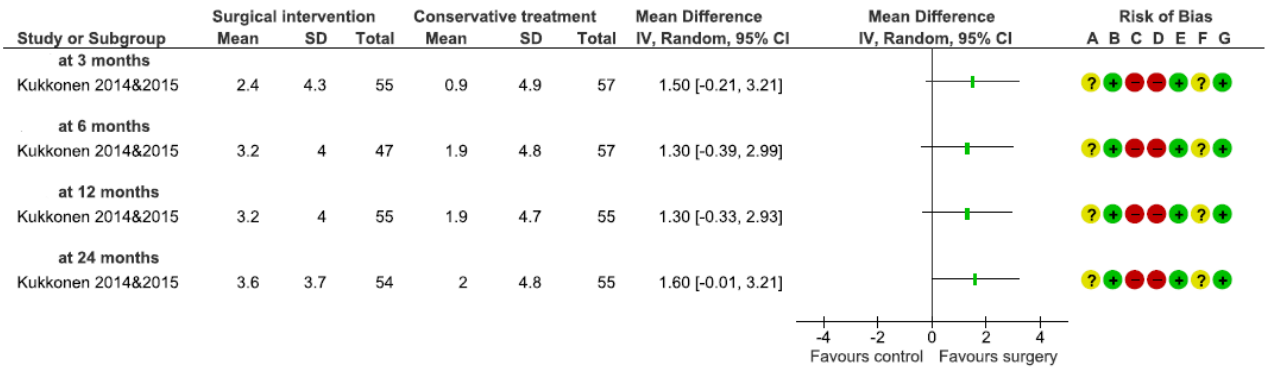


Risk of bias legend

(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
(**C**) Blinding of participants and personnel (performance bias)
(**D**) Blinding of outcome assessment (detection bias): Shoulder pain
(**E**) Incomplete outcome data (attrition bias): Shoulder pain
(**F**) Selective reporting (reporting bias)
(**G**) Other bias

B. Shoulder pain measured with a subscore of the CMS: means refer to the mean change from baseline.

CMS subscore: 0 – 15 points; 0 = worst, 15 = best outcome.



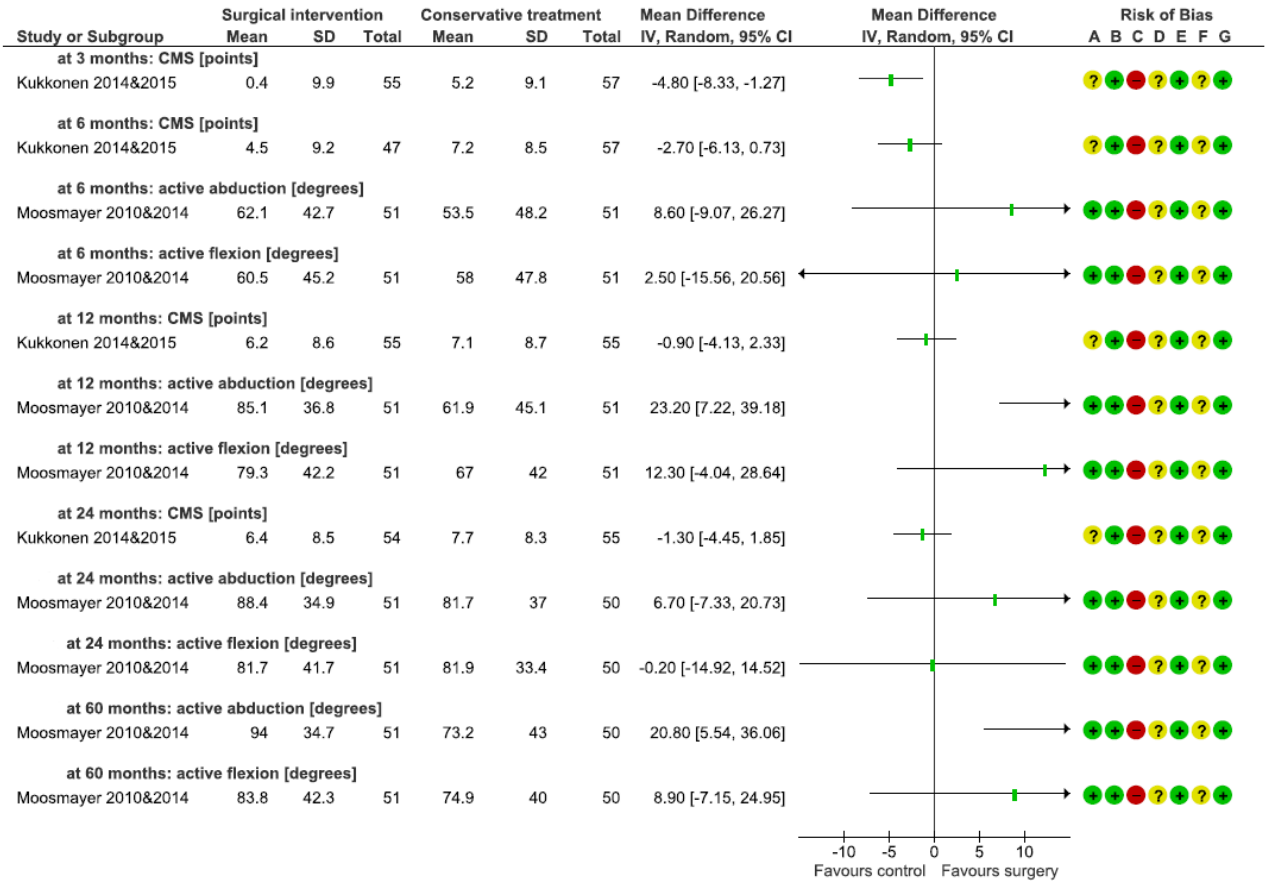
Risk of bias legend
(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
(**C**) Blinding of participants and personnel (performance bias)
(**D**) Blinding of outcome assessment (detection bias): Shoulder pain
(**E**) Incomplete outcome data (attrition bias): Shoulder pain
(**F**) Selective reporting (reporting bias)
(**G**) Other bias

ASES = American Shoulder and Elbow Surgeons Score; Chi^2 = Statistical Test Chi-square; CI = Confidence Interval; CMS: Constant Murley Score; DSST = Dutch Simple Shoulder Test; P = P value; SD = Standard Deviation; VAS Visual Analogue Scale.

Figure 6: Range of motion (RCTs)

Measured with the CMS subscore or a goniometer: means refer to the mean change from baseline.

CMS subscore: 0 – 40 points; 0 = worst, 40 = best outcome. Data of goniometer measurements are provided in degrees.



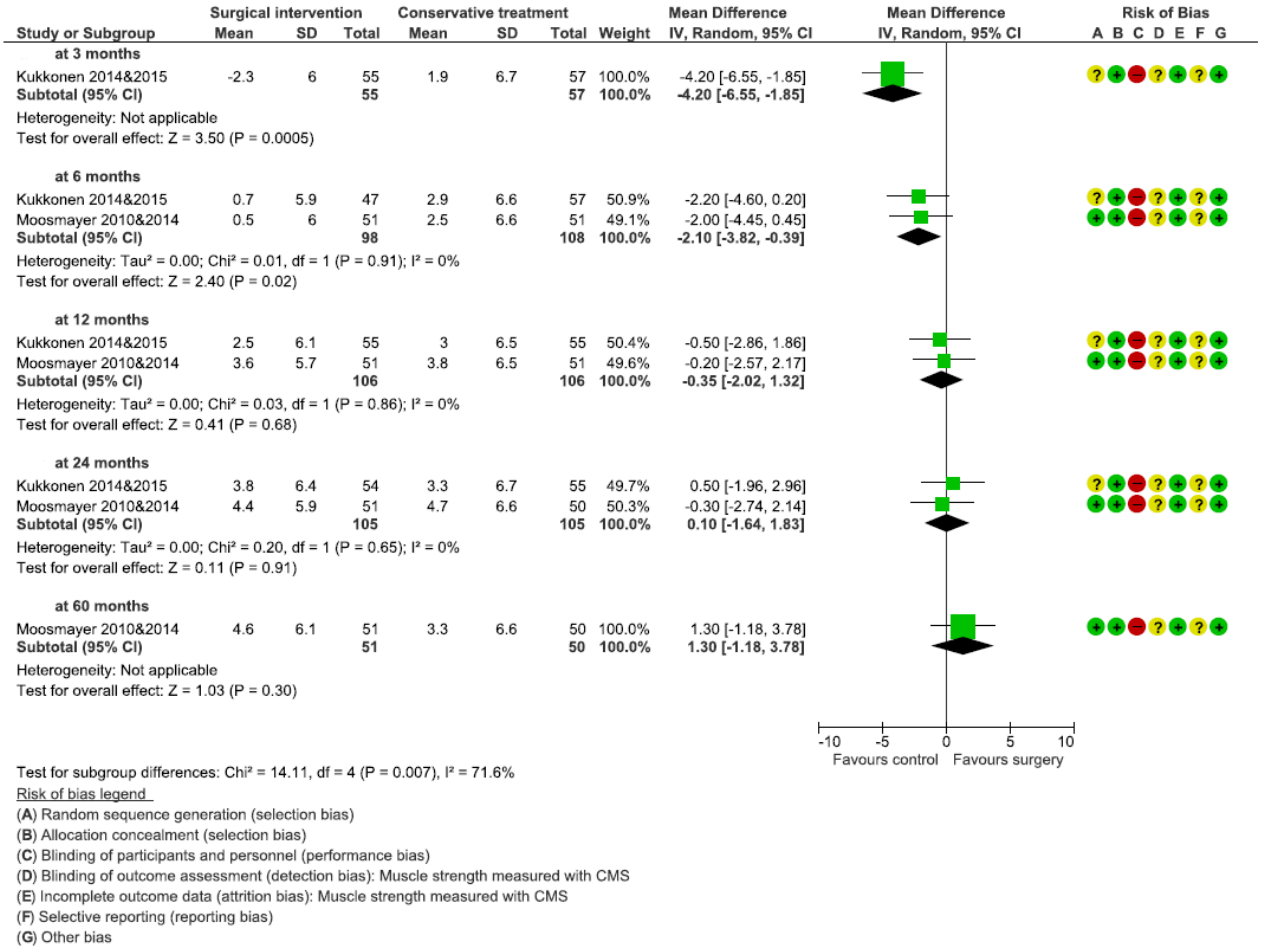
Risk of bias legend
(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
(**C**) Blinding of participants and personnel (performance bias)
(**D**) Blinding of outcome assessment (detection bias): Range of motion (ROM)
(**E**) Incomplete outcome data (attrition bias): Range of motion (ROM)
(**F**) Selective reporting (reporting bias)
(**G**) Other bias

CI = Confidence Interval; CMS: Constant Murley Score; SD = Standard Deviation.

Figure 7: Muscle strength (RCTs)

Measured with the CMS subscore: means refer to the mean change from baseline.

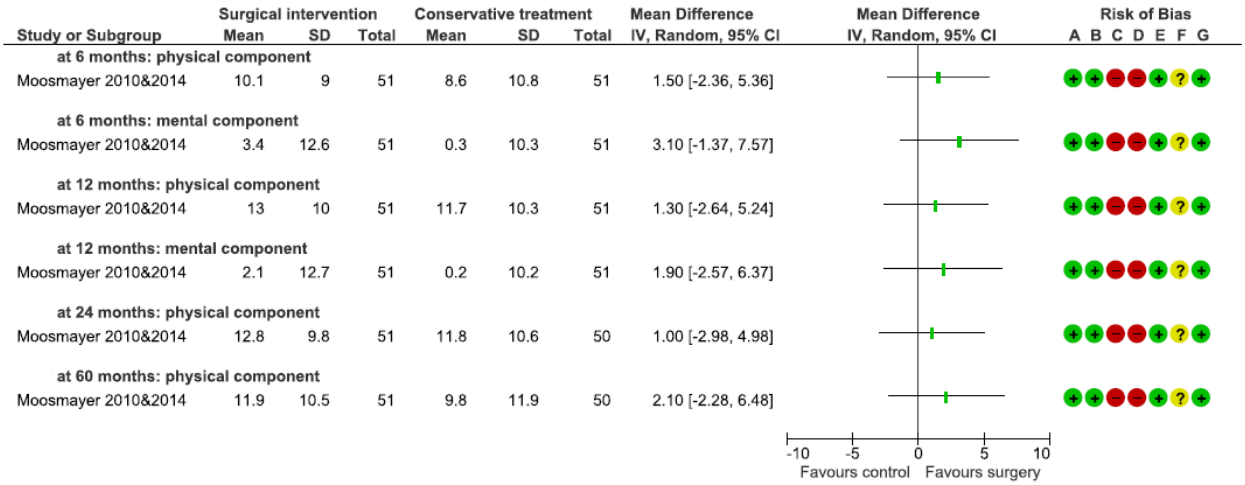
CMS subscore: 0 – 25 points; 0 = worst, 25 = best outcome.



Chi^2 = Statistical Test Chi-square; CI = Confidence Interval; CMS: Constant Murley Score; P = P value; SD = Standard Deviation.

Figure 8: Health-related quality of life (RCTs)

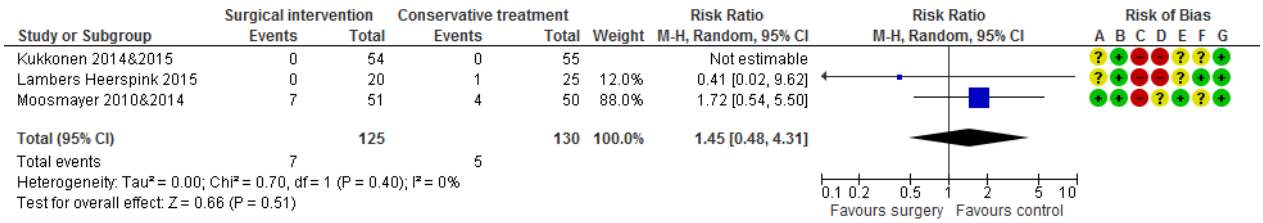
Measured with the SF-36: means refer to mean change from baseline.
SF-36: 0 – 100 points; 0 = worst, 100 = best outcome.



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias): Quality of life
(E) Incomplete outcome data (attrition bias): Quality of life
(F) Selective reporting (reporting bias)
(G) Other bias

CI = Confidence Interval; CMS: Constant Murley Score; SD = Standard Deviation; SF-36 = 36-Item Short Form Health Survey..

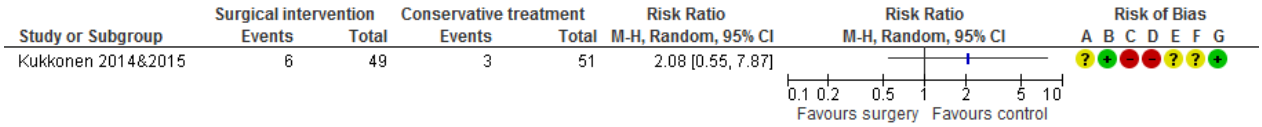
Figure 9: Any adverse events: at the longest follow-up (RCTs)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias): Adverse events
(E) Incomplete outcome data (attrition bias): Adverse events
(F) Selective reporting (reporting bias)
(G) Other bias

Chi^2 = Statistical Test Chi-square; CI = Confidence Interval; P = P value; SD = Standard Deviation.

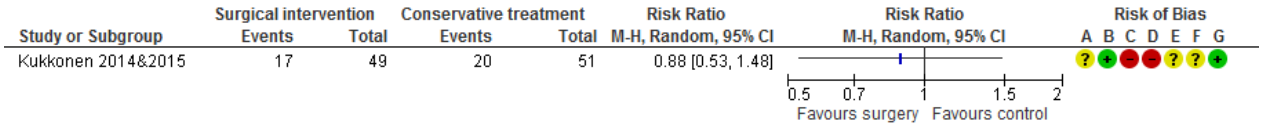
Figure 10: Fatty degeneration (Goutallier grade 3) at 24 months (RCTs)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias): MRI findings
(E) Incomplete outcome data (attrition bias): MRI findings
(F) Selective reporting (reporting bias)
(G) Other bias

CI = Confidence Interval.

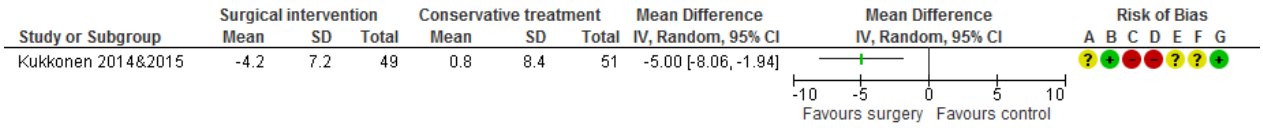
Figure 11: Muscle atrophy: at 24 months (RCTs)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias): MRI findings
(E) Incomplete outcome data (attrition bias): MRI findings
(F) Selective reporting (reporting bias)
(G) Other bias

CI = Confidence Interval.

Figure 12: Change in sagittal tear size (mm): means refer to the mean change from baseline (RCTs)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias): MRI findings
(E) Incomplete outcome data (attrition bias): MRI findings
(F) Selective reporting (reporting bias)
(G) Other bias

CI = Confidence Interval; SD = Standard Deviation.

6.3 Non-randomised studies (NRSs)

6.3.1 Study characteristics (NRSs)

The main study characteristics of the seven NRSs (eight publications)[54-61] meeting our inclusion criteria are displayed in Table 17 to Table 20.

Setting and key characteristics

The studies were published between 2000[60] and 2018.[61] All but one NRS (two publications)[54,55] were based on retrospective data. Yamada et al.[60] and Vad et al. [59] included the earliest data, from patients treated between 1979 and 1999. The included studies were conducted in Europe (Italy; two studies; 81 participants),[56,57] Asia (Korea and Japan; three studies; 406 participants)[58,60,61] and North America (Canada and USA; two studies; 180 participants).[54,55 59] Overall, 343 patients were assigned to surgical treatment and 313 to conservative treatment. In total, 656 participants (representing 656 shoulders) were investigated, of whom 93 were investigated prospectively. The shortest mean follow-up from baseline (assignment to the interventions) was two months,[58] and the longest follow-up was 60 months.[54,55] In Fabbri et al.,[57] the mean length of follow-up differed between the groups by 11 months: 50 months (surgical intervention group) and 61 months (conservative treatment group). Furthermore, Yamada et al.[60] reported a mean length of follow-up of 48 months with an upper limit of 276 months.

Participants

Across the NRSs, the mean patient age ranged between 58[54,55,57] and 70[60] years, and the percentage of female patients ranged from 12%[60] to 78%.[56] Six studies exclusively enrolled patients with full-thickness tears, and one included a mixed population (full-thickness and partial-thickness tears).[58] The results of this study were, however, reported separately for both patient populations, and only the population with full-thickness tears was considered. Five studies specified that MRI[54-57,59,61] was used as the imaging method for diagnosing the tears. Only one study specified the etiology of the tears and reported that almost half of the patients had traumatic tears.[24 25] The mean duration of symptoms at baseline was specified in four studies and ranged between six and 44 months.[54,55,59-61] In all but one of the NRSs,[57] more than 70% of patients showed an involvement of the dominant arm. Four studies explicitly excluded patients who had previously undergone shoulder surgery;[56,57,59,61] the remaining three studies provided no information on this aspect. The proportion of patients with co-morbidities was provided by only two studies.[56,61]

Surgical and conservative treatment

Four studies reported that the surgical intervention was done arthroscopically.[56-58,61] The remaining studies did not specify the type of surgery ([mini]-open or arthroscopic). Three studies reported that the surgical intervention included acromioplasty for selected participants.[56,58,60]

Patients in the conservative treatment group underwent physiotherapy with or without additional modalities (e.g., electrotherapy, thermotherapy). Furthermore, five studies[56,58-61] reported that oral medication and/or steroid injections were part of the treatment. The overall duration of the treatment was only specified in two studies.[56,57]

Table 17: Key study characteristics (NRSs)

Study	Design	Country	Total N enrolled	Intervention	Comparison	Recruitment/ data collection	Follow-up (months)	Patient flow
Boorman 2014&18[54,55]	Prospective cohort	Canada	93 patients (93 shoulders)	all patients: initial 3-month period of home-based treatment programme, then categorisation 'failure' group 23*	'success' group 70*	10/08-09/10	24 and 60	At 24 months: 10 patients crossed over: I: 4/23 4 did not go for surgery (but for conservative treatment); C: 6/70 6 did not go for control (but for surgery) => I: 25; C: 68 At 60 months: missing data: 30/93 (32%) I: 17/25; C: 46/68 death 3/93, unwilling to complete RC-QoL 16/93, unable to contact 11/93
De Carli 2017[56]	Retrospective cohort (clinical database)	Italy	40 patients (40 shoulders)	'all participants had indication for surgical repair'. 20	'refused surgery/ contraindication' 20 (18 analysed)	01/12-12/14	18 (± 2.5)	Missing data: 2/40 (5%) I: 0/20 C: 2/20 2 had undergone surgical repair
Fabbri 2016[57]	Retrospective cohort (clinical database)	Italy	41 patients (41 shoulders)	Surgical and conservative treatments options were discussed with the patient, depending on clinical symptoms and functional restrictions 19 (17 analysed)	22 (18 analysed)	2002-2008	mean (range) I: 50 (30-70) C: 61 (36-88)	Missing data: 6/41 (15%) I: 2/19 2 patients with a re-tear C: 4/22 no reasons provided
Lee 2016[58]	Retrospective cohort	Korea	229 patients (229 shoulders)	115§	114§	01/08-01/13	2-6 and 12	The authors report 'missing data', but numbers or reasons were not provided.
Vad 2002[59]	Retrospective cohort	USA	76 patients# (76 shoulders)	'patients failing a 6-months rehabilitation' 36	'not deemed feasible for surgery' 40	1990-1995	mean I: 38 / C: 37	no missing data reported
Yamada 2000[60]	Retrospective cohort	Japan (2 centres)	40 patients (40 shoulders)	not defined 26	'refused surgery' 14	1979-1999	mean (range) 48 (12-276)	no missing data reported
Yoo 2018[61]	Retrospective cohort	Korea	137 patients (137 shoulders)	all patients: initial ≥3-month period of conservative treatment, then categorisation 'agreed to surgery' 104	'refused surgery' 33	-	mean (range) 13.2 (12-15)	no missing data reported

C = Control; I = Intervention; N = Number of patients; NRS = Non-randomised Study; RC-QoL = Rotator cuff – Quality of Life.

* Boorman: The presented participant numbers relate to the 93 participants who were included after an initial 3-month period of conservative treatment.

§ Lee: The study includes both patients with a high-grade partial-thickness or small-to-medium-sized (≤ 3 cm) full-thickness tear. A total of 357 patients were enrolled, including 183 patients that received conservative and 174 patients that received surgical treatment. In the conservative and surgical groups, respectively, 69 and 59 patients showed a partial-thickness tear. These patients were excluded from the current systematic review, focusing on patients with full-thickness tear only.

Vad: This study also reports on an arthroscopic debridement group, which is not further considered in this review.

Table 18: Inclusion and exclusion criteria (NRSs)

Study	Key criteria
Boorman 2014&18[54,55]	**Inclusion**: - full-thickness rotator cuff tear of the SSP or ISP (confirmed by US or MRI) - symptoms for ≥ 3 months - age 40-85 years **Exclusion**: - exhausted non-operative treatment (i.e., patients who had already completed a minimum of 3 months of conservative treatment including exercises, medication or other modalities; with or without injections) - concomitant pathology of the affected shoulder (e.g., instability, osteoarthritis) - full-thickness tear of the SSC or TM - injury or onset of symptoms <3 months prior to presentation - elite athlete- substantial cervical spine pathology and/or radiculopathy and acute injury (symptoms for <3 months) - substantial medical issues precluding surgery and secondary gain issues (i.e., workers' compensation or litigation) and unable to complete study outcomes
De Carli 2017[56]	**Inclusion**: - small-to-medium (≤ 3 cm, based on Cofield criteria) symptomatic full-thickness SSP tears (evidenced by clinical and radiological assessment [MRI]) - indication for surgical repair - age 50-75 years **Exclusion**: - involvement of multiple tendons (not further specified) - previous shoulder surgery -- bilateral involvement (confirmed by US in symptomatic patients) - physiotherapy prior to orthopaedic examination - frozen shoulder, rheumatoid arthritis, neurological disorders, radiologic and symptomatic osteoarthritis of the glenohumeral or acromioclavicular joint
Fabbri 2016[57]	**Inclusion**: - medium-to-large full-thickness rotator cuff tear, diagnosed by MRI - age > 50 years - minimum follow-up of 24 months **Exclusion**: - presence of significant diseases involving the other shoulder (rotator cuff tears, glenohumeral arthritis) - previous surgery of the affected or the other shoulder
Lee 2016[58]	**Inclusion**: -high-grade partial-thickness* or small-to-medium-sized full-thickness tear (≤3 cm) **Exclusion**: - patients aged < 50 years - mini-open and open surgery - large-to-massive-sized full-thickness tear (≥3 cm) - paralysis of the shoulder girdle muscles and history of fractures, instability or septic shoulder

Vad 2002[59]	**Inclusion**: - full-thickness rotator cuff tear (involving at least two tendons, measuring 5 cm or longer, determined by MRI) **Exclusion**: - not specified
Yamada 2000[60]	**Inclusion**: - massive rotator cuff tear (confirmed by arthrography or surgery) **Exclusion**: - not specified
Yoo 2018[61]	**Inclusion**: - recommendation for surgical rotator cuff repair; thereby, full-thickness rotator cuff tear, confirmed by MRI - persistent pain and functional disability despite conservative treatment for more than 3 months **Exclusion**: - age < 18 years or > 75 years - presence of other local or systemic diseases affecting the shoulder and the presence of a medical contraindication for surgery or anaesthesia - prior history of trauma or surgery of the affected shoulder

SSP = Supraspinatus; ISP = Infraspinatus; US = Ultrasonography; MRI = Magnetic Resonance Imaging; NRS = Non-randomised Study; SSC = Subscapularis, TM = Teres Minor.
* Lee: These patients were not considered in the current systematic review.

Table 19: Patient characteristics (NRSs)

Study	Age (years) Mean (SD) or mean (range)		Sex N (%) females		Symptom duration (months) Mean (SD)		Shoulder-related functional disability Mean (SD) or mean (range)		Affected tendons N (%)		Affected arm N (%)		Co-morbidities N (%)		Previous surgery†		Patients with traumatic tears (%)	
	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C
Boorman 2014&18[54,55]	58 (8.9)	61 (9.4)	9 (39)	30 (43)	32 (45)	26 (37)	RC-QoL 33 (14.7)	49 (21.5)	-		dominant arm 18 (78)	49 (70)	-		-		10 (43)	36 (51)
De Carli 2017[56]	63.3 (4)	64.2 (3)	15 (75)	14 (78)	-		CMS 46 (6)	47 (5)	-		-		see footnote§		0 (0)	0 (0)	-	
Fabbri 2016[57]	58.7 (50-68)	61 (55-71)	12 (63)	10 (45)	-		-		SSP only 15 (88)	16 (89)	dominant arm 6 (32)	4 (18)	-		0 (0)	0 (0)	-	
									SSP + ISP 2 (12)	2 (11)								
Lee 2016[58$]	<61 years 35%	33%	-		-		-		-		-		-		-		-	
Vad 2002[59]	59.4 (-)	63.2 (-)	58 (54)		6 (1-17)		L'Insalata score 33 (1.2)	44 (1.7)	-		dominant arm 31 (86)	30 (75)	-		0 (0)	0 (0)	- -	
Yamada 2000[60]	62 (47-82)	70 (55-81)	3 (12)	5 (36)	13 (1-54)#	44 (12-132)#	JOA score 59 (43-73)	53 (40-65)	-		right arm 22 (85)	12 (86)	-		-		-	
Yoo 2018[61]	64.2 (8.9)	64.9 (7.6)	64 (62)	14 (42)	41 (75)	30 (45)	CMS 48 (17.8)	56 (15)	-		dominant arm 78 (75)	27 (82)	diabetes 26 (25)	8 (24)	0 (0)	0 (0)	-	

C = Control; CMS = Constant Murley Score; I = Intervention; ISP = Infraspinatus; JOA = Japanese Orthopaedic Association; N = Number of patients; RC-QoL = Rotator cuff - Quality of Life; SD = Standard Deviation; SSP = Supraspinatus; - = no information.

$ Lee: The study provides patients' characteristics solely for the entire patient population including patients with full-thickness and partial-thickness tear; therefore, the presented data must be interpreted cautiously because they do not exclusively refer to our patient population of interest (approximately 40% of the included patients showed a partial-thickness tear). Additionally, there were missing data under each category, which were not further explained by the study authors.

Yamada: The presented values relate to 'time from injury to evaluation' in the conservative group and 'time from injury to surgery' in the surgical group.

§ De Carli: 'The reasons for selecting conservative treatment were concomitant disorders contra-indicating surgery in 12 patients (pulmonary disease, 4 patients; previous cardiac disease, 7 patients; and unstable angina pectoris, 1 patient) (66.7%) and personal reasons in 8 patients (33.3%). Patients with diabetes or hormonal diseases were absent in both groups. Hypertension and hypercholesterolemia were equally distributed in both groups.'

† Previous surgery: The presented 0 values for 'previous surgery' relate to studies in which 'previous surgery' at the affected shoulder was an exclusion criterion.

Table 20: Characteristics of the surgical and conservative treatment (NRSs)

Study	Intervention		Control	
	Surgical treatment including postoperative treatment	**Additional medication**	**Conservative/comparison treatment**	**Additional medication**
Boorman 2014&18[54,55] *	**Surgical intervention**: - rotator cuff repair surgery (after an unsuccessful rehabilitation period of 3 months) **Postoperative treatment**: -not specified	-	**Duration**: not specified 'no operation'	-
De Carli 2017[56]	**Surgical intervention**: - arthroscopic repair, with/without acromioplasty and/or biceps tenotomy **Postoperative rehabilitation**: - brace in neutral shoulder position for 4 weeks; passive exercises from 2 weeks; assisted and active exercises from 5 weeks; full return to activities allowed after 3 months	NSAIDs as needed.	**Duration**: at least 12 sessions over 4 weeks (physiotherapy) followed by home-based exercises including passive, assisted and active exercises.	- NSAIDs as needed
Fabbri 2016[57]	**Surgical intervention**: - arthroscopic repair **Postoperative treatment**: - sling for 4 weeks; passive exercises after 2 weeks; active exercises after 5 weeks	-	**Duration**: minimum 3 months - prescription of physiotherapy; exercised-based therapy including instructions for self-stretching exercises	-
Lee 2016[58]	**Surgical intervention**: - arthroscopic repair (all), with/without acromioplasty, and debridement **Postoperative treatment**: - 5-6 weeks of immobilisation; shoulder exercises after immobilisation	pain medication or corticosteroid injection within 3 months postsurgery	**Duration**: not specified - active surveillance (patient education on activity modification, symptom control or prognosis) - therapeutic modality (TENS, heat therapy, therapeutic US) - shoulder exercises (passive and active exercises addressing ROM, strength and scapular stabilisation)	- steroid injections - NSAIDs or opioids
Vad 2002[59]	**Surgical intervention**: - surgical repair **Postoperative treatment**: no information provided	-	**Duration**: not specified - physical therapy (not further specified)	- oral medication and/or steroid injections
Yamada 2000[60]	**Surgical intervention**: - repair following acromioplasty (all) - additional procedures: tenorrhaphy (n = 12), fascia grafting (n = 8), lateral LHB tendon transfer (n = 2), teres minor muscle transfer (n = 3), supraspinatus muscle transfer (n = 1) **Postoperative treatment**: - physical therapy: from day 3: passive ROM, pendulum exercises; from day 14: passive extension and internal rotation; from day 36: active ROM and isometric exercises	-	**Duration**: not specified - early period (1-3 weeks): sling and injections - heat treatment (e.g., hotpacks) and rotator cuff strengthening exercises 'as needed', passive ROM exercises	- subacromial injections (lidocaine/dexamethasone; 1-2/week, up to 15 injections)
Yoo 2018[61]	**Surgical intervention**: - usually single row or transosseous equivalent arthroscopic repair **Postoperative treatment**: - 4 weeks of immobilisation in a sling with a small pillow; gentle passive ROM exercises, with advancement to active exercises ; from 3 months (with improved ROM): strengthening	-	**Duration**: not specified - activity modification - rehabilitation - regular clinical visits for evaluation of tear progression	- medication (unspecified) and/or steroid injections

LHB = Long head of the biceps; N = Number of patients; NSAID = Non-Steroidal Anti-Inflammatory Drug(s); ROM = Range of Motion; TENS = Transcutaneous electrical nerve stimulation; US = Ultrasonography; - = No information.

*The initial three-month conservative treatment period that all participants underwent before they were divided into two groups based on whether they had surgery or continued with non-surgical treatment included a supervised exercise-based rehabilitation programme and the optional use of anti-inflammatory medications.

6.3.2 Risk of Bias (NRSs)

(i) Bias due to confounding

Relevant prognostic factors (e.g., age, tear size, involvement of multiple tendons, fatty degeneration, insurance claims, history of trauma, duration of symptoms or psychological aspects),[62-65] were generally insufficiently considered in the study pool. Although all the studies reported some 'selected' baseline data for both groups, the study authors neither adjusted for potential imbalances nor justified their relevance. Notably, in all but one study,[58] either the patient chose the treatment they wanted to have, or clinical characteristics including tear size, functional restrictions, or other clinical symptoms were used as criteria for assigning patients to their respective group. Consequently, the observed differences in outcomes between the interventions may largely be attributable to confounding rather than to the effects of the interventions.

(ii) Bias in the selection of patients into the study

In four[54-57,61] of the seven studies, bias in the selection of patients into the study was not associated with a risk for bias as patients were either selected consecutively or predefined inclusion and exclusion criteria were applied. Three studies,[58-60] however, selected their patient population based on methods associated with a serious risk of bias (e.g., two comparable treatment groups were selected from different hospitals at different times, or 'convenient sampling' was based on selected demographic data [sex, age, tear on dominant side, pain onset, trauma]).[58]

(iii) Bias in the classification of the intervention

Owing to the nature of the compared interventions (surgical intervention, conservative treatment [non-surgical treatment]), a risk of misclassification can generally be excluded.

(iv) Bias due to deviations from the intended interventions

There was either no or insufficient information on the actual intake of additional medication (e.g., pain relievers) or on the provision of cointerventions, including insufficient information on whether cointerventions were balanced across the groups.

(v) Bias due to missing data

In four[56,59-61] of the seven studies, attrition bias due to missing data may not be an issue. The remaining three studies showed a serious risk for attrition bias due to a relatively high proportion of drop-outs (up to 30%) and either no or only limited information on why these data were not available.[54,55,57,58]

(vi) Bias in the measurement of outcomes

The nature of studies comparing surgical with non-surgical interventions generally precludes the blinding of participants. Consequently, the observed differences may, to an undeterminable extent, be attributable to the influence of patients' perceptions and preferences regarding the interventions rather than to the effects of the interventions.

(vii) Bias in the selection of the reported results

Risk of bias due to the selection of the reported outcomes could not be judged for any of the studies due to a lack of published protocols or registration records.

(viii) Overall bias

Overall, all the included non-randomised studies were judged to be at a serious or critical risk of bias. Bias due to confounding and the selection of participants (selection bias) into the groups were the key reasons for this judgement.

Table 21: Risk of Bias after ROBINS-I (NRSs)

Study	Bias caused by confounding*	Bias in the selection of participants	Bias in the classification of the intervention#	Bias due to deviations from the intended interventions	Attrition bias due to missing data	Detection bias in the measurement of outcomes	Reporting bias in the selection of the reported results	Overall judgement
Boorman 2014&18[54,55]	critical categorisation after participating in a 3-month home-based treatment programme: responder (assigned to conservative treatment) and failure (assigned to surgery) no adjustment for confounding	low 93 patients prospectively included	low	no information$	serious missing data: up to 32% at the longest follow-up	serious/moderate both the sport medicine physician and surgeon were blinded to the RC-QoL results but not the patient	unclear	**CRITICAL**
De Carli 2017[56]	critical categorisation: assignment to surgery or conservative treatment was based on contraindications and personal reasons no adjustment for confounding	low 40 consecutive patients retrospectively included	low	no information$	low/moderate missing data: 2%	serious no blinding described	unclear	**CRITICAL**
Fabbri 2016[57]	critical categorisation: assignment to surgery depended on clinical symptoms and functional restrictions no adjustment for confounding	low 63 patients retrospectively identified meeting inclusion criteria	low	no information$	serious missing data: 11%-18%, reasons not fully provided)	serious/moderate clinical examination was performed by an independent blinded examiner, but the patient was not blinded	unclear	**CRITICAL**
Lee 2016[58]	serious approaches to control for predefined prognostic factors were described, but only a selection of known confounders were addressed no adjustment for confounding	serious patients from 3 centres were identified retrospectively; data were randomly extracted, then 'convenient sampling' was based on sex, age, tear on dominant side, pain onset and trauma	low	no information$	serious missing data: '[…] sample size was too small due to missing data excluding the calculation of SDs […]' - for some outcomes	critical no blinding described; telephone interview to assess pain and ROM in patients who were lost to follow-up in a year	unclear	**SERIOUS**

Vad 2002[59]	critical categorisation based on tear size and tissue quality: surgery (patients failing a ≥6-month rehabilitation programme), conservative treatment (patients not feasible for surgery) no adjustment for confounding	serious 78 patients were retrospectively identified	low	no information[$]	low data reported for all participants initially included	serious no blinding described	unclear	**CRITICAL**
Yamada 2000[60]	critical categorisation: conservative treatment was selected by the patients no adjustment for confounding	serious groups selected retrospectively from 2 hospitals treated at different time ranges: group I: conservative treatment (1979-99) group II: surgery between (1982-97)	low	no information[$]	low data reported for all participants initially included	serious no blinding described	unclear	**CRITICAL**
Yoo 2018[61]	critical categorisation after participating in a ≥3-month conservative treatment programme: patients agreeing with or declining surgery (dependent on improvement of symptoms, economic burden, worry for rehabilitation) no adjustment for confounding	low 137 consecutive patients retrospectively identified (all recommended for surgery)	low	no information[$]	low data reported for all participants initially included	critical no blinding described; outcomes and intervention evaluated by telephone surveys at 58.1 months	unclear	**CRITICAL**

RC-QoL = Rotator Cuff- Quality of Life: SD = Standard deviation.

* Baseline confounders (i.e., factors that [may] predict whether an individual receives one or the other intervention of interest) identified in systematic reviews on the prognostic factors influencing the outcome measurements in rotator cuff repair: age, tear size, involvement of multiple tendons, fatty degeneration, insurance (workers compensation) claims, history of trauma (traumatic origin), diabetes, duration of symptoms, disability, shoulder range of motion, shoulder strength, level of activity (sports), tendon retraction, bone mineral density, patient expectations, obesity and psychological/psychosocial factors (e.g., anxiety, fear-avoidance, pain catastrophising).[62-65]

Bias in the classification of the intervention: due to the nature of the comparison groups (surgical intervention, conservative treatment [non-surgical treatment]) misclassification can be excluded.

$ Bias due to deviations from the intended interventions: @retrospective study design: there is no or insufficient information on the actual intake of additional medications (e.g., pain relievers) or on the use of cointerventions and whether these cointerventions were balanced across the groups.

6.3.3 Outcomes (tabular form, NRSs)

The outcomes reported in the identified studies, including the corresponding results, are displayed in Table 22 to Table 29. These data provide the basis for the forest plots (graphical view of the outcome data), quantitative results (pooled estimates) (section 6.3.4), and the GRADE evidence profile for the selected outcomes (Table 31; section 6.4.2).

Although all but three (adverse events, health-related QoL, occupational impairment, and/or hospital length of stay) of our predefined outcomes (section 4.4) were addressed, important data were often missing, making the interpretation of the results difficult. In brief, shoulder function was measured with eight different scales: (i) CMS (0 – 100, 100 = best outcome);[56,57,61] (ii) VAS for function (0 – 10, 10 = worst outcome),[56,57] (ii) Quick Disability of the Arm, Shoulder and Hand score (QuickDASH; 0 – 100, 100 = worst outcome),[56] (iv) Rotator Cuff QoL (RC-QoL; 0 – 100, 100 = best outcome),[54,55] (v) DSST (0 – 12, 12 = best outcome),[57] (vi) L'Insalata Shoulder Questionnaire (0 – 100, 100 = best outcome),[59] (vii) Japanese Orthopaedic Association score (JOA; 0 – 100, 100 = best outcome)[60] and (viii) University of California at Los Angeles score (UCLA; 0 – 35, 35 = best outcome).[61] Furthermore, the Jobe test (with external rotation and internal rotation) was used to assess shoulder function.[57] Shoulder pain was measured with the (i) VAS for pain (0 – 10; 10 = worst outcome),[58,61] (ii) JOA subscore (0 – 30; 30 = best outcome)[60] and the L'Insalata pain subscore (0 – 45; 45 = best outcome).[59] Range of motion was measured with the JOA subscore (0 – 30; 30 = best outcome)[60] or by a goniometer assessing forward flexion and internal rotation (degrees).[59] For the outcome muscle strength, only a descriptive summary was provided by two study authors, disallowing us to estimate any effect estimates.[56,60] Structural findings including failed surgery defined as a re-tear of the repaired tendon and/or tear progression in non-operative patients were derivable from three studies.[56-58]

Table 22: Shoulder function (continuous outcome; NRSs)

Study	Definition of outcome measurement	Follow-up (months)	Surgical group		Conservative group	
			N total	Mean (SD)	N total	Mean (SD)
Boorman 2014&18[54,55]*	**RC-QoL (0-100%)** 0 = worst, 100 = best outcome	**baseline**	**23**	**38.0 (21)**	**70**	**82.0 (12)**
		24	25	78.0 (23) mean change: 40.0 (26.1)	68	80.0 (18) mean change: -2 (18.4)
		60	17	89.0 (11) mean change: 51.0 (20.6)	46	83.0 (16) mean change: 1 (16.9)
De Carli 2017[56]*	**CMS (0-100 points)** 0 = worst, 100 = best outcome	**baseline**	**20**	**46.1 (6)**	**18**	**47.1 (5)**
		6	20	-	18	70.2 (2.2) mean change: 23.1 (4.8)
		18	20	80.2 (3.4) mean change: 34.1 (5.9)	18	68.6 (5.2) mean change: 21.5 (6.0)
	QuickDASH (0-100 points) 0 = best, 100 = worst outcome	**baseline**	**20**	**46.2 (3)**	**18**	**47.4 (4)**
		6	20	-	18	19.5 (1.5) mean change: -7.9 (3.8)
		18	20	18.2 (2.8) mean change: -28.0 (3.4)	18	22.3 (1.3) mean change: -25.1 (3.8)
	VAS (0-10 cm) 0 = best, 10 = worst outcome!	**baseline**	**20**	**7.0 (1)**	**18**	**6.9 (2)**
		6	20	-	18	3.3 (1) mean change: -3.6 (1.9)
		18	20	2.1 (1) mean change: -4.9 (1.2)	18	4.4 (2.2) mean change: -2.5 (2.5)
Fabbri 2016[57]		**baseline#**	**17**	**-**	**18**	**-**
	CMS (0-100 points) (see above)	50-61	17	82.7 (6.0)	18	75.1 (12.4)
	Relative CMS (adjusted for age and gender) (see above)		17	92.0 (6.0)	18	81.0 (10.6)
	DSST (0-12 points), 0 = worst, 12 = best outcome		17	10.6 (2.5)	18	8.6 (2.4)
	VAS (0-10 cm) (see above)		17	2.4 (1.9)	18	5.1 (2.3)
Vad 2002[59]*	**L'Insalata Shoulder Questionnaire (overall, 0-100 points)** 0 = worst, 100 = best outcome	**baseline**	**36**	**33.0 (1.2)**	**40**	**44.4 (1.7)**
		37-38	36	83.6 (1.4) mean change: 50.6 (1.5)	40	70.5 (1.4) mean change: 26.1 (1.8)
	L'Insalata activities of daily living subscore (0-25 points)§ 0 = worst, 25 = best outcome	**baseline**	**36**	**9.3 (-)**	**40**	**13.1 (-)**
		37-38	36	22.2 (-) mean change: 12.9 (-)	40	19.4 (-) mean change: 6.3 (-)
	L'Insalata athletic activity subscore (15 points)§	**baseline**	**36**	**5.2 (-)**	**40**	**6.6 (-)**

	0 = worst, 15 = best outcome	37-38	36	11.0 (-) mean change: 5.8 (-)	40	11.0 (-) mean change: 4.4 (-)
Yamada 2000[60*$]	**JOA score (overall assessment, 0-100 points)** 0 = worst, 100 = best outcome	**baseline**	**26**	**58.8 (9.4)**	**14**	**53.2 (9.6)**
		48	26	85.9 (9.1) mean change: 27.1 (10.9)	14	71.1 (14.6) mean change: 18 (14.9)
	JOA subscore (0-20 points)[$] 0 = worst, 20 = best outcome	**baseline**	**26**	**12.8 (3.6)**	**14**	**10.9 (3.8)**
		48	26	17.2 (2.8) mean change: 4.4 (3.8)	14	13.9 (3.9) mean change: 3.0 (4.6)
Yoo 2018[61*]	**CMS (0-100 points)** (see above)	**baseline**	**104**	**48.0 (17.8)**	**33**	**56.3 (15.1)**
		13.2	72	83.2 (17.0) mean change: 35.2 (20.6)	17	78.2 (20.8) mean change: 22 (21.7)
	UCLA score (0-35 points) 0 = worst, 35 = best outcome	**baseline**	**104**	**13.2 (3.5)**	**33**	**14.7 (3.1)**
		13.2	72	30.0 (6.2) mean change: 16.8 (6.1)	17	28.9 (7.8) mean change: 14.2 (7.5)
	DSST (0-12 points) (see above)	baseline[#]	104	-	33	-
		58.1	104	9.6 (2.7)	33	9.2 (3.6)
	ASES (0-100 points) 0 = worst, 100 = best outcome	**baseline[#]**	**104**	**-**	**33**	**-**
		58.1	104	83.9 (19.4)	33	77.0 (23.6)

ASES = American Society of Shoulder and Elbow Surgeons; CMS = Constant Murley Score; DASH = Disabilities of the Arm, Shoulder and Hand; DSST = Dutch Simple Shoulder Test; JOA = Japanese Orthopaedic Association; N = Number of patients; RC-QoL = Rotator cuff - Quality of Life; SD = Standard Deviation; UCLA = University of California Los Angeles; VAS = Visual Analogue Scale.
* The studies did not provide sufficient information to directly calculate the SD for the mean changes from baseline; therefore, they have been imputed as described in the Cochrane Handbook.[1]
# Fabbri, Yoo: no baseline values provided by study authors.
§ Vad: No standard deviations were provided by the study authors; therefore, these subscore results cannot be displayed in a forest plot.
$ Yamada: means and/or standard deviations are calculated from the values reported by the study authors.

Table 23: Shoulder function (dichotomous outcome; NRSs)

Study	Definition of outcome measurement*	Follow-up (months)	Surgical group		Conservative group	
			N total	N with event* (%)	N total	N with event* (%)
Fabbri 2016[57]	Jobe test (present/absent)	50-61	17	0 (0)	18	14 (77)
	External rotation (present/absent)		17	1 (5.8)	18	4 (22)
	Internal rotation (present/absent)		17	0 (0)	18	2 (11)

N = Number of patients.
* Fabbri: 'A positive test (event) is the provocation of pain or abnormal weakness.'

Table 24: Shoulder pain (NRSs)

Study	Definition of outcome measurement	Follow-up (months)	Surgical group		Conservative group	
			N total	Mean (SD)	N total	Mean (SD)
Lee 2016[58*+]	**VAS (0-10 cm)** 0 = best, 10 = worst outcome	**baseline**	**115**	**6.5 (2.3)**	**114**	**7.1 (1.7)**
		2-6	115	1.6 (2.1) mean change: - 4.9 (2.6)	114	3.0 (-) mean change: -4.1 (-)
		12	115	0.9 (1.4) mean change: -5.6 (2.3)	114	1.0 (1.3) mean change: -6.1 (1.8)
Vad 2002[59§+]	**L'Insalata pain subscore (0-45 points)** 0 = worst, 45 = best outcome	**baseline**	**36**	**16.3 (-)**	**40**	**20.8 (-)**
		37-38	36	40.5 (-) mean change: 24.2 (-)	40	30.7 (-) mean change: 9.9 (-)
Yamada 2000[60$+]	**JOA subscore (0-30 points)** 0 = worst, 30 = best outcome	**baseline**	**26**	**7.9 (4.7)**	**14**	**7.9 (3.8)**
		48	26	25.8 (3.1) mean change: 17.9 (4.8)	14	18.6 (5.0) mean change: 10.7 (5.3)
Yoo 2018[61]	**VAS** (see above)	**baseline#**	**104**	**-**	**33**	**-**
		58	104	1.6 (2.2)	33	2.1 (2.5)

JOA = Japanese Orthopaedic Association; N = Number of patients; SD =Standard Deviation; VAS = Visual Analogue Scale; - = data not provided by the study authors.
* Lee: Pain was adjusted for sex, age, tear on dominant side, symptom onset, trauma history and tear classification. The study authors report 'missing data' and 'small sample sizes' for follow-up visits but gave no numerical values for these missing data. Our calculations are based on the originally included patient population, as no other data were available.
§ Vad: No standard deviations were provided by the study authors; therefore, these subscore results cannot be displayed in a forest plot.
$ Yamada: means and/or standard deviations are calculated from the values reported by the study authors.
# Yoo: no baseline values were provided by the study authors.
+ The studies did not provide sufficient information to directly calculate the SD for the mean changes from baseline; therefore, they have been imputed as described in the Cochrane Handbook.[1]

Table 25: Shoulder range of motion (NRSs)

Study	Definition of outcome measurement	Follow-up (months)	Surgical group		Conservative group	
			N total	Mean (SD)	N total	Mean (SD)
Lee 2016[58*#]	Passive forward flexion (degrees)	baseline	115	154.1 (20.3)	114	161.1 (11.4)
		2-6	-	159.6 (20.3) mean change: 5.5 (24.0)	-	160.8 (12.0) mean change: -0.3 (13.9)
		12	-	173.5 (9.7) mean change: 19.4 (19.7)	-	166.0 (13.4) mean change: 4.9 (14.8)
	Passive internal rotation (degrees)	baseline	115	10.5 (3.0)	114	9.8 (3.1)
		2-6	-	10.8 (2.5) mean change: 0.3 (3.3)	-	8.9 (2.6) mean change: -0.9 (3.4)
		12	-	11.1 (1.8) mean change: 0.6 (3.0)	-	13.0 (-) mean change: 3.2 (-)
Vad 2002[59§#]	Abduction (not further specified, ROM degrees)	baseline	36	72.0 (-)	40	68.0 (-)
		37-38	36	116 (-) mean change: 44.0 (-)	40	108 (-) mean change: 40.0 (-)
Yamada 2000[60$#]	JOA subscore (0-30 points) 0 = worst, 30 = best outcome	baseline	26	20.2 (6.4)	14	18.0 (6.0)
		48	26	24.6 (5.9) mean change: 4.4 (7.3)	14	21.9 (6.8) mean change: 3.9 (7.6)

JOA = Japanese Orthopaedic Association; N = Number of patients; ROM = Range of Motion; SD = Standard Deviation; - = data not provided by the study authors.
* Lee: Pain was adjusted for sex, age, tear on dominant side, symptom onset, trauma history and tear classification. The study authors report 'high rates for missing data' and 'small sample sizes' for follow-up visits but gave no numerical values for these missing data. Therefore, we decided not to provide effect estimates for these outcomes addressing ROM.
§ Vad: No standard deviations were provided by the study authors; therefore, these subscore results cannot be displayed in a forest plot.
$ Yamada: means and/or standard deviations are calculated from the values reported by the study authors.
# The studies did not provide sufficient information to directly calculate the SD for the mean changes from baseline; therefore, they have been imputed as described in the Cochrane Handbook.[1]

Table 26: Muscle strength (NRSs)

Study	Definition and result of outcome measurement
De Carli 2017[56]	'The dynamometric evaluation showed, in group A, 93% of strength of involved versus uninvolved side, while in group B, a 76,8% was detected with a statistically better performance in the surgically treated group (p=0.0014).'
Yamada 2000[60]	'Evaluation of muscle strength by isokinetic muscle testing by Cybex; none of the 14 patients in group I were able to comply with the exercises because of motion pain. The 9 patients in group II had greater isokinetic strength on supine (flexion/extension) at follow-up than pre-operatively. Isokinetic evaluation of internal and external rotation at 30° and 90° of abduction did not demonstrate a statistically significant difference in pre-operative strength between the involved and uninvolved sides. There were no significant differences in strength between the pre-operative state and at follow-up on the involved side.'

Table 27: Failed surgery (re-tears; NRSs)

Study	Definition of outcome measurement	Follow-up (months)	Surgical group (repair)		Conservative group	
			N total	N with events (%)	N total	N with event (%)
De Carli 2017[56]	re-tear (by US)	18	20	2 (10%)	outcome not applicable	

N = Number of patients; US = Ultrasonography.

Table 28: Structural findings (dichotomous outcomes; NRSs)

Study	Definition of outcome measurement	Follow-up (months)	Surgical group		Conservative group	
			N total	N with event (%)	N total	N with event (%)
De Carli 2017[56]	Progression of tear in conservative group (present, absent; US)	outcome not applicable			18	2 (11)
Lee 2016[58]	Progression of tear in conservative group (present, absent; US, MRI, MRA)				45	3 (6.7)
Fabbri 2016[57]	Progression of tear in conservative group (present, absent; MRI)				18	12 (67)

MRA = Magnetic Resonance Arthrography; MRI = Magnetic Resonance Imaging; N = Number of patients; US = Ultrasonography.

Table 29: Structural findings (continuous outcomes; NRSs)

Study	Definition of outcome measurement	Follow-up (months)	Surgical group		Conservative group	
			N total	Mean (SD)	N total	Mean (SD)
Fabbri 2016[57]	Fatty degeneration (MRI; mean stage after Goutallier classification [0-4, 4 = worst])	baseline	17	1.82 (0.38)	18	1.72 (0.44)
		50-61		1.94 (0.41)		3.05 (0.52)
	Muscular atrophy (MRI; 'mean atrophy' modified after Zanetti et al.[66] [not further defined])	baseline		1.52 (0.60)		1.61 (0.48)
		50-61		1.29 (0.57)		2.39 (0.47)
	Tendon retraction (MRI; mean stage, Patte classification [1-3, 3 = worst])	baseline		outcome not applicable		2.06 (0.66)
		50-61				2.66 (0.49)

MRI = Magnetic Resonance Imaging; N = Number of patients; SD = Standard Deviation.

6.3.4 Outcomes (forest plots, NRSs)

The outcomes stated in section 6.3.3 are displayed in forest plots either as single-study results or as pooled effect sizes (quantitative analyses), given that more than one study reported the same outcome using a comparable scale at a given time point (Figure 13 to Figure 16).

Shoulder function (based on the CMS [0 – 100 points])

When surgery was compared to conservative treatment, effect estimates (expressed as MD) favoured surgical treatment (for example, at 18 months: MD 11.6; 95%-CI 8.8, 14.3; 38 patients; 1 studies[56] and at 50 to 61 months: MD 7.6; 95%-CI 1.2, 14.0; 35 patients; 1 study[57] [Figure 13A]).

Shoulder function (based on other scores than the CMS)

In general, effect estimates were in favour of surgery when compared with conservative treatment (Figure 13B-F). However, the corresponding 95%-CIs were wide, and statistical significance was not always reached.

Shoulder pain (based on the VAS [0 – 10 cm] or JOA subscore [0 – 30 points])

Similar to the outcome shoulder function, changes in effect estimates at 12, 48 and 58 months favoured the surgical intervention (Figure 14A and Figure 14B). Thereby, the largest effect was observed at 48 months using the JOA subscore: MD 7.2; 95%-CI 4.3, 10.1; 40 patients; 1 study[60] (Figure 14B). Of note, at 12 and 58 months, pain improvement measured with the VAS was in favour of surgery but did not reach statistical significance: MD 0.1; 95%-CI -0.3, 0.5; 229 patients; 1 study[58] and MD 0.5; 95%-CI -0.5, 1.5; 137 patients; 1 study,[61] respectively.

Shoulder range of motion (based on the JOS subscore [0 – 30 points] or goniometer [degrees])

Changes in range of motion measured with the JOA subscore did not show any significant differences between the interventions (at 48 months: MD 2.7; 95%-CI -1.5, 6.9; 40 patients; 1 study[60] [Figure 15]). Furthermore, Lee et al.[58] reported no differences in forward flexion and internal rotation between surgical- and conservative-treated patients between two and six months and at 12 months. Of note, due to missing data in the primary study, this result could not be displayed graphically.

Failed surgery defined as a re-tear (surgery group)/ tear progression (non-surgery group)

One study reported a re-tear rate of 10% (2/20 patients) at 18 months (Table 28).[51] The proportions of participants with tear progression (categorised as absent or present) ranged between 11% and 67% of patients treated conservatively (Table 28).[56-58]

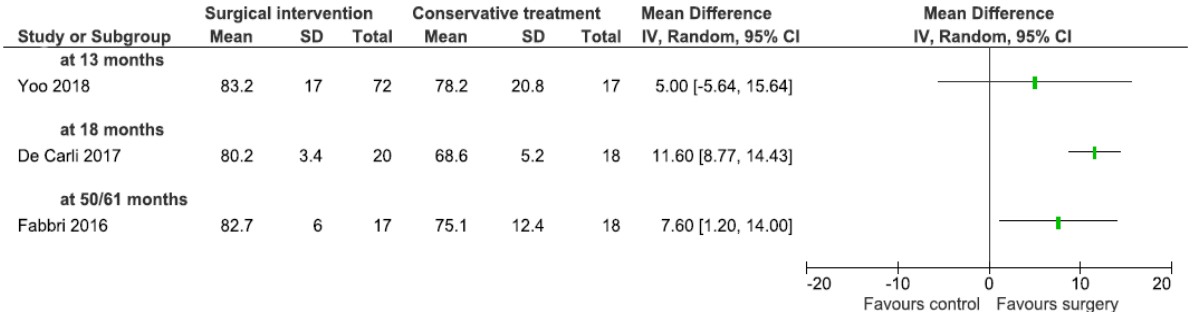
Structural findings, supraspinatus tear characteristics

Effect estimates for both fatty degeneration and muscle atrophy were in favour of the surgical intervention when measured at between 50 and 61 months (35 patients, 1 study):[57] (i) fatty degeneration (mean Goutallier classification 1-4): MD -1.1; 95%-CI -1.4, -0.8 (Figure 16A); (ii) muscle atrophy: ('mean atrophy', not further specified): MD -1.1; 95%-CI -1.5, -0.8; 35 patients (Figure 16B).

Figure 13: Shoulder function (NRSs)

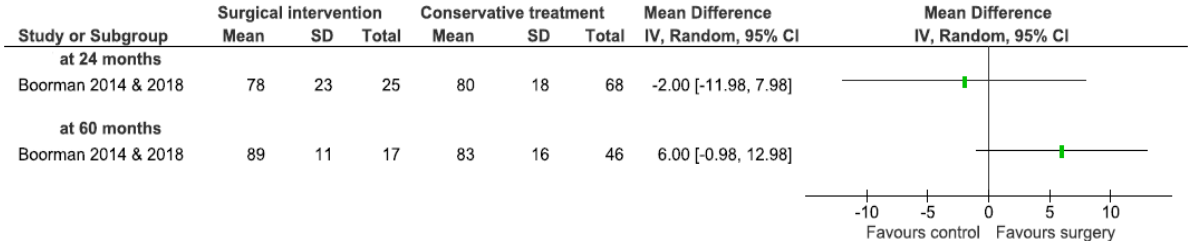
A. Measured with the CMS: means refer to scores reported at the given follow-ups

CMS: 0 – 100 points; 0 = worst, 100 = best outcome.



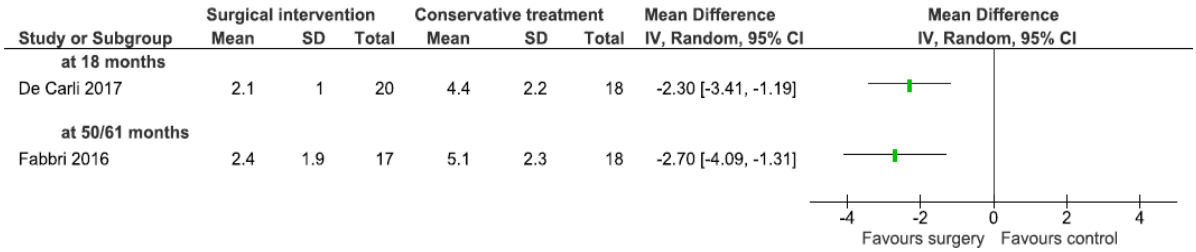
B. Measured with the RC-QoL: means refer to scores reported at the given follow-ups

RC-QoL: 0 – 100 percent; 0 = worst, 100 = best outcome.



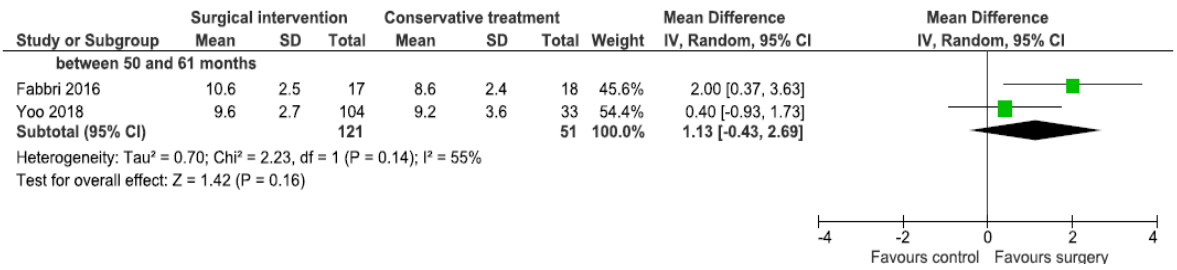
C. Measured with the VAS: means refer to scores reported at the given follow-ups

VAS: 0 – 10 points; 0 = best, 10 = worst outcome. NOTE: Axes are labelled vice versa in comparison to the other forest plots; this is due to the VAS reporting better outcomes with lower scores.



D. Measured with the DSST: means refer to scores reported at the given follow-ups

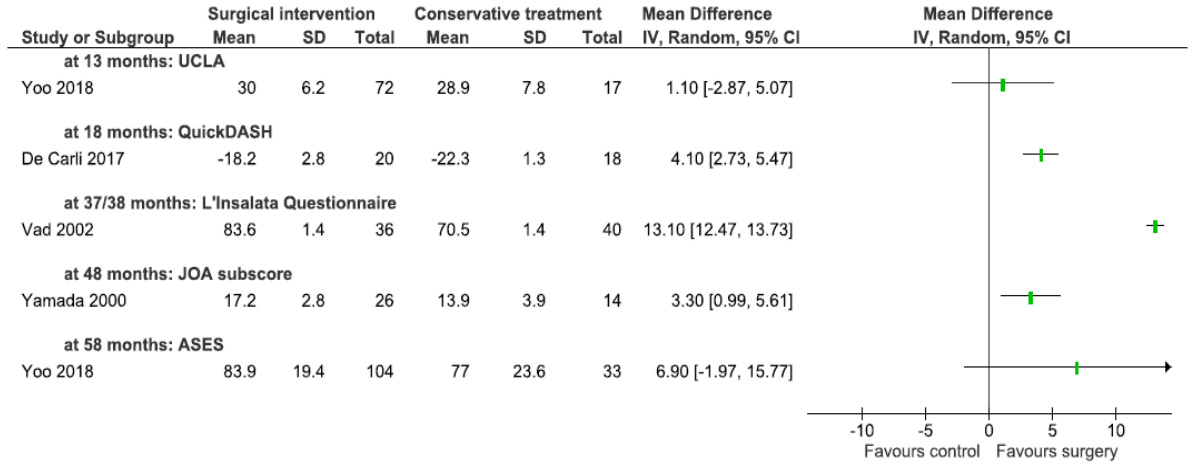
DSST: 0 – 12 points; 0 = worst, 12 = best outcome.



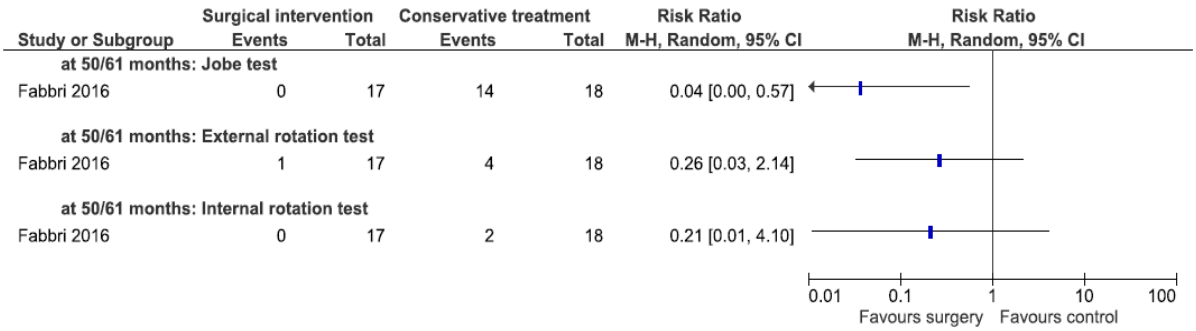
E. Measured with different scores: means refer to scores reported at the given follow-ups

JOA subscore:	0 – 20 points	0 = worst, 20 = best outcome.
UCLA:	0 – 35 points	0 = worst, 35 = best outcome.
ASES:	0 – 100 points	0 = worst, 100 = best outcome.
L'Insalata Shoulder Questionnaire:	0 – 100 points	0 = worst, 100 = best outcome.
QuickDash:	0 – 100 points	0 = best, 100 = worst outcome.

NOTE: The algebraic sign of the means measured with the QuickDash were inverted to be in alignment with the other scores reporting better outcomes with increasing scores (compare data with Table 22)



F. Measured with different scores and expressed a dichotomous outcome: events refer to the number of patients with pain or abnormal weakness



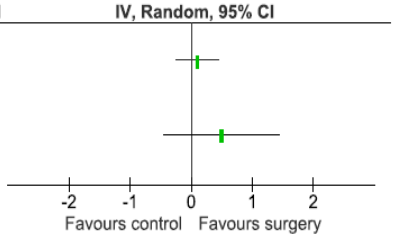
ASES = American Shoulder and Elbow Surgeons Score; Chi^2 = Statistical Test Chi-square; CI = Confidence Interval; CMS: Constant Murley Score; DSST = Dutch Simple Shoulder Test; JOA = Japanese Orthopaedic Association; P = P value; QuickDASH = Quick Disability of the Arm, Shoulder and Hand; RC-QoL = Rotator Cuff Quality of Life; SD = Standard Deviation; UCLA University of California at Los Angeles; VAS Visual Analogue Scale.

Figure 14: Shoulder pain (NRSs)

A. Measured with the VAS: means refer to scores reported at the given follow-ups

VAS: 0 – 10 cm; 0 = no, 10 = worst pain. NOTE: The algebraic sign of the means measured with the VAS were inverted to be in alignment with the other score reporting better outcomes with increasing scores (compare data with **Fehler! Verweisquelle konnte nicht gefunden werden.**).

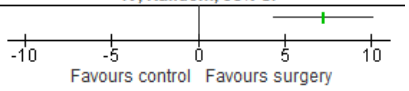
	Surgical intervention			Conservative treatment			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Random, 95% CI	IV, Random, 95% CI
at 12 months								
Lee 2016	-0.9	1.4	115	-1	1.3	114	0.10 [-0.25, 0.45]	
at 58 months								
Yoo 2018	-1.6	2.2	104	-2.1	2.5	33	0.50 [-0.45, 1.45]	



B. Measured with the JOA subscore: means refer to scores reported at 48 months

JOA subscore: 0 – 30 points; 0 = worst, 30 = no pain.

	Surgical intervention			Conservative treatment			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Random, 95% CI	IV, Random, 95% CI
Yamada 2000	25.8	3.1	26	18.6	5	14	7.20 [4.32, 10.08]	



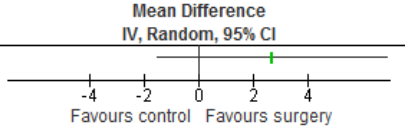
CI = Confidence Interval; JOA = Japanese Orthopaedic Association; SD = Standard Deviation; VAS Visual Analogue Scale.

Figure 15: Range of motion (NRSs)

Measured with the JOA subscore: means refer to scores reported at 48 months.

JOA subscore: 0 – 30 points; 0 = worst, 30 = best outcome.

	Surgical intervention			Conservative treatment			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Random, 95% CI	IV, Random, 95% CI
Yamada 2000	24.6	5.9	26	21.9	6.8	14	2.70 [-1.52, 6.92]	

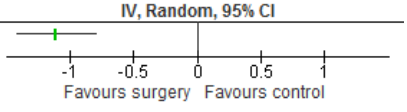


CI = Confidence Interval; JOA = Japanese Orthopaedic Association; SD = Standard Deviation.

Figure 16: Structural outcomes between 50 and 61 months (NRSs)

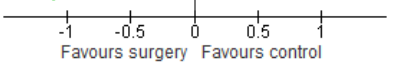
A. Fatty degeneration (after Goutallier classification)

	Surgical intervention			Conservative treatment			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Random, 95% CI	IV, Random, 95% CI
Fabbri 2016	1.94	0.41	17	3.05	0.52	18	-1.11 [-1.42, -0.80]	



B. Muscular atrophy (not further defined)

	Surgical intervention			Conservative treatment			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Random, 95% CI	IV, Random, 95% CI
Fabbri 2016	1.29	0.57	17	2.39	0.47	18	-1.10 [-1.45, -0.75]	



CI = Confidence Interval; SD = Standard Deviation.

6.4 GRADE evidence profiles

6.4.1 GRADE evidence profile for RCTs

A GRADE evidence profile[42] of the currently best available evidence (based on RCTs) was constructed for the following outcomes: shoulder function (measured with the CMS), shoulder pain (measured with the VAS), shoulder range of motion (measured with the CMS subscore), muscle strength (measured with the CMS subscore) and any adverse events (Table 30).

The effect estimates for shoulder function (measured with the CMS) and shoulder pain (measured with the VAS) at 12, 24 and 60 months showed statistical significant differences in favour of surgery when compared to conservative treatment. Considering a published estimate for the minimal clinically important difference (MCID) for a shoulder function of 10.4 points[1] and for pain of 1.4 cm,[2] the clinical relevance of these differences, however, are questionable. For example, at 12 months, the effect estimate expressed as the MD for shoulder function (CMS based) was 6.9 points higher with surgery and with corresponding upper and lower boundaries of the 95%-CIs of 1.6 points and 12.3 points, respectively; and the effect estimate expressed as the MD for shoulder pain (VAS based) favoured surgery with a MD of 1.1 cm and upper and lower boundaries of the 95%-CI of 0.4 cm and 1.8 cm, respectively. The overall certainty of evidence was rated as moderate for shoulder function and low for pain.

Effect estimates for shoulder range of motion (measured with a CMS subscore), muscle strength (also measured with a CMS subscore), and adverse events were not found to be statistically different when surgical treatment was compared to conservative treatment at 12, 24 and/or 60 months. The overall certainty of evidence was rated as low for adverse events and moderate for shoulder range of motion and muscle strength.

The moderate to low certainty of evidence can be explained by (i) a possible risk of performance and detection bias due to the nature of the studies, as adequate blinding was not possible (for details, see section 6.2.2 and **Table 30**); (ii) a lack of clinical relevance particularly regarding the lower limit of the 95%-CI when shoulder function and pain was assessed; or (iii) 95%-CIs that are consistent with the possibility for benefit and the possibility of harm (dichotomous outcome: adverse events) or the possibility of improving and the possibility of worsening symptoms (continuous outcomes: shoulder range of motion and muscle strength).

Table 30: GRADE evidence profile (RCTs)

Study setting: Adults with full-thickness rotator cuff tears from Finland, Norway and the Netherlands.

Certainty assessment							Summary of findings				
N patients (studies), follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Overall certainty of evidence (rating starts at high quality)[67]	N patients		Relative effect (95%-CI)	Baseline mean with control	MD with surgery
							control	surgery			
Shoulder function (assessed with the CMS, 0 [worst] - 100 points [best outcome])											
257 (3 RCTs) 12 months	not serios	not serious	not serious	serious [b]	none	⊕⊕⊕◯ MODERATE	131	126	-	baseline range: 38.4-57.1	**6.9 points higher*** (1.6 to 12.3 higher)
210 (2 RCTs) 24 months	not serious	not serious	not serious	serious [b]	none	⊕⊕⊕◯ MODERATE	105	105	-	baseline range: 38.4-57.1	**4.4 points higher*** (0.04 to 8.8 higher)
101 (1 RCT) 60 months	not serious	not serious	not serious	serious [b]	none	⊕⊕⊕◯ MODERATE	50	51	-	baseline: 38.4	**8.7 points higher*** (1.3 to 16.1 higher)
Shoulder pain (assessed with the VAS, 0 [best] – 10 cm [worst outcome])											
257 (3 RCTs) 12 months	serious [a]	not serious	not serious	serious [b]	none	⊕⊕◯◯ LOW	131	126	-	baseline range: 2.7-6.3	**1.1 cm lower*** (0.4 to 1.8 lower)
210 (2 RCTs) 24 months	serious [a]	not serious	not serious	serious [b]	none	⊕⊕◯◯ LOW	105	105	-	baseline range: 2.7-5.3	**0.9 cm lower*** (0.3 to 1.5 lower)
101 (1 RCT) 60 months	serious [a]	not serious	not serious	serious [b]	none	⊕⊕◯◯ LOW	50	51	-	baseline: 5.3	**1.3 cm lower*** (0.5 to 2.1 lower)
Shoulder range of motion (assessed with the CMS subscore, 0 [worst] – 40 points [best outcome])											
110 (1 RCT) 12 months	not serious	not serious	not serious	serious [c]	none	⊕⊕⊕◯ MODERATE	55	55	-	baseline: 29.3	**0.1 points lower** (0.5 lower to 0.3 higher)
109 (1 RCT) 24 months	not serious	not serious	not serious	serious [c]	none	⊕⊕⊕◯ MODERATE	55	54	-	baseline: 29.3	**0.2 points lower** (0.5 lower to 0.2 higher)
Muscle strength (assessed with the CMS subscore, 0 [worst] - 25 points [best outcome])											

Certainty assessment							Summary of findings				
212 (2 RCTs) 12 months	not serious	not serious	not serious	serious [c]	none	⊕⊕⊕◯ MODERATE	106	106	-	baseline range: 8.1-8.4	**0.35 points lower** (2.02 lower to 1.32 higher)
210 (2 RCTs) 24 months	not serious	not serious	not serious	serious [c]	none	⊕⊕⊕◯ MODERATE	105	105	-	baseline range: 8.1-8.4	**0.1 points higher** (1.64 lower to 1.83 higher)
101 (1 RCT) 60 months	not serious	not serious	not serious	serious [c]	none	⊕⊕⊕◯ MODERATE	50	51	-	baseline: 8.1	**1.3 points higher** (1.18 lower to 3.78 higher)
Any adverse events: at the longest follow-up											
255 (3 RCTs)	serious [a]	not serious	not serious	serious [c]	none	⊕⊕◯◯ LOW	5/130 (3.8%)	7/125 (5.6%)	**RR 1.45** (0.48-4.31)	**Risk with control** 38 per 1.000	**RD with surgery 17 more per 1.000** (20 fewer to 127 more)

CI = Confidence Interval; CMS = Constant Murley Score; N = Number of patients; MD = Mean Difference; RD: Risk Difference; RR = Risk Ratio, VAS = Visual Analogue Scale.

a. Risk of bias downgraded by one level: concerns about adequate blinding (due to the nature of the studies). Hence, a high risk of detection bias exists for all subjectively reported outcomes (in our case pain and adverse events).

b. Imprecision downgraded by one level: clinical relevance regarding the lower limit of the 95%-CI is questionable.

c. Imprecision downgraded by one level: 95%-CI consistent with the possibility for benefit and the possibility of harm (dichotomous outcome) or the possibility of improving and the possibility of worsening symptoms (continuous outcome).

* Favours surgery.

6.4.2 GRADE evidence profile for NRSs

In addition to the GRADE evidence profile on the best available evidence from RCTs presented in Table 30, such a profile was also constructed for specific outcomes reported in the NRSs. The addressed outcomes were similar to the outcomes reported in the RCTs, including shoulder function (measured with the CMS), shoulder pain (measured with the VAS), and shoulder range of motion (measured with the JOA subscore) (Table 31). In contrast to the data from RCTs, the outcomes muscle strength and any adverse events could not be addressed in the GRADE evidence profile for NRSs due to a lack of data from this study type.

The effect estimates for shoulder function (measured with the CMS) at a follow-up of 18 months and at 50 to 61 months showed statistical significance in favour of surgery when compared to conservative treatment. But again—similar to the results of the RCTs—taking into account a MCID for a shoulder function of 10.4 points,[1] the clinical relevance of these differences is questionable: for example, the effect estimate (expressed as MD) at 50 to 61 months was 7.6 points higher with surgery, and the upper and lower boundaries of the 95%-CI were 1.2 points and 14.0 points, respectively. The overall certainty of evidence for this outcome was very low.

Effect estimates for the outcomes pain (measured with the VAS) and range of motion (measured with a JOA subscore) were not found to be statistically different when surgical treatment was compared to conservative treatment at 12, 48 and 58 months. The overall certainty of evidence was also rated as very low for both outcomes.

The very low certainty of evidence in the NRSs can be explained by (i) a very serious risk of bias due to major confounding, selection bias, and a lack of blinding applying to all outcomes; (ii) lacking clinical relevance; and/or (iii) 95%-CIs that are consistent with the possibility of improving and the possibility of worsening symptoms (pain and range of motion) and/or (iv) inadequate group sizes (i.e., low number of patients or varying group sizes) within one study.

Table 31: GRADE evidence profile (NRSs)

Study setting: Adults with full-thickness rotator cuff tears from Canada, Italy, Korea, Japan, and the US.

Certainty assessment							Summary of findings				
N patients (studies) follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Overall certainty of evidence (rating starts at high quality)[67]	N patients		Relative effect (95%-CI)	Baseline mean with control	MD with surgery
							control	surgery			
Shoulder function (assessed with the CMS, 0 [worst] - 100 points [best outcome])											
38 (1 NRS) 18 months	very serious [a]	not serious	not serious	serious [b]	none	⊕◯◯◯ VERY LOW	18	20	-	baseline: 47	**11.6 points higher*** (8.8 to 14.3 higher)
35 (1 NRS) 50-61 months	very serious [a]	not serious	not serious	very serious [c]	none	⊕◯◯◯ VERY LOW	18	17	-	not reported	**7.6 points higher*** (1.2 to 14.0 higher)
Shoulder pain (assessed with the VAS, 0 [non] – 10 cm [worst pain])											
229 (1 NRS) 12 months	very serious [a]	not serious	not serious	serious [d]	none	⊕◯◯◯ VERY LOW	114	115	-	baseline: 7.1	**0.1 cm lower** (0.3 higher to 0.5 lower)
137 (1 NRS) 58 months	very serious [a]	not serious	not serious	very serious [e]	none	⊕◯◯◯ VERY LOW	33	104	-	not reported	**0.5 cm lower** (0.5 higher to 1.5 lower)
Shoulder range of motion (assessed with the JOA subscore, 0 [worst] – 30 points [best outcome])											
40 (1 NRS) 48 months	very serious [a]	not serious	not serious	very serious [e]	none	⊕◯◯◯ VERY LOW	14	26	-	baseline: 18	**2.7 points higher** (1.5 lower to 6.9 higher)

CI = Confidence Interval; CMS = Constant Murley Score; JOA = Japanese Orthopaedic Association; MD = Mean Difference; N = Number of patients; NRS = Non-Randomised Study; VAS = Visual Analogue Scale.

a. Risk of bias downgraded by two levels: major confounding, selection bias, and lack of blinding (obviously, due to the nature of the studies, the blinding of patients was not possible).

b. Imprecision downgraded by one level: low number of patients.

c. Imprecision downgraded by two levels: clinical relevance regarding the lower limit of the 95%-CI is questionable and low number of patients.

d. Imprecision downgraded by one level: 95%-CI consistent with the possibility of improving and the possibility of worsening symptoms.

e. Imprecision downgraded by two levels: 95%-CI consistent with the possibility of improving and the possibility of worsening symptoms and low number of patients (range of motion) or varying group size (pain at 58 months).

* Favours surgery.

7 Clinical assessment – Discussion and conclusion

7.1 Main findings

This systematic review addressed the comparative effectiveness and safety of surgical versus non-surgical treatment in patients with full-thickness rotator cuff tears. It is the first review on this topic that considers both the best available evidence from RCTs (N=3) and also the results from NRSs (N=7). Overall, our findings suggest that surgery may be more effective than conservative treatment. However, the clinical relevance of these differences is questionable. As an example, our meta-analysis of the RCT data for shoulder function (measured with the CMS) showed a difference (expressed as MD) of 6.9 (out of a maximum of 100 attainable) points, with a 95%-CI of 1.6 to 12.3 points. Very limited evidence is yet available on estimates of the MCID of the CMS for most shoulder outcome measures. However, applying a published estimate for the MCID of 10.4 points[1] for patients undergoing rotator cuff surgery, the observed difference is below this threshold of clinical relevance, and the 95%-CI includes both values above and below it. As another example, the upper and lower boundaries of the 95%-CIs for the MD in pain, measured by a 10-cm VAS, which favoured surgery, ranged between 0.4 and 1.8 cm. Applying a published MCID estimate of 1.4 cm[2] to this interval, there is again a possibility of both a difference below and above the threshold of clinical relevance.

For other patient-relevant outcomes such as shoulder range of motion, muscle strength, QoL and adverse events, only very limited data were available, showing no differences between the groups. Overall, adverse events were poorly reported. In most of the studies, adverse events were either not addressed (particularly in the NRSs) or insufficiently defined, and/or it was unclear how systematically the data had been collected. Moosmayer et al.[52,53] was the only study providing a detailed account of adverse events with the supplementary materials to the published reports, which appeared to have been documented systematically. Considering that any surgical intervention carries a potential serious risk for complications such as thromboembolism or infections,[68,69] poor reporting or the unsystematic assessment of such events may underestimate the true complication rate. Aspects of tendon integrity as a structural outcome were reported in relation to fatty degeneration, muscle atrophy, tendon retraction and changes in tear size (tear progression). Where data were compared between the surgical and non-surgical groups, the observed differences mostly favoured surgery. However, the findings need to be viewed cautiously, as only a limited number of studies contributed data on these structural aspects, and they varied considerably in their measurements.

Recommendations for surgery are often made based on concerns regarding tear progression.[70] However, reported rates vary across the literature. The reported proportions of participants with tear progression in the conservative treatment groups varied between 7% (at 12 months)[58] and 67% (at 61 months)[57] in our review. In comparison, a recently published systematic review summarising the evidence on tear progression in conservatively treated full-thickness rotator cuff tears found an overall rate of 41% (at 47 months).[71] Of note, the tear progression of conservatively treated rotator cuff tears needs to be balanced against the re-tear rates of surgically treated patients, which also differed widely across the studies: 74% (at 12 months)[51], 8% and 13% (at 12 and 60 months, respectively)[52,53] and 10% (at 18 months).[56] These varying

rates, however, are in accordance with other review data describing re-tear rates ranging between 0% and 94% after surgical repair. [72] Up to a follow-up of 24 months, the "overall" crossover rates were under 10% (in the RCTs), which may suggest that the majority of patients accept conservative treatment, at least within this time frame.

Despite various outcomes being assessed in the current study pool, meta-analyses of the results were limited and the provided effect estimates which are based on either single study results or a maximum of outcome data of three studies need to be interpreted cautiously. Furthermore, the choice of outcome measures and the timing of measurements varied considerably across studies, making any synthesis even more challenging. For example, shoulder function (the outcome that was most often assessed) was measured with more than ten different scales, and multiple scales (up to four) were often used in a single study. Particularly in the NRSs, the quality of reporting was poor and often inconsistent. For example, single components included in the conservative treatment 'programme' were often not specified, and the additional use of steroid injections or oral medications was insufficiently described.[e.g. 54,55,57,59,61] Surgery was either performed arthroscopically, mini-open or open. In addition, acromioplasty was applied widely but not standardised according to the surgical technique. Obviously, the heterogeneity of the treatment protocols hampered the comparison of the interventions even more. Moreover, the comparability of the results across the studies is limited by differences in baseline tear characteristics, which may or may not have affected outcomes. For example, Kukkonen et al.[47,48] limited their inclusion to isolated supraspinatus tears, whereas the other two RCTs included both infraspinatus and subscapularis tears in addition to tears of the supraspinatus. Massive cuff tears, another potential prognostic factor influencing outcome measurements,[73] were also not adequately considered within the current research.

Although the effect estimates of the RCTs and NRSs were similar, the certainty of evidence varied by study type. Whereas in the RCTs the certainty of evidence was judged to be moderate to low, it was judged to be very low in the NRSs. Overall, the certainty of evidence was hampered by serious imprecision (due to the lower limits of the 95%-CIs being of questionable clinical relevance or the 95%-CIs including the possibility of a benefit or harm with either intervention) — in the GRADE evidence profiles for both the RCTs and NRSs. However, the risk for bias was judged as more serious in the GRADE evidence profile based on the NRSs: Whereas all included studies (independent of the study type) were judged to be at a (high) risk of performance and partly of detection bias (depending on whether the outcome is based on a subjective or objective measurement) due to a lack of blinding, the observed differences between the interventions in the NRSs may additionally be attributable to critical confounding rather than to the effects of the interventions. Selective outcome reporting may also have introduced bias. However, it was not possible to make a final judgement on this aspect of bias as, for most of the studies, no published protocols or registration records were available. Likewise, it was not possible to assess the risk of publication bias or even single-study results for the individual outcomes because of the small numbers of studies.

7.2 Comparison with other reviews

Numerous systematic reviews and guidelines addressing the management of rotator cuff diseases exist.[e.g. 73 16,35,74-76] Recently, a systematic review including a network meta-analysis of

RCTs of different rotator cuff tear treatments was published.[75] This review included 13 RCTs comparing different surgical interventions (not referenced because irrelevant to our review question) and two RCTs[47,53] comparing surgical interventions with non-surgical interventions. The authors concluded for the comparison 'surgery and physiotherapy vs. physiotherapy alone' that functional improvements and pain release was in favour of surgery, but it is not clear whether this statistically significant difference is related to clinical effectiveness (relevance).[77] Another review from 2010 focused on non-operative and operative treatments for rotator cuff tears and included over 130 studies.[16] The authors concluded that the comparative effectiveness and harms of various operative and non-operative treatments is often of low quality and inconclusive. Particularly, evidence that compared the relative effectiveness of operative versus non-operative treatments was sparse. We also identified two systematic reviews focusing exclusively on patients with full-thickness rotator cuff tears.[35,74] Although these reviews are based on the same RCTs as the current systematic review, not all available study data were analysed in these publications. For example, Piper et al.[74] did not consider the five-year data from Moosmayer et al.,[53] and Ryösä et al.[35] did not consider the two-year data of the Kukkonen et al. study.[48] Moreover, the review of Piper et al. made no attempt to carry out a risk of bias assessment—one of the most crucial parts of a systematic review.[74] The other review assessed the risk of bias by taking into account the Cochrane methodology, but their overall rating differed from ours. Whereas we assume a (serious) risk of performance and detection bias due to the nature of these studies excluding adequate blinding, Ryösä et al.[35] judged an overall low risk of bias. Additionally, in contrast to our review addressing a wide range of outcomes, these reviews focused solely on shoulder function,[35,74] pain,[35,74] range of motion[74] and QoL.[74] Despite these differences, the overall conclusions, however, are in line with our findings.

Regarding guidelines, there are also no definite recommendations regarding the type of intervention (surgery or conservative treatment). For example, different international guidelines, including a German guideline on the management of rotator cuff tears, advocate conservative treatment (including physiotherapy) as the first-line therapy, with surgery to be considered only if conservative treatment fails (defined as 'insufficient' improvements of symptoms and disability) or in patients with acute (traumatic) rotator cuff tears.[76,78-80] Moreover, the American Academy of Orthopaedic Surgeons has developed the Appropriate Use Criteria that considers the response of 'previous treatment' (which is not defined in detail) and prognostic factors such as tear size to determine the appropriate treatment.[73]

7.3 Implications for future research

Given the overall high rates of surgical treatment, high-quality research in patients with rotator cuff tears should consider: (i) the determination of the optimal duration, content and dose of conservative treatment and clarifying the questions 'what constitutes "failed conservative treatment"' and 'what justifies a subsequent recommendation to undergo surgery'; (ii) the achievement of a consensus on core outcome measures, i.e., consistency in their choice, definition and application to facilitate the comparability of outcome measures across trials; (iii) the provision of thresholds of clinical relevance based on reliable estimates of MCIDs for all patient-relevant outcomes; (iv) the need to establish the effectiveness of treatment options for specific subgroups of people with rotator cuff tears (e.g., different age-groups or levels of

physical activity/demands) considering relevant prognostic factors; and (v) the need to improve the reporting of studies following the recently published CONSORT (Consolidated Standards of Reporting Trials) statement for RCTs of non-pharmacologic treatments[81] and/or a STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement[82] to avoid bias and poor quality when designing such studies.

7.4 Conclusions

Overall, our findings suggest that surgery may be more effective than conservative treatment to improve shoulder function and reduce pain. However, the clinical relevance of these differences is questionable. For other patient-relevant outcomes such as shoulder range of motion, muscle strength, quality of life, and adverse events, only very limited data were available, showing no differences between the groups.

It was striking that only three RCTs (the currently best available evidence) are published, and that, judged on the identified registered and unpublished studies, results from further randomised studies (ongoing studies) can be expected to be available not before 2022. To complement the available evidence, we also considered NRSs. However, our systematic review revealed that the observed differences in the outcomes between the interventions may largely be attributable to confounding rather than to the effects of the interventions in those studies.

8 Health economic assessment - Methods

The health economic assessment included a systematic review of the currently published literature, a *de novo* cost-effectiveness or cost analysis, and a budget impact analysis (BIA). The systematic review focused primarily on economic evaluations reporting results in terms of cost per QALY gained or cost per LYG gained. In addition, we reviewed cost studies corresponding to our PICO. To the extent data would allow, we planned to perform a *de novo* cost-effectiveness analysis for Switzerland. In case there would be costs but no sufficient utility data available, the fall-back option was to perform a *de novo* cost analysis. Finally, a BIA combining the costs of surgery or conservative treatment with the estimated number of patients with full-thickness rotator cuff tears in Switzerland was performed.

8.1 Systematic literature review

We undertook a systematic review of the current economic literature. The aim was to identify and evaluate literature on the costs and cost-effectiveness of any surgical intervention in comparison to no or conservative treatment in patients with full-thickness rotator cuff tears. All types of economic evaluation studies were considered and checked for relevant content.

8.1.1 Literature search strategy

We developed a search strategy to identify all relevant economic literature in the following electronic databases: Medline, Embase and the Cochrane Library. For both the Medline and the Embase search, we used Ovid. The Medline search included Ovid MEDLINE(R), Ovid MEDLINE(R) Epub Ahead of Print, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, and Ovid MEDLINE(R) Daily Update. The clinical search strategies already developed by the clinical systematic review team for the Medline, Embase and Cochrane databases, were combined with economic search strings. For the economic search strategy for Medline and Embase, we used the NHS EED filter.[83] Because the NHS EED economic filter has not been published for Cochrane searches, we translated the Medline NHS EED filter into a Cochrane search string with the help of an online application.[84] Minor adaptations were subsequently made as required. All search strategies are presented in Appendix E.

8.1.2 Screening of the search results

The results of the literature search were screened by title, abstract and, if necessary, by full text review. In a first step, title and abstracts were screened for relevant quantitative results (e.g. costs, LYG, QALYs, or ICERs) or for sentences suggesting potentially relevant content in the full text version.

Potentially relevant abstracts proceeded to the next step, in which full texts were screened. Articles were then classified as being relevant or as potentially providing important additional information (for more details, please refer to the bullet points below).

For validation purposes, 20% of the screening was duplicated by an independent second reviewer. Discrepant screening results were discussed and resolved by consensus or otherwise would have led to involvement of a third party. In case there would have been more than 5% discrepancies, a further 20% of the literature would have been screened by a second reviewer and the same procedure would have been applied. However, this was not the case.

- Relevant articles needed to meet the following criteria:
    - The article reported a full-scale incremental cost-effectiveness analysis, ideally but not necessarily with an endpoint of cost per QALY gained or cost per life year gained.
    - The 'PIC' of the PICO corresponded to the one defined in the scoping document and used in the clinical systematic review part of this HTA.
    - The analysis was performed for a jurisdiction with broadly similar socioeconomic characteristics as Switzerland (e.g. North, Central and Western European countries, the USA, Canada, Australia and New Zealand).
- Studies potentially providing important additional information were defined as not meeting the criteria for the 'relevant' category but potentially containing useful additional information on effectiveness or costs, and thus being 'partially relevant' (e.g. comparative cost studies). Depending on the quality and quantity of information available from relevant articles, partially relevant articles would be considered for use as an additional source of information.

8.1.3 Extraction of information and quality assessment

For eligible cost-effectiveness studies (i.e. relevant articles as defined above), we planned to perform data extraction, covering the following information:

- Study population (including country, age and BMI range of the patients)
- Intervention
- Comparator(s)
- Setting and perspective of the study
- Cost types included and cost year
- Type of model
- Time horizon
- Discount rate
- Approach to sensitivity analysis
- Effectiveness
- Costs
- Incremental cost-effectiveness ratio (ICER)

A brief, qualitative characterisation of each eligible study was planned to be prepared, covering methodological approaches taken, main data sources, particularities, methodological issues and potential meaningfulness of the results for Switzerland.

Quality of reporting would be assessed with the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) 24-item checklist, recommended by the ISPOR Health Economic Evaluations Publication Guidelines Task Force.[85]

Assessment of transferability and adaptation of cost-effectiveness results to Switzerland
Transferability of the findings to Switzerland and implications for Switzerland were planned to be evaluated and discussed. Numerical adaptation to Switzerland was planned to be considered as sensible.

8.2 Cost-effectiveness analysis / cost analysis

As previously mentioned, we considered a *de novo* cost-effectiveness analysis for Switzerland using a decision tree model. In case there would be costs but no sufficient utility data available, the fall-back option was to perform a *de novo* cost analysis instead.

In the absence of data suitable for a cost-effectiveness analysis, we developed a *de novo* cost model. Utility values were available for patients undergoing surgery, but not conservative treatment, and for a short follow-up period of two years only. On this basis, we performed brief supplemental calculations to understand which utility and QALY differences between the initial surgery strategy and the conservative treatment strategy would lead to a cost-effective situation for the initial surgery strategy.

The *de novo* cost model is described in the following sections.

8.2.1 Population

The model population corresponded to the population stated in the PICO. This population consisted of patients with full-thickness rotator cuff tears, irrespective of etiology of the tear (degenerative or traumatic), time of diagnosis, patient age and comorbidities. The PICO was therefore broad and left open if the patients already had, and even might have failed, prior surgery or conservative treatment, and for how long the rotator cuff tear symptoms already persisted.

We assumed that asymptomatic patients do not receive any treatment. Therefore, the population for the health economic analysis consisted of symptomatic full-thickness rotator cuff tear patients with or without prior treatment.

8.2.2 Intervention and comparator

The intervention consisted of any full-thickness rotator cuff tear repair surgery as defined in the PICO (section 4). Feedback from the clinical expert group which was involved in this HTA indicated that full-thickness rotator cuff tear repair surgeries in Switzerland are only performed in the inpatient setting.

The comparator treatment as defined in the PICO included the options of placebo, sham, no treatment, 'watchful waiting', or any conservative treatment such as physiotherapy or pharmacological treatment including injection therapies. We planned to include the whole range of these comparator treatments and to assign costs to all those utilized in the RCTs ultimately selected by the clinical systematic review team, as well as to the ones mentioned by clinical experts as being applied in clinical practice in Switzerland as an alternative to repair surgery of full-thickness rotator cuff tears.

Since no data were available for other types of comparator treatment than conservative physiotherapy and pharmacological treatment including injection therapies, we assumed in the remainder of this report that comparator treatment would consist of physiotherapy and pain medication only.
Costs for no treatment itself were assumed to be zero. As a result of the systematic literature review, high quality data on consequences of patients with no treatment were not available. Hence, our cost analysis focused on symptomatic patients receiving either inpatient repair surgery or conservative treatment.

8.2.3 Time horizon and initial treatment strategies

A time horizon of six months was selected for a short-term economic analysis (from now on called 6-month analysis) as it included both the time of repair surgery plus subsequent physiotherapy treatment, as well as one complete block of physiotherapy treatment of several sessions in the case of conservative treatment. Not all relevant consequences of the initial treatment strategies will have occurred for six months. However, after approximately six months, a certain number of patients switch from conservative treatment to surgery, and patients who previously had surgery and subsequent physiotherapy may need additional physiotherapy and pharmacological treatment. The original treatment strategies (initial surgery, initially conservative treatment) would therefore mix. The 6-month analysis will therefore provide the costs of the initial treatments "repair surgery with subsequent physiotherapy and pharmacological treatment" versus "physiotherapy and pharmacological treatment".

In order to develop an estimation of the Swiss costs of full-thickness rotator cuff tear treatment for a longer time horizon, we developed a 5-year treatment scheme for Switzerland. Five years was the longest time horizon available from the RCTs included in the clinical systematic review part of this HTA.

8.2.4 Endpoints

Health economic endpoints of interest included total costs, sub-categories of total costs as well as their drivers. Drivers included e.g. treatment failures (crossovers to surgery), re-operations, resource use for physiotherapy, resource use for medications (e.g. cortisone injections and pain killers), outpatient physician visits, resource use for intra- and post-operative complications, and time off work – to the extent data was available.

8.2.5 Costs

The health economic model covered surgery costs, costs for outpatient specialist and general practitioner (GP) visits, costs for physiotherapy as well as medication costs. In addition, we examined whether an inclusion of "treatment-related adverse event costs" and "indirect costs due to time off work" in our Swiss model would be feasible.

8.2.6 Perspective

Data were to be assessed from a health insurance law perspective (considering the full direct medical costs of all health care services principally covered by the Swiss statutory health insurance, irrespective of payer) and, if possible, from a societal perspective (including indirect costs).

8.2.7 QALYs

In order to measure the effectiveness of the surgery and of conservative treatment, standardized, generic, preference-based instruments for health-related QoL, like e.g. the Euro-QoL (EQ-5D) were considered. We also considered conventional, generic instruments such as the 36-Item Short Form Health Survey (SF-36), if algorithm were available to estimate utilities.

8.2.8 Discounting

An annual discount rate of 2% was anticipated for Switzerland for the costs after 12 months, consistent with the preferences of the Swiss Medical Board (SMB).[86]

8.2.9 Sources of economic information

To obtain the information required for the economic analysis we considered the following sources:

- The clinical systematic review part of this assessment
- The results of the economic systematic literature review of this assessment
- The Swiss Tarmed reimbursement system for outpatient physician care (including physiotherapy) and the Swiss Diagnosis Related Group (SwissDRG) system for inpatient care[7]
- Swiss Hospital Statistics (SHS) 2016 of the Swiss Federal Statistical Office (SFSO)[8]
- Diagnosis-related case costs statistics ("Statistik diagnosebezogener Fallkosten") of the SFSO[87]
- Drug unit costs from the Swiss specialist list ("Spezialitätenliste")[4] and compendium[3]
- Input from the Swiss clinical expert group already involved by the SMB during the scoping of this HTA
- Additional targeted searches, complemented with hand-searches of grey literature and the World Wide Web (non-systematic) in order to identify manuscripts for prevalence and incidence rates, health resource use and costs that were not available from the above-mentioned sources.

8.2.10 Base case and scenario analyses of the cost model

We report on a base case analysis for the cost model. To verify the validity of the model, we performed uncertainty analyses in the form of univariate sensitivity analyses and scenario analyses. The selection of the base case and the scenario analyses to be performed depended on intermediate results and will therefore be described later in this document (see section 9.2.7). One-way deterministic sensitivity analysis was performed for all relevant input parameters. The parameter value estimates used in the base case were varied by ± 25%.

8.3 Budget impact analysis

The aim of the BIA was to investigate the overall costs of full-thickness rotator cuff tear repair surgeries in comparison to conservative interventions in Switzerland. The estimation of the yearly number of surgeries performed in Switzerland was based on a combination of SwissDRG, International Classification of Diseases (ICD) and Swiss operation classification (CHOP) codes, extracted from the SHS of the SFSO (year 2016).[8] The SHS is a collection of data on all patients who were hospitalised in a Swiss hospital during a specific year. This database included a total of 1,467,947 hospitalisations in 2016. It was possible to approximate the number of general rotator cuff tear surgeries. However, it was not possible to separate out the number of full-thickness rotator cuff tear surgeries from the rotator cuff tear surgeries. In the absence of a good estimator, we used the number of rotator cuff tear surgeries as an upper limit for full-thickness rotator cuff tear surgeries. More details are given in section 8.3.1.

Since outpatient physician (GP and specialist) visits and physiotherapy treatment are not coded in the Tarmed system in relation to their medical indication (in this case full-thickness rotator cuff tear), it was not possible to estimate the number of patients with full-thickness rotator cuff tear undergoing conservative treatment in Switzerland. An estimation based on the international literature was considered. However, the available data were judged insufficient as a basis for a realistic estimation for Switzerland. In other words, it was not possible to determine how many patients undergo conservative full-thickness rotator cuff tear treatment in Switzerland.

The prevalence of rotator cuff tears reported in the trial published by Minagawa et al. showed inconstant results if applied to Switzerland.[28] The overall prevalence for subjects older than 20 years (22%) would lead, if applied to the Swiss population over 20 years of age (i.e. 6.74 million persons in 2017), to 1.47 million rotator cuff tears cases. [24,28,88] Assuming that approximately only one third of them would be symptomatic, the number of patients eligible for conservative treatment would be close to half a million subjects. If age specific prevalence rates (0% in the 20s to 40s, 10.7% in the 50s, 15.2% in the 60s, 26.5% in the 70s, and 36.6% in the 80s) were applied to the Swiss population, the number of rotator cuff tears would however reach 616,224.

Furthermore, there is also paucity of information on the incidence of full-thickness rotator cuff tear in Switzerland and the duration of the disease. Beside the issues related to the estimation of the potentially eligible patients, the percentage of symptomatic patients that may be diagnosed and that may effectively start a conservative treatment is unknown. Considering this, we

pursued the following approach: the same number of cases were applied to both the surgery and the conservative treatment strategies. The costs according to the initial surgery strategy would represent the actual cost of full-thickness rotator cuff tear surgery and subsequent physiotherapy in Switzerland. In contrast, the costs according to the conservative treatment strategy would represent the potential costs for the same patients in case of initial conservative treatment and a secondary repair surgery for a certain percentage of patients.

It is important to emphasize that this BIA will provide information on the actual costs of surgery and standard follow-up physiotherapy for full-thickness rotator cuff tears in Switzerland, on the cost difference between initial surgery and conservative treatment strategy, but not on the total costs of the conservative treatment strategy.

The costs were calculated over a time period of five years (from 2018 until 2022), for the Swiss healthcare system using a health insurance system perspective.

8.3.1 Number of full-thickness rotator cuff tear repair surgeries in Switzerland in 2016

The identification of potentially relevant codes (addressed below) was supported by coding/pricing specialists of two Swiss hospitals.

SwissDRG codes

SwissDRG is a diagnosis-related group-type (DRG-type) system to classify hospital cases, as a basis for reimbursement. Each inpatient case receives one single SwissDRG classification code. The SwissDRG code is assigned according to patient characteristics, ICD-10 diagnoses and the treatments provided to the patient (CHOP codes). In particular, the main diagnosis and the main treatment play a fundamental role, as they are the main drivers of the classification. Depending on how coders in hospitals code the diagnoses and treatments of cases (i.e. depending on their sequence), patients with similar diagnoses and treatments may be assigned to different SwissDRG codes.

For this analysis, three SwissDRG codes potentially suggesting the relevant repair surgery were identified in the SHS 2016.[8]

- I29A: Complex interventions to the shoulder joint with complex procedure ("Komplexe Eingriffe am Schultergelenk mit bestimmtem aufwendigen Eingriff"), possibly used for multiple tendons tears
- I29B: Complex interventions to the shoulder joint, possibly used for single tendon tears
- I27D: Interventions at the soft tissue ("Eingriffe am Weichteilgewebe»), possibly used for single tendon tear

Since it was unclear as to whether the code I29B or the code I27D were used in 2016 for single tendon rotator cuff tears, we started with considering both SwissDRG codes.

It should also be emphasized that the mentioned SwissDRG codes may have been used to code interventions for other problems than the repair surgeries relevant for our PICO. Therefore, these SwissDRG codes were compared and combined with relevant diagnosis (ICD-10 codes, see below) and treatment (CHOP) codes.

ICD-10 diagnosis codes

The ICD is a health care classification system providing standardized diagnostic codes for classifying diseases. For this analysis, the following ICD-10 codes suggested a relevant diagnosis of rotator cuff tear:

- For atraumatic/degenerative rotator cuff tears (not specified as traumatic):
  M75.1: Rotator cuff tear or rupture, not specified as traumatic
- For traumatic rotator cuff tears:
  S46.0: Strain of muscle(s) and tendon(s) of the rotator cuff of shoulder

However, there is no distinction between partial and full-thickness tears.

It is important to keep in mind that a patient may have multiple concurrent diagnoses. For this reason, in the SHS, a patient can receive simultaneously one main diagnosis ("Hauptdiagnose") and several secondary diagnoses ("Nebendiagnosen"). Depending on the severity of the diseases, hospital coders decide on the principal reason for hospitalisation (the main diagnosis) and which ones are secondary problems (secondary diagnoses). For example, a person involved in a car accident may arrive at the hospital with a cranial fracture and a rotator cuff tear. In this case, the cranial fracture would probably be the main diagnosis, whereas the rotator cuff tear would be a secondary diagnosis. For the present assessment, the main diagnosis and up to 10 secondary diagnoses were considered for each hospitalisation. All diagnoses were considered equally, independent of the sequence.

For the cost calculation, all cases with at least one relevant ICD-10 code were considered as equally important (i.e. cases with only one relevant diagnosis were considered like those with multiple relevant ICD-10 codes).

CHOP treatment codes

CHOP is the Swiss classification of surgical interventions (www.medcode.ch). The following potentially relevant codes were extracted from the SHS 2016:

- *83.63 Plastische Rekonstruktion an der Rotatorenmanschette*
- *83.62.11 Sekundäre Naht einer Sehne, Schulter*
- *83.64.11 Sonstige Naht einer Sehne, Schulter*
- *83.71.11 Sehnenvorverlagerung, Schulter*
- *83.72.11 Sehnenrückverlagerung, Schulter*
- *83.73.11 Reinsertion einer Sehne, Schulter*
- *83.75.11 Sehnentransfer oder –transplantation Schulter*
- *83.88.41 Tenodese, Schulter*

According to the Swiss clinical expert group, CHOP codes 83.71.11, 83.72.11, 83.75.11, and 83.88.41 are often used in combination with a plastic reconstruction (CHOP code 83.63) but are per se not necessarily related to a full-thickness rotator cuff tear. Therefore, in an additional scenario analysis, these four codes were excluded from the estimation of the number of full-thickness rotator cuff tear surgeries.

Patient identification in the Swiss Hospital Statistics

For this BIA, two analytical approaches were compared: in the first, only patients who reported, at the same time, a relevant SwissDRG code, at least one relevant diagnosis (ICD-10 code), and at least one relevant treatment (CHOP code) were included. In the second approach, all patients who had at the same time at least one relevant diagnosis (ICD-10 code) and one relevant treatment (CHOP code), irrespective of the reported SwissDRG codes, were included.

8.3.2 Estimated number of full-thickness rotator cuff tear cases in Switzerland between 2014 and 2022

In order to estimate the budget impact of full-thickness rotator cuff tear surgery between 2018 and 2022, we needed to estimate the number of full-thickness rotator cuff tear cases from 2014 to 2022, since patients operated between 2014 and 2017 were assumed to have follow-up costs during five years. Costs after five years follow-up were assumed to be zero. The proportional occurrence of full-thickness rotator cuff tear cases identified through the SHS in the Swiss population aged 40 years or more in 2016 was applied to the estimated number of 40 years old persons between 2014 and 2022. Projection data concerning the Swiss population size as well as the age distribution until 2025 published from the SFSO were used as basis for the calculations.[89-91]

8.3.3 Base case budget impact analysis

In a first BIA, we applied 6-month treatment costs for patients initiating treatment over a 5-year time period, from 2018 until 2022 (from now on called 6-month-cost BIA). In this BIA, follow-up costs after six months were not considered. In a second BIA we considered 5-year treatment costs per patient over the same time period of five years (from now on called 5-year-cost BIA). In the base case BIAs, the 6-month and undiscounted 5-year costs per patient identified in the *de novo* cost analysis were applied to the estimated number of cases over the time period of five years.

For the 5-year-cost BIA, total treatment costs for each year included the follow-up costs of all patients with treatment start in the previous four years. For example, the costs in 2018 included the first year costs for patientes who started treatment in 2018, the second year costs for patients who started treatment in 2017, the third-year costs for those who started in 2016, the fourth-year costs for those who started in 2015, and the fifth-year costs for those who started in 2014.

As mentioned above, the same number of cases was applied to both initial surgery and conservative treatment strategies, meaning that this BIA provided information on the potential costs of surgery for full-thickness rotator cuff tears in Switzerland, on the potential cost difference between surgery and conservative strategies, but not on the total costs of conservative treatment.

8.3.4 Scenario analyses

In a first scenario analysis, the assumed annual number of patients undergoing surgery was varied from 0 to 20,000. Results were graphically illustrated. We assumed that each year the same number of patients underwent surgery.

In a second scenario analysis the number of eligible cases was reduced by excluding patients who received exclusively CHOP codes 83.71.11, 83.72.11, 83.75.11, and 83.88.41 (according to the clinical expert group. these codes are often used in combination with a plastic reconstruction but are per se not necessarily related to a full-thickness rotator cuff tear).

8.4 Approach for retrieval of Swiss resource use and cost information

Table 32 summarises all sources for resource use estimation and related costs in Switzerland.

Table 32: Swiss resource use and cost sources

Element *De novo* cost model	Source
full-thickness rotator cuff tear repair surgery costs (inpatient)	Relevant SwissDRG cost, because repair surgery in this HTA combines a mix of surgeries: e.g. arthroscopic, open and mini-open surgery, with or without acromioplasty, as well as with single or double suture row.[5]
Costs of physician visits (ambulant or outpatient)	Tarmed[7]
Physiotherapy costs (outpatient)	Tarmed (Specific physiotherapy tariff: physio swiss)[7]
Drug costs	Swiss specialist list («Schweizer Spezialitätenliste»)[4], Compendium[3]
6-month and 5-year treatment scheme development	Swiss clinical expert group (consisting of two clinical experts already involved by the SMB during the scoping process of this HTA), international literature
BIA	
Overall number of rotator cuff repair surgeries in 2016 identified by diagnoses and CHOP-codes	SHS 2016, identified through relevant treatments (CHOP codes) and diagnostic codes (ICD-10 codes according to the inclusion criteria)[8]
Overall number of patients with conservative treatment	It was not possible to quantify this number. Physician visits and physiotherapy treatment are not coded in relation to their indication in the Tarmed outpatient system[7]

Abbreviations: BIA = budget impact analysis, CHOP = Swiss classification of surgeries, ICD = International classification of diseases, SFSO = Swiss Federal Statistical Office, SHS = Swiss Hospital Statistics

9 Health economic assessment - Results

9.1 Health economic literature search results

Although the systematic literature search identified a considerable amount of economic analyses, none of them reported information concerning the effectiveness or cost-effectiveness of the interventions in terms of QALYs, LYG, or ICERs for the predefined PICO.

Cost-effectiveness studies were in general restricted to the comparison of different operative interventions. An example is the HTA UK analysis from 2015 about arthroscopic versus open surgery of the rotator cuff tear alongside the UK Rotator Cuff Surgery (UKUFF) trial.[92] Since many patients (77%) moved from the non-surgical treatment to the surgical intervention, an original third treatment arm of conservative treatment was closed prematurely.

A total of 210 citations were identified from the electronic database searches (Figure 17). Following removal of duplicates (n=62), 148 citations were reviewed. Based on titles and abstracts, 100 citations were excluded due to inappropriate comparator or non-comparative design, character of a review or commentary piece, inappropriate outcome measure, or no relevant cost information given. A total of 48 citations were included for full text review. As already stated above, there were no full-scale cost-effectiveness studies among the 48 citations for the PICO under investigation. However, of these citations, 28 provided additional information on health economic outcomes, costs or utilities of one of the treatments, but not on the effectiveness of repair surgery versus no or conservative treatment, in terms of QALYs or life years gained. These 28 studies were considered partially relevant and were reviewed to identify input variables and unit costs. For example, partially relevant information was found in the UK HTA comparing arthroscopic with open rotator cuff tear repair.[92]

Given the very limited health economic literature and other required data available, performance of a full-scale cost-effectiveness analysis was deemed non-feasible. We thus decided to perform a *de novo* model-based cost study as the main economic analysis. Utility values were available for the surgery group but not for the conservative group, and for a follow-up period of two years only, from the above-mentioned UK HTA report.[92] On this basis, we performed brief supplemental calculations to understand which utility and QALY values in the conservative treatment strategy would lead to a cost-effective situation for the initial surgery strategy.

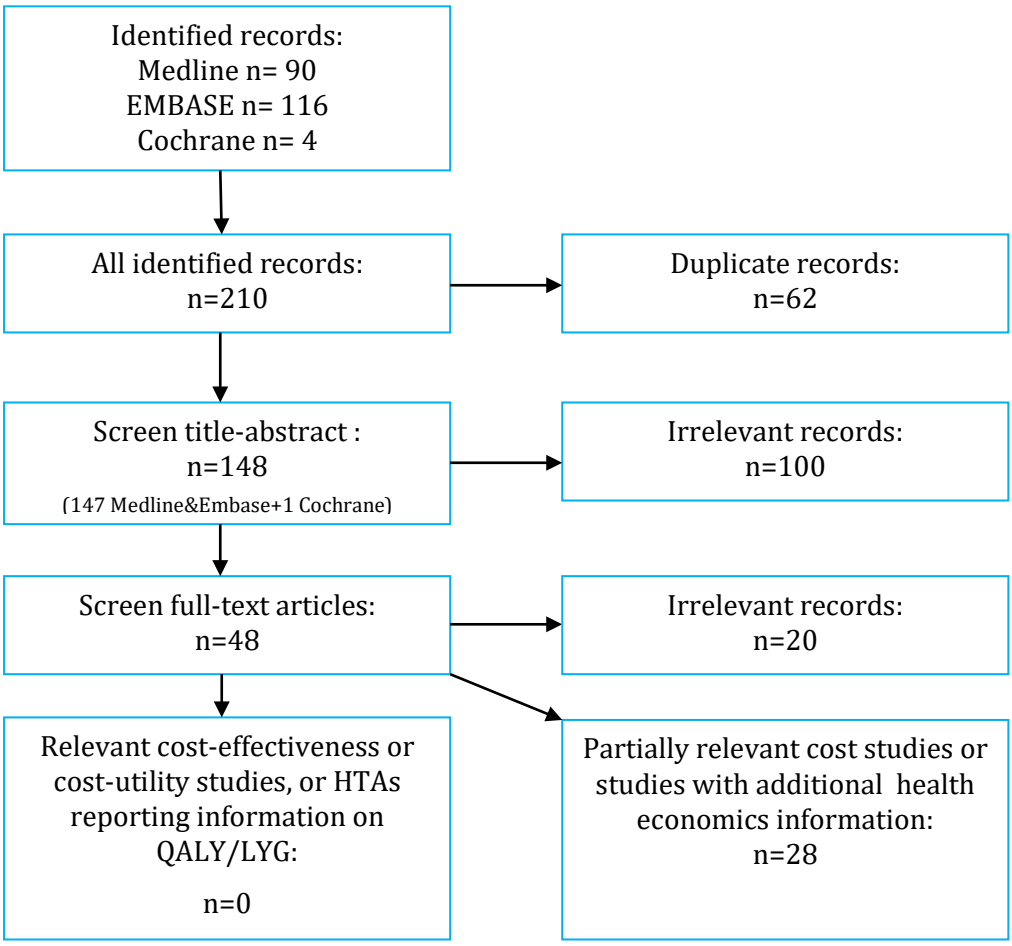


Figure 17: Results of the health economic literature search and study selection process
Abbreviations: LYG = life year gained; QALY = quality-adjusted life year

9.2 Data availability and implications for the *de novo* cost analysis

9.2.1 Population

The clinical systematic review part of this HTA determined three relevant RCTs for the PICO under investigation.[51-53,93,94] For more details please see the clinical systematic review part of this HTA.

In total, only patients with either a mean symptom duration of approximately one year[51,53] or of approximately 2.5 years[93] were included in these studies. No patient had undergone previous surgery of the same shoulder. However, patients had undergone previous physiotherapy and medical treatment, to a large extent.

Two of the studies (Kukkonen et al., Lambers Heerspink et al.) included patients with only degenerative full-thickness rotator cuff tears with single and multiple tendon tears.[51,94,93] The third study by Moosmayer et al. was based on full-thickness rotator cuff tear patients with traumatic and degenerative tears, however only of small to medium sizes (up to 3cm). The full-

thickness rotator cuff tear subgroup of patients with traumatic, large (and therefore probably multiple) tendon tears is therefore not present in any of the three selected studies of the clinical systematic review part. Since there is no good quality data available for this subgroup, it could not be considered in our cost analysis.

9.2.2 Resource consumption in the 6-months analysis

9.2.2.1 Intervention resource consumption

All patients undergoing repair surgery received physiotherapy directly after surgery in our *de novo* cost model. Physiotherapy is part of the initial repair surgery treatment. This is in accordance with the postoperative treatment given in the three RCTs included in the clinical systematic review part of this HTA. In all three studies, patients received physiotherapy after an immobilisation period of either three or six weeks after surgery.

After consultation with the clinical expert group, we assumed that the same outpatient physiotherapy treatment (18 sessions overall: two prescriptions of nine sessions each) would be given after repair surgery, as is the case for the conservative treatment.

We further assumed that there would be one GP visit of 15 minutes and two specialist visits necessary around initial surgery. One of the two specialist visits was again assumed to last 15 minutes and the second visit to consisted of 10 minutes plus 30 minutes pre-discussion of the intervention, plus 10 minutes studying the patient record, and the writing of a report of maximum 35 lines. More details on the relevant Tarmed codes are given in Table 33. For comparison, the UK HTA analysis mentioned approximately three physician visits (one GP and two outpatient visits) between surgery and 12 months follow-up for patients in the surgery group.[92]

With regard to medications given after initial full-thickness rotator cuff tear repair surgery, we assumed opioid treatment (e.g. TRAMADOL Helvepharm®) for three to five days, anti-inflammatory medication (e.g. ibuprofen) as well as pain killers like paracetamol, based on expert consultation. Generally, cortisone injections are not administered neither just before nor after surgery according to the clinical expert group. For comparison, Moosmayer et al. only mentioned when describing physiotherapy treatment that no supplemental treatment, such as cortisone injections or pain medication, were given.[52,53] Costs for medications were included in the UKUFF economic analysis between surgery and 12 months.[92]

Regarding complications, we assumed no complications in our cost model except treatment failure leading to re-operation. Generally, the occurrence of complications of full-thickness rotator cuff tear repair surgeries, expect re-tears, seems to be low (Carr et al.[92], feedback from medical experts). As reported in the clinical systematic review part of this HTA, occurrence of adverse events was zero in both the Kukkonen and the Lambers Heerspink trials[51,94,93], and low in the Moosmayer trial.[52,53]

9.2.2.2 Comparator treatment resource consumption

For patients receiving initial conservative treatment, we anticipated outpatient physiotherapy treatment of 18 sessions overall: two prescriptions of 9 sessions each. We also assumed one GP visit of 15 minutes and two specialist visits during the first six months in the conservative

treatment group. Table 33 presents the details. Finally, we assumed that patients undergoing conservative treatment received, next to ibuprofen and paracetamol as pain medication, one injection of cortisone (e.g. KENACORT®), during the initial six months. These decisions were based on clinical expert group advice.

9.2.2.3 Time off work

The outcome of "occupational impairment" was not reported in the three RCTs considered in the clinical systematic review part of this report. The clinical systematic review also investigated NRSs, case-control studies and controlled before-after studies. It was however not possible to obtain good quality estimates for this endpoint. Therefore, it was not possible to perform the *de novo* cost analysis from a societal perspective.

9.2.3 Resource consumption after six months - five years treatment scheme

In order to gain an understanding of how costs may evolve after six months, we developed a possible treatment scheme for a time horizon of five years, following feedback from the clinical expert group, the Moosmayer study, and the UK HTA analysis.

The outline of the treatment scheme is mapped out in section 9.2.3.1. More details as well as justifications for the assumptions on resource consumption are given from section 9.2.4 onwards. For the first six months, the above-described assumptions apply, except where otherwise stated.

9.2.3.1 Outline of the 5-year treatment scheme

For patients in the initial surgery strategy, we assumed no revision surgery during the first year after surgery and a small percentage between years one and five. Also, a certain percentage of patients were supposed to need additional follow-up treatment consisting of a specialist visit, 18 sessions of physiotherapy, and pain medication.

Patients in the conservative treatment strategy could crossover to secondary surgery.[52,53,93,94] In Moosmayer et al. this was the possible for patients whose outcomes did not adequately improve during at least 18 sessions of physiotherapy.[52,53] According to Boorman et al., most patients became more symptomatic during the first two years, and only very few during three to five years.[95] Therefore, in the present model, we assumed that patients would only crossover to secondary surgery during the first two years. In case of secondary surgery, we assumed that the patients had the same risk of revision surgery as for patients in the initial surgery treatment scheme.
The 5-year treatment scheme is graphically depicted in Figure 18.

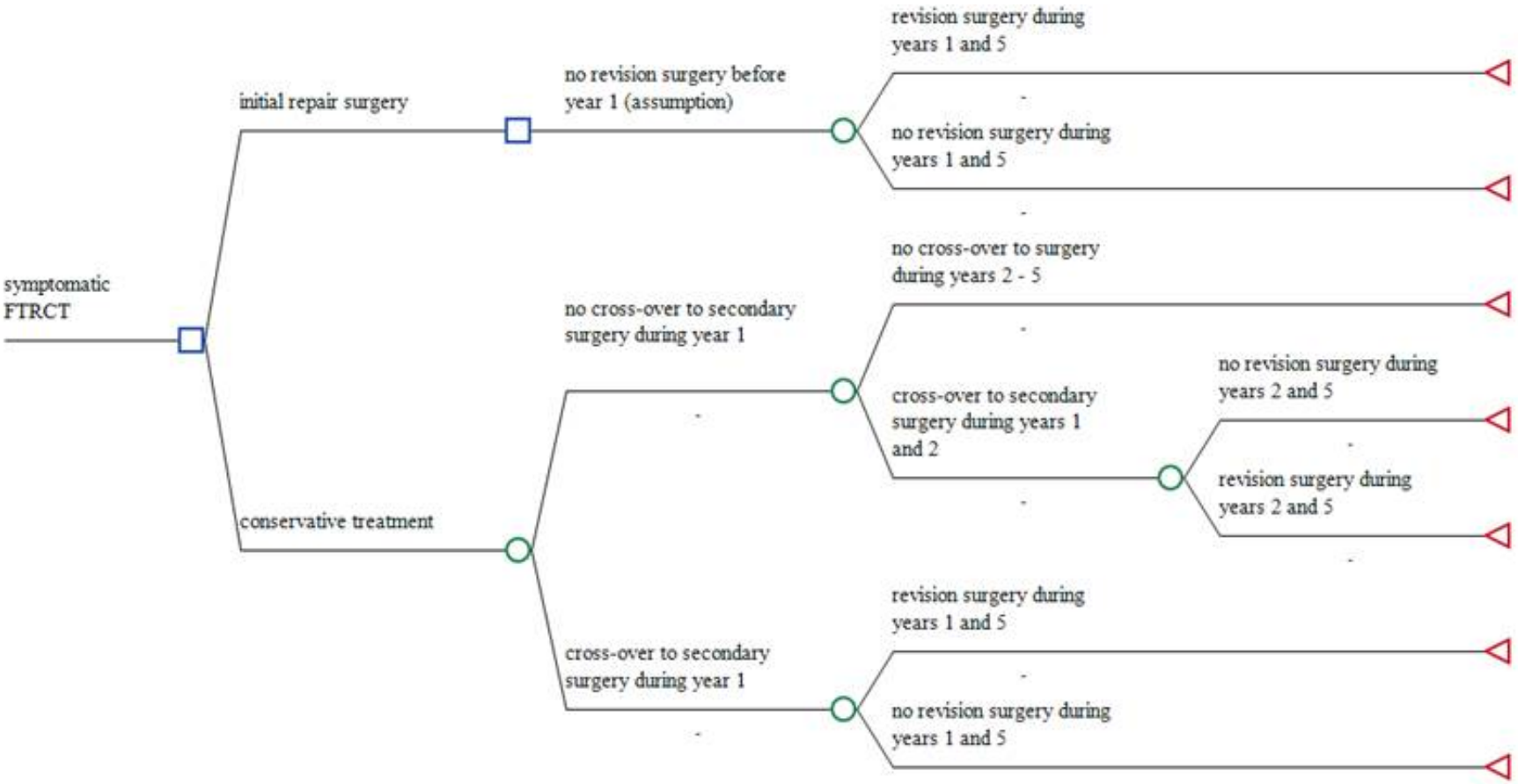


Figure 18: 5-year treatment scheme of the *de novo* cost model

9.2.3.2 Crossover from conservative treatment to secondary surgery

Crossover rates at 12 months

In the Moosmayer study, 18% of the patients in the conservative treatment strategy had crossed-over to secondary surgery after one year.[52] Since the crossover rate of the UKUFF study could not be utilized because the treatment arm was closed prematurely, we chose a crossover rate of 18% after one year as reported by Moosmayer et al.[52]

Crossover rates after 12 months

At five years, Moosmayer reported an overall crossover rate of 24%.[53] Boorman et al. mentioned a very similar rate of 25% following non-operative treatment of patients with full-thickness rotator cuff tears at the same follow-up time point.[95] We assumed an overall crossover rate of 24% consistent with the Moosmayer study. We further assumed that all crossovers would occur in the first two years as previously outlined in 9.2.3.1.

9.2.4 Revision surgery rate after six months

As mentioned in the previous section we included the possibility of a revision surgery for a certain number of FTCRT patients between years one and five after surgery. We assumed an overall revision rate of 1.9% as in the Moosmayer study.[53] The revision rate was distributed equally among the considered follow-up years, starting from year two.

For comparison, the re-operation rate in the UKUFF study was 1.5%.[92]

9.2.4.1 Physiotherapy after six months

Moosmayer et al. reported that 1.9% (1/52) of patients in the surgery group and 5.9% (3/51) of patients in the conservative group underwent additional physiotherapy after six months.[53] It is however unclear if the latter patients belonged to the subgroup of patients having moved from the initial physiotherapy group to secondary surgery or not. In the UKUFF study, patients in the initially conservative group were not supposed to receive standard physiotherapy but a high-quality booklet with an accompanying compact disc for home exercises[92]. It is not mentioned in the UK report if patients in the full-thickness rotator cuff tear repair surgery group generally received this booklet after surgery too, or a different physiotherapy program. Their resource consumption list shows a mean of 6.2 physiotherapist visits per person between surgery and 12-months follow-up. These visits reduced to 0.85 between 12 and 24 months for a 40% patient population with re-tears. Therefore, a certain number of patients still needed physiotherapy.

In this cost analysis we applied the additional physiotherapy rates (1.9% and 5.9%) reported by Moosmayer et al.[53] Additional physiotherapy treatment was distributed equally among the considered follow-up years, starting from year two.

9.2.4.2 Medication and physician visits after six months

Medication patterns after surgery or during conservative treatment were not described in detail in the identified literature. As previously mentioned, Moosmayer et al. only briefly mentioned that no supplemental treatments, such as cortisone injections or pain medication, was given.[52,53] We based medication assumptions on the advice of the clinical expert group. We assumed that the same patients who needed additional physiotherapy as reported in Moosmayer et al. would

also need additional medication and an additional physician visit. After expert consultation, we integrated costs for ibuprofen and paracetamol in our cost model. Costs for cortisone injections were added in case of absence of previous surgery.

9.2.4.3 Re-tear rates after surgery

According to several studies, re-tears after repair surgery are frequent. For example, in the Moosmayer study a re-tear rate of 20% during the first 12 months after surgery and of overall 25% after five years have been reported (included in the clinical systematic review).[52,53] In the UK HTA assessment (HTA not included in the clinical systematic review), the authors reported a re-tear rate of 40% over a follow-up period of 12 months.[92] A very high re-tear rate of 74% was reported in the small study by Lambers and Heerspink et al. following 25 patients with degenerative full-thickness rotator cuff tear for one year (included in the clinical systematic review).[51] In a retrospective data analysis of the medical records of a Swedish hospital's database for the period between January 1999 and December 2011, Zhaeentan et al. observed an overall re-tear rate of 24% after open repair of traumatic rotator cuff tears.[96] The average follow-up time of the study was 56 months.

Despite such high re-tear rates, the functional outcome for patients with a re-rupture is not well known.[97] Also, no correlation between anatomic outcomes (i.e. re-tear or re-tear size) after full-thickness rotator cuff tear repair surgery and functional outcomes could be demonstrated in a prospective study performed in South Korea.[98] The clinical expert group involved in this assessment confirmed that patients with re-tears are mostly asymptomatic and do not require any additional surgery nor treatment.[97,99] In fact, the high frequency of re-tears reported in the clinical trial may mostly be driven by follow-up investigations of the participating patients planned a priori, independently from their health status or symptoms.

For this reason, we did not integrate re-tear rates in the present cost model.

9.2.4.4 Sagittal tear size

There is ongoing debate if non-repaired tears, especially larger tears, are at risk of deterioration. For example, Moosmayer et al. reported that 37% of the tears treated with physiotherapy had tear size increases of more than 5mm after five years (based on sonographic evaluations).[53] Kukkonen reported that mean sagittal tear size after two years increased in the physiotherapy group and decreased in the surgery group.[93]

Although results for the outcome of sagittal tear size were in favour of the initial surgery strategy at 24 months as reported in the clinical assessment, it was not possible to quantify related costs. The *de novo* cost model did therefore not consider this parameter.

9.2.5 Costs

9.2.5.1 Surgery

We assumed full-thickness rotator cuff tear repair surgery costs of CHF 9,379.12 in 2018.
In more detail, we approximated the costs for inpatient full-thickness rotator cuff tear surgery using the costs of SwissDRG code I29. In 2014, mean costs of CHF 8,316 were reported for code I29 representing "Complex interventions at the shoulder joint" ("Komplexe Eingriffe am Schultergelenk") according to the SwissDRG 2014 report.

Since SwissDRG costs are currently available for 2014 only, we projected the costs to the year 2017, by applying the increase in overall hospital costs in Switzerland ("Gesamtspitalkosten") between 2014 and 2017 to the 2014 SwissDRG costs for I29. The year 2017 was the latest year with overall hospital costs available. In 2014, the overall hospital costs were 26.2 billion[100] and in 2017 approximately 29.4 billion[101], which implies an increase of approximately 12%. In addition, the Swiss Consumer Price Index was applied to project the costs further to 2018 (inflation rate of 1%[102]).

9.2.5.2 Outpatient visits and medication costs

Costs for outpatient (GP and specialist) visits and physiotherapy were calculated based on tax points according to Tarmed codes (Table 33). We used the sum of the Tarmed tax points for physician and technical services from the Tarmed system. The obtained tax points were multiplied with an average tax point for Switzerland of 0.87.[103] Based on the medical controlling department of a University hospital, the examining physician does not always fulfil the criteria for the coding of a specialist visit (but only a generalist visit) in Tarmed. For this reason, we assigned GP costs for both specialist and GP visits.

Medication costs were determined based on the public prices given in February 2019 in the Swiss specialist list ("Spezialitätenliste") and in Compendium for the drugs listed in Table 33.

Table 33: Resource consumption in the initial surgery and conservative treatment strategies up to six months

Resource use	Initial surgery	Initial conservative treatment	Costs and cost sources
Surgery	1	-	Surgery costs estimated with the help of the SwissDRG code I29 ("Complex interventions at the shoulder joint")[5]
Physiotherapy	18 sessions	18 sessions	Outpatient physiotherapy only. Sessions of 30 minutes twice a week. Same physiotherapy for conservative treatment and after initial surgery. Physiotherapytarif code 7301 per session (TP48) and for the very first session the supplement 7350 (TP 24) (Tarmed system[7])
Visits	GP: 1 visit (15min) Specialist: 1 visit (15 min) 1 visit (10min + pre-discussion surgery 30min + studying patient dossier 10min + report max 35 lines)	GP: 1 visit (15min) Specialist: 1 visit (15 min) 1 visit (15min + studying patient dossier 10min + report max 35 lines)	GP and specialist visit (10 or 15 min): Tarmed codes 00.0010, (00.0020), 00.0030 Pre-discussion of diagnostic/therapeutic intervention (30 min: 6 times: AL 10.42, TL 8.19). Tarmed code 00.00560 Studying patient dossier (10 min, 00.0141, 10 times: AL 2.08, TL 1.64) Report writing (up to 35 lines, Tarmed code 00.2285, AL 22.90, TL 18.03) Tarmed[7]
<u>Medications:</u>	Medication related to surgery:	Medication related to conservative treatment:	
Cortisone injections	N.A.	1 injection	KENACORT® 40mg/ml CHF 18.70 Swiss specialist list ("Spezialitätenliste")[4] Compendium[3]

Resource use	Initial surgery	Initial conservative treatment	Costs and cost sources
Opioids	1*100mg/ml for 3-5 days after surgery:	-	E.g. TRAMADOL Helvepharm® oral drops, whole flask assumed to be acquired by patient after hospital discharge (PP=CHF 8.10 for 10 ml flask with 100mg/ml)[3]
NSAID	3*600mg per day for 3-5 days (patient to buy after discharge)	3*600mg per day for 2 weeks	Ibuprofen (tablets 600mg (20 pieces PP=CHF 8.65, 50 pieces PP=CHF 18.05, 100 pieces= CHF 34.70)[3]
Paracetamol	3*1g per day for 4 weeks (patient to buy after discharge)	2*1g per day for 4 weeks	1000mg 100 pieces PP=CHF 19.35, 50 pieces PP= CHF 14.50, 30 pieces PP= CHF 8.05[3]

AL = "Ärztliche Leisung" (Tarmed tax points for physician performance); CHF = Swiss franc; g = gram; mg = milligram; ml = millilitre; NSAID = Non-steroidal anti-inflammatory drugs; PP = "Publikumspreis" (public price); TL = "Technische Leistung" (Tarmed tax points for technical performance); TP = Tax point of the Tarmed system

9.2.6 Summary of model assumptions

In summary, our *de novo* cost model was based on the following assumptions and decisions:

- Patients with asymptomatic full-thickness rotator cuff tear do not receive any treatment and were therefore not regarded in the economic analysis. Also, patients with traumatic, large (> medium sized) tears were not considered in the model since this patient subpopulation was not represented in the RCTs considered in the clinical systematic review part of this assessment.
- We assumed that sponteneous healing of a full-thickness rotator cuff tear would not happen since it is currently unclear if a healing of e.g. small tears is possible.[97]
- Conservative treatment consisted of physiotherapy and medication only (there is lack of data for other conservative approaches).
- Patients did not receive any other treatment (like e.g. reverse total shoulder arthroplasty) next to repair surgery or conservative treatment during the 5-year time horizon.
- All patients in the initial surgery strategy received physiotherapy directly after surgery.
- We assumed no adverse events or complications due to surgery. Re-tears were not included in the model for reasons explained in section 9.2.4.3.
- We included costs for surgery, physiotherapy, physician visits and medication. No costs for magnet resonance imaging or ultrasound examinations were considered.
- Our 6-month analysis compared the short-term treatment costs of initial surgery with subsequent physiotherapy versus initially conservative treatment.
- We developed a 5-year treatment scheme in order to get an idea of the mid-term costs of possible combinations of repair surgery and physiotherapy treatment (either starting with surgery or starting with conservative treatment).
- Patients in the conservative treatment strategy could crossover to secondary surgery in case their outcomes did not adequately improve after at least 18 sessions of physiotherapy. We further assumed that patients would only crossover to surgery during the first two years.

- After an initial or secondary surgery, we assumed no further cortisone injections. Also no cortisone injections were given before a planned surgery.
- For the secondary surgery costs, we considered the full costs of surgery and subsequent physiotherapy, medications and specialist visits, but no additional GP visit.
- Revision surgery (after initial or secondary sugery) was only assumed for 1.9% of patients. Occurrence of revision surgery was equally distributed between years one and five after surgery for the initial surgery strategy, and between years two and five for the conservative treatment strategy.
- For a certain percentage of patients, additional follow-up treatments consisting in a physician visit, medication and one block of physiotherapy (18 sessions) were possible between years one and five.
- Costs for prosthesis or other costs for end-stages of the disease were not included into the model due to the 5-year time horizon and lack of data.

9.2.7 Base case and uncertainty analysis of the cost model

As already outlined in section 9.2.3.1 we report on a base case 6-month analysis and a base case 5-year model. One-way deterministic sensitivity analyses as well as scenario analyses were performed for the 5-year time horizon. We did not perform sensitivity analyses for the 6-month analysis. Since a crossover from the conservative treatment strategy to secondary surgery was assumed to be only possible after six months, the most influential costs up to six months were surgery costs, followed by costs of physiotherapy.Table 34 summarizes the input parameters of the *de novo* cost model.

One-way deterministic sensitivity analyses

In deterministic sensitivity analyses, we varied by all parameter values used in the model and that were expected to have a relevant effect on the 5-year cost difference between the two treatment strategies. Variation was on a one-by-one basis and by ±25%.

Scenario analysis 1 (90% overall crossover rate at 24 months)

In a first scenario analysis, we increased the crossover rate at one year from 18% to 80% and after two years from overall 24% to 90%. This scenario represented an extreme case and assumed that almost all patients in the conservative treatment strategy would switch to secondary repair surgery.

Scenario analysis 2 (40% additional follow-up treatment for patients in the initial surgery strategy)

In a second scenario analysis we assumed that 40% of the patients in the initial surgery strategy would need additional follow-up treatment (consisting of one block of additional physiotherapy, one physician visit and medication) during one to five years after surgery. This was based on an observation of a 40% re-tear rate in the UKUFF study.[92]

Table 34: Summary of model input parameters for base case and scenario analyses

Input	Base case point estimate	Sensitivity analysis for 5-year model		Scenario values of 5-year model	Comment/Source
		Low	High		
Time horizon (years)	0.5 and 5				6-month analysis and 5-year model (Moosmayer et al. 2014)
Cost discount per year, after year 1 (%)	2				SMB standard rate
PART I: CLINICAL					
Initial surgery strategy					
Revision surgery after initial surgery (%)	1.9	1.4	2.4		Moosmayer et al. 2014
Additional follow-up treatment rate (%)	1.9	1.4	2.4	40	Moosmayer et al. 2014
Conservative treatment strategy					
Crossover rate to secondary surgery					
up to 12 months	18	13.5	22.5	80	Moosmayer et al. 2014
up to 24 months	24	18	30	90	Moosmayer et al. 2014 (24%), Boorman et al. 2018 (25%)
Revision surgery after secondary surgery (%)	1.9	1.4	2.4		Moosmayer et al. 2014. Applied only to the patients in the conservative treatment strategy who crossed-over to surgery
Additional follow-up treatment rate (%)	5.9	4.4	7.4		Moosmayer et al. 2014
PART II: COSTS (in CHF)					
full-thickness rotator cuff tear repair surgery	9,379.12	7,034.34	11,723.90		Mean costs of SwissDRG code I29 from 2014 projected to 2018, I29="Complex interventions at the shoulder joint"
Physiotherapy	772.56	579.42	965.70		Feedback from clinical expert group and medical controlling department of a University hospital: 18 sessions, supplement for first session (Tarmed codes 7301 and 7350)
GP/specialist visit (15 min)	40.48	-	-		Feedback from clinical expert group and the medical controlling department of a University hospital, Tarmed codes 00.0010,

Input	Base case point estimate	Sensitivity analysis for 5-year model		Scenario values of 5-year model	Comment/Source
		Low	High		
					00.0020, 00.0030
Specialist visit prior repair surgery	189.41	-	-		Feedback from the medical controlling department of a University hospital, Tarmed codes 00.0010, 00.0030, 00.0050, 00.0141, 00.2285
Specialist visit prior conservative treatment start	108.45	-	-		Feedback from the medical controlling department of a University hospital, Tarmed codes 00.0010, 00.0020, 00.0030, 00.0141, 00.2285
Opioid after surgery	8.10	-	-		Feedback from clinical expert group: Tramadoli hydrochloridum (TRAMADOL Helvepharm®)
Cortisone injection	18.70	-	-		Feedback from clinical expert group: Cortisone (KENACORT®) 40 mg/ml For conservative treatment only
NSAID	8.65 (20 pieces) 18.05 (50 pieces)	-	-		Feedback from clinical expert group : Ibuprofen (IBUPROFEN Sandoz®) tablets 600 mg
Analgetic	19.35	-	-		Feedback from clinical expert group : Paracetamol (Paracetamol Mepha®) 1000 mg 100 pieces

Abbreviations: GP = General practitioner; mg = milligram; ml = millilitre; NSAID = Non-steroidal anti-inflammatory drugs; SMB = Swiss Medical Board

9.3 Results of the *de novo* cost model

9.3.1.1 Initial cost analysis up to six months

For the initial cost analysis, we performed a direct comparison of surgery plus subsequent physiotherapy and pharmacological treatment versus conservative treatment (i.e. physiotherapy and pharmacological treatment). Hence, the same patients were assumed to be either assigned to the initial surgery strategy or to the conservative treatment strategy. Table 35 shows the base case results of each treatment strategy.

Table 35: Cost results of initial treatment up to six months

	Estimated costs during 6 months (in CHF)		
	Surgery plus physiotherapy	**Conservative physiotherapy**	**Difference (Surgery –Conservative)**
Repair surgery	9,379	-	9,379
Physiotherapy	773	773	0
Physician visits (GP, specialist)	270	189	81
Medication	36	56	-20
Total	**10,458**	**1,018**	**9,440**

Abbreviation: GP = General practitioner; CHF = Swiss francs

Overall, costs per patient for the initial surgery strategy amounted to CHF 10,458 and for the initial conservative treatment to CHF 1,018, leading to a cost difference of CHF 9,440 over six months.

Surgery costs of CHF 9,379 per patient constituted the highest cost factor. Costs for one block (18 sessions) of physiotherapy were estimated to be CHF 773. Costs for both physician visits and medications for full-thickness rotator cuff tear were low. The slightly higher costs for the outpatient physician visit in the surgery group are due to the costs of the pre-operative discussion (i.e. surgeons explaining to the patients the benefits and risk of surgery). Slightly higher costs for medication in the conservative group are mainly due to the additional costs of a cortisone injection.

In conclusion, focusing purely on the direct costs during the first six months, expenses for surgery plus subsequent physiotherapy are approximately 10 times higher than for physiotherapy alone.

9.3.1.2 Costs for the 5-year treatment scheme

Table 36 presents the results of the base case analysis for the 5-year time horizon.

Costs per patient for the initial surgery strategy remained stable over five years (CHF 10,458 at six months, CHF 10,662 at year five), whereas costs for the conservative treatment strategy more than tripled (from CHF 1,018 at six months to CHF 3,599 at five years).

The cost results need to be carefully related to the clinical outcomes which are described in the clinical part of the overall HTA.

Table 36: Base case cost results for the 5-year treatment scheme

	Estimated costs per patient (CHF)		
Timepoint	**Initial surgery strategy**	**Conservative treatment strategy**	**Difference (Surgery – Conservative)**
6 months	**10,458**	**1,018**	**9,440**
1 year	10,458	2,893	7,565
2 years	10,511	3,518	6,992
5 years	**10,662**	**3,599**	**7,063**

Abbreviations: CHF = Swiss francs

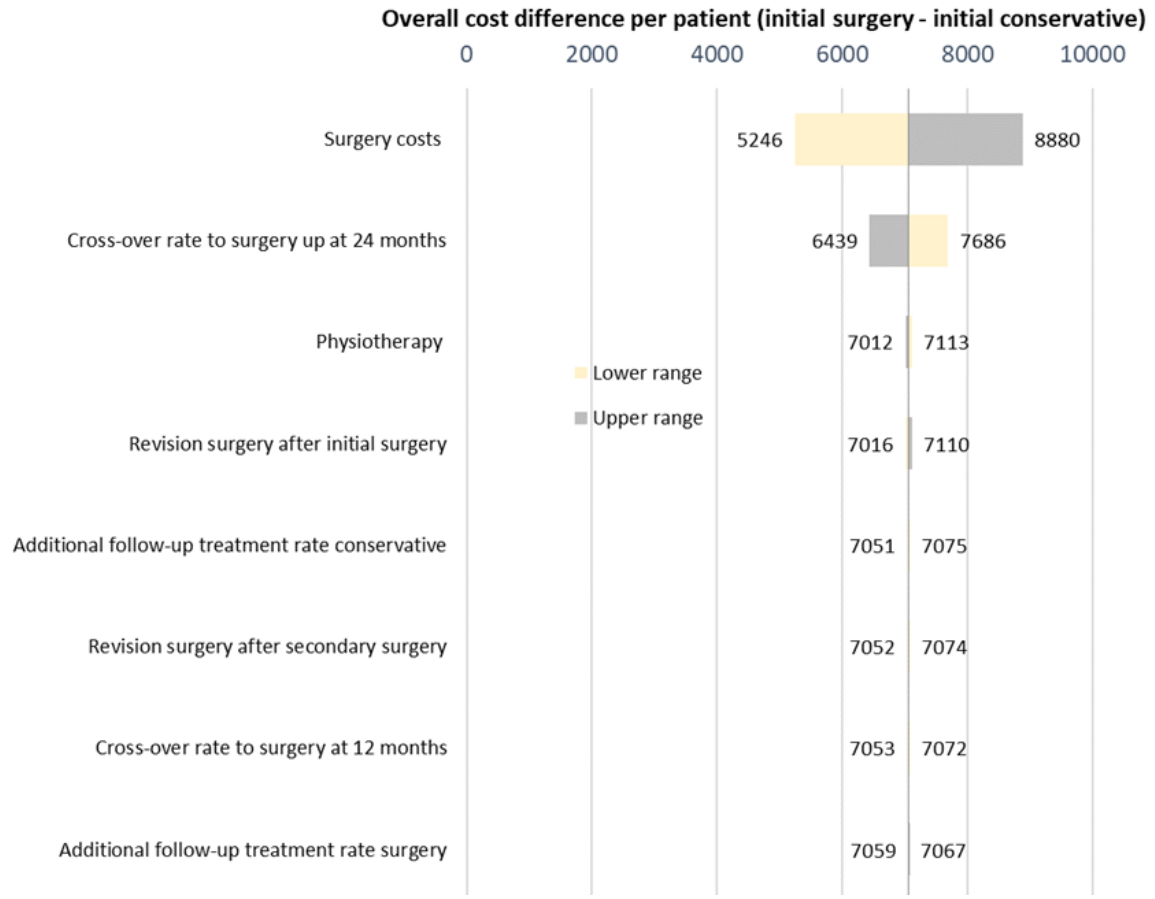
9.3.1.3 One-way deterministic sensitivity analysis for the 5-year treatment scheme

In deterministic sensitivity analyses, we varied all parameters individually that were expected to have a relevant impact on the overall cost difference at five years. Table 37 and Figure 19 presents the results, in descending order of impact.

The most influential variable was the cost of surgery, followed by the overall crossover rate at 24 months (crossover from conservative treatment to secondary surgery). All other variables only had a minor impact.

Table 37: Tornado one-way sensitivity results of influential parameters

		Input		Cost difference per patient in CHF (Surgery-Conservative)	
Parameter	**Default**	**Lower**	**Upper**	**Lower**	**Upper**
Surgery costs (CHF)	9,379	7,034	11,724	5,246	8,880
Crossover rate to secondary surgery up to 24 months (%)	24	18	30	7,686	6,439
Physiotherapy (CHF)	773	579	966	7,113	7,012
Revision surgery after initial surgery (%)	1.9	1.4	2.4	7,016	7,110
Additional follow-up treatment rate for conservative treatment strategy (%)	5.9	4.4	7.4	7,075	7,051
Revision surgery after secondary surgery (%)	1.9	1.4	2.4	7,074	7,052
Crossover rate to secondary surgery up to 12 months (%)	18	13.5	22.5	7,072	7,053
Additional follow-up treatment rate for initial surgery strategy (%)	1.9	1.4	2.4	7,059	7,067



Abbreviations: CHF = Swiss francs

Figure 19: Tornado graph of one-way sensitivity results of influential parameters

Scenario analysis 1 (90% overall crossover rate at 24 months) for the 5-year treatment scheme

In a first scenario analysis, we increased the crossover rate at one year from 18% to 80% and after two years from overall 24% to 90%. Therefore, the scenario assumed that almost all patients starting with a conservative treatment strategy switched to repair surgery during two years.

Costs per patient after five years stayed the same for the initial surgery strategy (CH 10,662). For the conservative treatment strategy costs increased from to CHF 3,599 to CHF 10,589, leading to a new cost difference per patient of CHF 73 (Table 38). Hence, the overall 5-year costs for the two strategies became very similar.

Scenario analysis 2 (40% additional follow-up treatment for patients in the initial surgery strategy) for the 5-year treatment scheme

The second scenario analysis assumed that 40% of the patients in the initial surgery strategy would need additional follow-up treatment (consisting of additional physiotherapy, physician visit and medication) one to five years after surgery. As shown in Table 38, the costs of the initial surgery strategy increased by approximately CHF 300 per patient over five years, suggesting that the impact of additional follow-up treatment in the initial surgery strategy was minimal.

Table 38: Scenario analysis results for the 5-year treatment scheme

	Mean 5-year costs per patient (CHF)		
Scenario analyses	**Initial surgery strategy**	**Conservative treatment strategy**	**Difference (Surgery – Conservative)**
Base case 1	10,662	3,599	7,063
Scenario 1 (80% crossover year 1, 90% crossover year 2)	10,662	10,589	73
Scenario 2 (40% additional follow-up in initial surgery strategy	10,970	3,599	7,371

Abbreviation: CHF = Swiss francs

9.4 Cost-effectiveness considerations

The economic systematic literature review of this HTA indicated that no cost-effectiveness studies for the predefined PICO were available.

We found EQ-5D utilities covering a period of 24 months after FTCRT (arthroscopic and open) repair surgery, in the UK HTA report of Carr et al.[92] However, we did not find any utility values for conservative physiotherapy treatment.

In the three available RCTs included in the clinical systematic review part of this HTA, one study reported health-related quality of life collected through the SF-36.[52,53] In the small-to medium size full-thickness rotator cuff tear population of the Moosmayer study, after five years, no significant difference in mean change from baseline between the surgical group (mean at five years = 50.1, baseline mean = 38.2, mean change = 11.9) and the conservative group (mean at five years = 48.4, baseline mean = 38.6, mean change = 9.8) was reported for the physical component summary scale of the SF-36 (MD = 2.1, 95%-CI -2.28, 6.48). (On this scale, a general population sample would be expected to have a mean of 50 and a standard deviation of 10).[104] The translation of the SF-36 score into utilities was not possible for us since patient level data would be required for such step.

Considering the lack of information concerning the QoL after surgery or conservative treatment, a proper cost-effectiveness analysis was not possible.

9.4.1 Cost-effectiveness calculations

We performed supplementary calculations in order to determine what differences in utilities and QALYs gained over periods of two and five years, between the initial surgery strategy and the conservative treatment strategy, would be necessary so that an ICER of CHF 50,000 or 100,000 per QALY could be obtained. Table 39 and Figure 20 present the results.

For an estimated cost difference of CHF 7,063 at five years, a QALY difference of 0.141 and 0.071 would be needed in order to obtain an ICER of CHF 50,000 and CHF 100,000, respectively. At two years, an estimated cost difference of CHF 6,992 would require a similar QALY difference of 0.140 and 0.070 in order to obtain an ICER of CHF 50,000 and CHF 100,000 per QALY gained.

Based on a simplifying assumption of constant utility differences across the 2-year or 5-year time horizons, a utility difference of 0.070 and 0.035 would be required over a 2-year time horizon to meet an ICER threshold of CHF 50,000 and CHF 100,000, respectively. For a 5-year time horizon, a utility difference of 0.028 and 0.014 would be necessary.

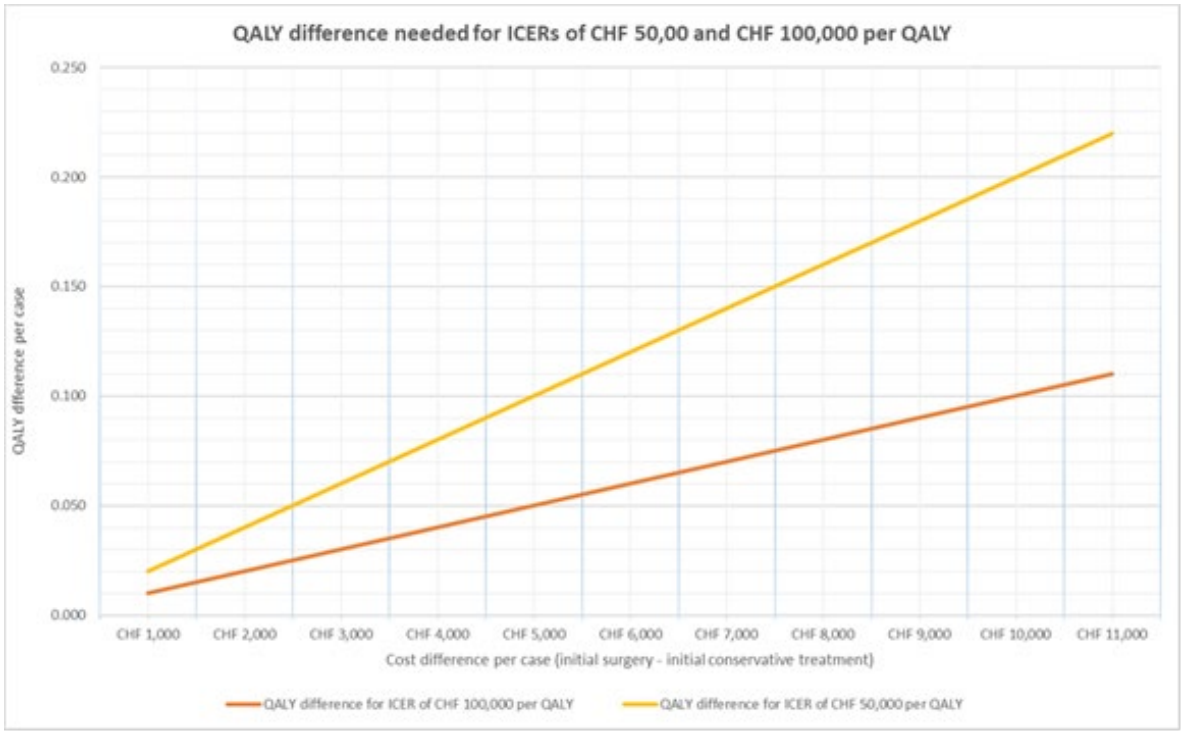


Figure 20: QALY difference at five years for an ICER of CHFF 50,000 and CHF 100,000 per QALY gained

Abbreviations: ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year

Table 39: Utility and QALY differences needed at two and five years for an ICER of CHF 50,000 and CHF 100.000 per QALY gained

		Time horizon	
	ICER threshold	**2-years**	**5-years**
Utility difference needed	CHF 50,000	0.070	0.028
	CHF 100,000	0.035	0.014
QALY difference needed	CHF 50,000	0.140	0.141
	CHF 100,000	0.070	0.071

Abbreviation: CHF = Swiss franc; QALY = quality-adjusted life year

9.5 Budget impact analysis

The aim of the BIA was to investigate the overall costs of repair surgery of full-thickness rotator cuff tears in comparison to alternative conservative treatment in Switzerland. The costs were calculated for the Swiss healthcare system using a health insurance system perspective.

The available data allowed the investigation of actual surgery costs for full-thickness rotator cuff tears in Switzerland as well as a cost comparison between surgery and conservative treatment at a patient level. In contrast, total costs for conservative treatment in Switzerland could not be estimated as the frequency of conservative treatment for full-thickness rotator cuff tears in Switzerland is unknown.

9.5.1 Number of surgeries in Switzerland

Table 40 shows the total number of possible rotator cuff tear surgeries in Switzerland in 2016 according to the two approaches to selection previously described in section 8.3.1.

The number of rotator cuff tear surgeries is similar between the two approaches. The addition of the SwissDRG code to the ICD-10 and CHOP codes did not have a big effect. Since it was not entirely clear which SwissDRG code was relevant in 2016 for single tendon tears, we assumed that there were overall 11,830 rotator cuff tear surgeries in Switzerland in 2016, based on ICD-10 and CHOP codes only (second approach).

When the CHOP codes 83.71.11, 83.72.11, 83.75.11, and 83.88.41 were excluded in a scenario analysis, the number of eligible cases decreased to 10,960 for the first approach and to 11,415 for the second approach.

Table 40: Estimated number of eligible surgery cases in 2016

	N
First approach (based on relevant SwissDRG, ICD-10 and CHOP codes)	11,278
Second approach (based on relevant ICD-10 and CHOP codes only)	11,830

As mentioned above, the removal of the SwissDRG code did not have a big effect on the estimated number of eligible cases. Nevertheless, as illustrated below, a comparison between the SHS 2016 and 2017 revealed unexplained differences in the SwissDRG code distribution.

Table 41 shows results separately for the three eligible SwissDRG codes. The number of cases for SwissDRG codes I27D and I29B, both possible candidates for rotator cuff tear surgeries of single tendon tears, were low. There were only 222 cases (2.4%) with relevant ICD-10 and CHOP codes for I27D. The SwissDRG code I29B resulted in 1,134 cases (10.8%) with relevant ICD-10 and CHOP codes. For assumed multiple tendon tears (I29A), there were 9,922 cases (88.3%) found in the 2016 database.

Table 41: Estimated number of eligible surgery cases by SwissDRG code in 2016

SwissDRG	N total	Relevant ICD-10		Relevant CHOP		Relevant ICD-10 AND CHOP	
		N	%	N	%	N	%
I27D	9,343	279	3.0%	471	5.0%	222	2.4%
I29A	11,243	9,938	88.4%	10,130	90.1%	9,922	88.3%
I29B	10,484	2,255	21.5%	2,026	19.3%	1,134	10.8%
Total	31,070	12,472	40.1%	12,627	40.6%	11,278	36.3%

The SFSO recently published online data from the SHS 2017. Cross-analyses between SwissDRG, ICD-10 and CHOP codes were not available. However, the number of cases hospitalised with a specific SwissDRG code was provided. In total, 30,385 cases were classified with one of the above mentioned SwissDRG codes. Although this number seems to be comparable with the 31,070 cases in 2016, the numbers for the single codes were very different with 9,869 I27D codes, 6,606 I29A codes, and 14,210 I29B codes. It is possible that many patients that in 2016 would have been classified under code I29A received, in 2017, a I29B code. Feedback from the medical controlling of a university hospital suggested that in 2017 I29A was used for rotator cuff tear surgeries with multiple tendon tears and I27D was used for single tendon tears, whereas I29B wasn't used at all. This would implie a significant but unrealistic decrease in the number of eligible cases. Since the distribution of cases according to SwissDRG shows unexplained discrepancies among different years, for this BIA, we decided to use the second approach only to estimate number of surgeries (i.e. based on ICD-10 and CHOP codes).

It should be emphasized that the estimated number of 11,830 surgeries (i.e. 142 per 100,000 persons) based on the SHS 2016 represents an upper bound since it was not be possible to assess how many of the rotator cuff tear surgeries were full-thickness rotator cuff tear repair surgeries or other types of surgeries. As a comparison, Dornan et al. reported that 275,000 rotator cuff repairs of symptomatic rotator cuff tears (i.e. 86 per 100,000 persons) are being performed every year in the United States.[24]

To estimate the number of cases treated between 2018 and 2022, the number of cases undergoing surgery between 2014 and 2022 was estimated (Table 42). Following the assumptions in the base case of our *de novo* cost model, we assumed that 1.9% of the patients who underwent surgery between 2014 and 2017 would still need follow-up treatment in the period of interest (2018-2022). In total we assumed 63,051 cases undergoing surgery between 2018 and 2022, and 896 (1.9% of 47,148) cases who underwent surgery between 2014 and 2017 and still required follow-up treatment between 2018 and 2022.

Table 42: Estimated number of full-thickness rotator cuff tear in Switzerland between 2014 and 2022

Year	2014	2015	2016	2017	2018	2019	2020	2021	2022
Estimated Swiss population (million)	8.140	8.238	8.327	8.420	8.532	8.645	8.758	8.838	8.919
% above 40 years of age	53.7	53.3	53.4	53.6	53.8	54.0	54.2	54.5	54.7
Persons above 40 years of age (million)	4.375	4.387	4.446	4.512	4.589	4.667	4.749	4.813	4.878
Estimated number of cases	11,641	11,672	**11,830**	12,004	12,210	12,417	12,637	12,808	12,979

9.5.2 Budget impact model results

In the base case BIA, undiscounted costs per patient identified in the *de novo* cost analysis were applied to the estimated number of cases, for each of the two treatment strategies.

Estimated total costs in the 6-month-cost BIA, comparing an initial surgery strategy with the alternative of a conservative treatment strategy are shown in Table 43. Total costs reached CHF 659.4 million between 2018 and 2022 if all cases were assumed to follow an initial surgery strategy. In contrast, in case of use of an initially conservative treatment strategy, the total costs would be CHF 64.2 million (i.e. approximatively one tenth if compared to surgery).

Table 43: Estimated costs of 6-month treatment costs of full-thickness rotator cuff tear in Switzerland between 2018 and 2022

Year	2018	2019	2020	2021	2022	Total
Total costs initial surgery strategy (million CHF)	127.7	129.9	132.2	133.9	135.7	**659.4**
Total costs conservative treatment strategy (million CHF)	12.4	12.6	12.9	13.0	13.2	**64.2**
Cost difference (initial surgery – conservative treatment strategy) (million CHF)	115.3	117.2	119.3	120.9	122.5	**595.2**

Abbreviations: CHF = Swiss francs

Following the *de novo* cost model, the 5-year-cost BIA assumed the following: In the initial surgery strategy 1.9% of the patients receive a revision surgery and also 1.9% additional conservative follow-up treatment. In the conservative treatment strategy, the crossover rate to secondary surgery is 18% up to 12 months, and overall 24% up to 24. In the patients who receive crossover surgery, the occurrence of revision surgery is also 1.9%. Of all patients in the conservative treatment strategy, 5.9% receive additional, conservative follow-up treatment.

The estimated total costs of the 5-year-cost BIA in case of initial surgery or conservative treatment strategy (allowing for the possibility of crossover surgery) between 2018 and 2022 is shown in Table 44. Total costs reached CHF 672.4 million if all cases were assumed to follow an initial surgery strategy. In contrast, in case of use of an initially conservative treatment strategy, the total costs would be CHF 227.2 million (i.e. approximatively one third if compared to surgery).

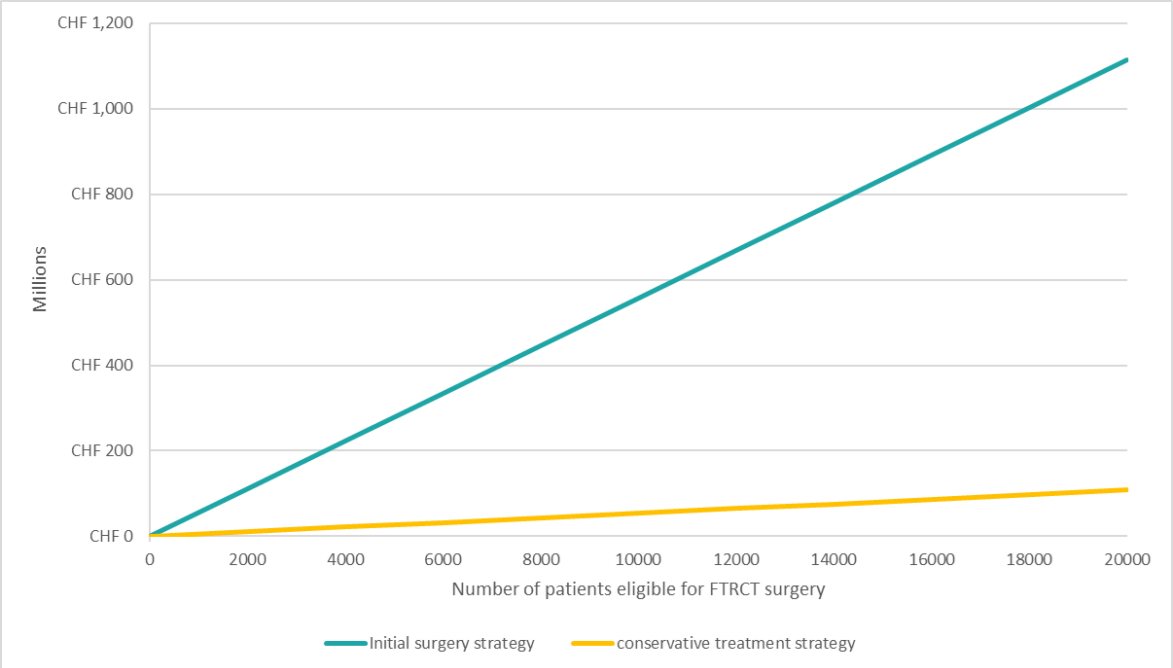
9.5.3 Scenario analyses

Scenario analyses for the 6-month-cost BIA and 5-year-cost BIA: number of eligible patients

Figure 21 (6-month-cost BIA) and Figure 22 (5-year-cost BIA) illustrate the results of the first scenario analysis varying the number of eligible patients (in 2016) overall from 0 to 20,000.

Table 44: Estimated costs of 5-year treatment costs of full-thickness rotator cuff tear in Switzerland between 2018 and 2022

Year	2018	2019	2020	2021	2022	Total
Total costs initial surgery strategy (million CHF)	130.2	132.4	134.8	136.6	138.4	**672.4**
Total costs conservative treatment strategy (million CHF)	44.0	44.7	45.5	46.2	46.8	**227.2**
Cost difference (initial surgery – conservative treatment strategy) (million CHF)	86.2	87.7	89.2	90.4	91.6	**445.2**



Abbreviations: CHF = Swiss francs

Figure 21: 5-year budget impact of initial surgery strategy or conservative treatment strategy assuming 6-month treatment costs per patient

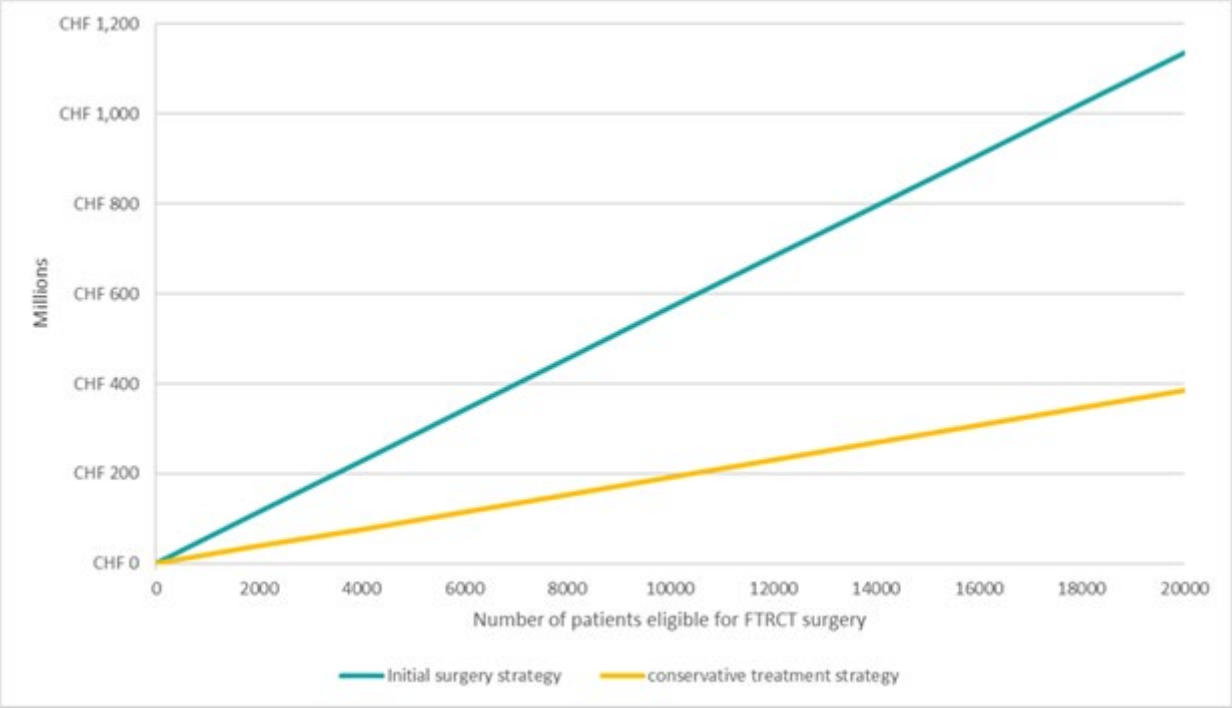


Figure 22: 5-year budget impact of initial surgery strategy or conservative treatment strategy assuming 5-year treatment costs per patient

Scenario analysis for the 5-year-cost BIA: number of eligible surgery cases

In a second scenario analysis reducing the number of eligible surgery cases (from 11,830 to 11,415) by excluding patients who exclusively received any of CHOP codes 83.71.11, 83.72.11, 83.75.11 or 83.88.41 the total costs of full-thickness rotator cuff tear between 2018 and 2022 would reach CHF 648.8 million in case of surgery and CHF 219.1 in case of initial conservative treatment.

In general, with an increasing number of cases the cost difference between the initial surgery strategy and the conservative treatment strategy would increase linearly.

The overall costs for the initial surgery strategy were similar between the 6-month-cost BIA and the 5-year-cost BIA. In contrast, the overall costs for the conservative treatment strategy in the 6-month-cost BIA were much lower if compared to those in the 5-year-cost BIA. This difference was obviously driven by the crossovers to secondary surgery in the 5-year-cost BIA.

10 Health economic assessment - Discussion and conclusion

The aim of the present report was to assess the health economic properties of surgical versus non-surgical treatment of patients with full-thickness rotator cuff tears in Switzerland. The report is part of an HTA. The clinical part of the HTA addressed comparative effectiveness and safety of surgical versus non-surgical treatment in patients with full-thickness rotator cuff tears in the form of a systematic review. The protocol of the clinical systematic review has been registered in PROSPERO (https://www.crd.york.ac.uk/prospero/) on 14/08/2018 (PROSPERO ID CRD42018100343).

Our health economic assessment consisted of a systematic review of the currently published health economic literature, a *de novo* cost analysis with supplemental cost-effectiveness considerations and a BIA for Switzerland.

The results of the health economic systematic review indicated absence of published cost-effectiveness analyses. Due to lack of suitable data, we could not perform a proper cost-effectiveness analysis, but developed a *de novo* cost model instead. The resulting cost analysis provided a cost estimation and comparison for the treatment strategies defined in the PICO: initial repair surgery (plus subsequent physiotherapy and pharmacological treatment) versus conservative treatment (i.e. physiotherapy and pharmacological treatment with the possibility to crossover to secondary repair surgery). Some additional specifications were required, as addressed below. Costs were assessed from a Swiss health insurance law perspective. Next to a cost estimation over six months (6-month analysis), we also developed a 5-year treatment scheme to gain an understanding of possible cost differences over a longer time horizon. The BIA remained limited in that we could well estimate the number of full-thickness rotator cuff tear surgeries performed in Switzerland, but not the total occurrence of (surgical and conservative) full-thickness rotator cuff tear treatments.

10.1 *De novo* cost analysis results

The results of the de novo cost analysis suggested that the 6-month costs per patient of initial repair surgery of full-thickness rotator cuff tear plus subsequent physiotherapy are approximately 10 times higher than physiotherapy alone in a Swiss setting. During the first six months, costs per person for surgery plus subsequent physiotherapy were estimated as CHF 10,458, whereas costs for physiotherapy alone were CHF 1,018. This led to a cost difference of CHF 9,440 per person over six months. Surgery costs of CHF 9,379 constituted the highest cost factor. Costs for 18 sessions of physiotherapy treatment were estimated to be CHF 773.

In the cost model with a time horizon of five years, costs per person for the initial surgery strategy amounted to CHF 10,662, whereas costs for the conservative treatment strategy

reached CHF 3,599. The cost difference between the treatment strategies of CHF 9,440 at six months decreased to CHF 6,992 at two years, and slightly rose again to a difference of CHF 7,063 at five years.

Deterministic sensitivity analysis of the 5-year model showed these results to be most strongly influenced by surgery costs, followed by the overall crossover rate at 24 months (crossover from conservative treatment to surgery). All other variables only had a minor impact.

10.2 Cost comparison with other studies

Our cost results for Switzerland were comparable with the results of earlier international cost analyses.[22,24,93,94,105,106] This holds primarily for the cost estimates of repair surgery. Cost estimates of the conservative treatment strategy were often lower in our Swiss model. For example, for Finland, the RCT of Kukkonen et al. reported mean direct costs after two years of follow-up of EUR 9,185 for the surgery group and of EUR 5,104 for the conservative group (cost year, 2015).[93] If compared to our cost estimate of the conservative treatment strategy after two years, of CHF 3,518, the conservative treatment costs in Kukkonen et al. of EUR 5,104 appeared to be high, especially as the authors assumed that only 9.1% of the patients in conservative group crossed-over to surgery (vs. 24% in the present analysis).[93]

Furthermore, Kukkonen et al. reported mean direct treatment costs after one year that were approximately half of their costs at two years (EUR 5,709 in the surgery group and EUR 2,417 in the conservative group at one year).[94] In contrast, our costs for the initial surgery strategy stayed almost constant during two years. Kukkonen et al. mentioned that 31% of the patients in the surgery group had full-thickness rotator cuff tear re-tears. Structured questionnaire forms were collected at each control visit and costs estimated using 2013 prices.[93,94]. A possible explanation for increase in costs in the surgery group of the Kukkonen trial may be a peculiar categorisation of costs into direct costs and indirect societal costs. In fact, in their work, 'direct' costs included expenses for transportation, hospital, physician, physiotherapist, medication and lost income. In contrast, 'indirect societal costs' included surgery, supplies, and patient care. Unfortunately, resource use or unit costs were not reported in detail. The absence of such detail and the non-standard definition of direct and indirect costs may reduce the comparability of these study results with the present assessment.

In the UK HTA on full-thickness rotator cuff tear repair surgeries, Carr et al. reported mean total costs per patient over 24 months of GBP 2,567 in the arthroscopic surgery group and of GBP 2,699 in the open surgery group, for the cost year 2012-2013 (ITT analysis, no adjustment for covariates).[92] These UK costs for a time horizon of two years were low in comparison to the SwissDRG costs for full-thickness rotator cuff tear repair of CHF 9,379 estimated for 2018. This difference is not surprising considering that UK healthcare costs are typically low if compared to those in Switzerland.

As a further comparison, an Italian study published by Castagna et al. reported total costs of EUR 24,312 per patient with irreparable and massive rotator cuff tears undergoing arthroscopic

partial rotator cuff repair.[22] The total costs per patient in an initial non-surgical, conservative treatment group were estimated to reach EUR 16,805 for 2017. An explanation for such high costs may be the fact that patients had more severe disease (irreparable and massive) and that patients in the non-operative group proceeded to expensive surgery (total reverse shoulder arthroplasty or InSpace™) if symptoms worsened.

A USA modelling study by Makhni et al. reported total costs per case of USD 22,300 for initial arthroscopic rotator cuff repair and of USD 11,300 for non-operative treatment, for 2014.[106] In another USA study, Dornan et al. reported that the costs for single arthroscopic rotator cuff repair for massive rotator cuff tears in patients with pseudoparalysis and nonarthritic shoulder accounted for USD 14,983 in 2016.[24]

10.3 Cost-effectiveness considerations

Since a proper cost-effectiveness analysis was not possible, we determined in supplementary calculations what differences in utilities and QALYs (between the initial surgery strategy and the conservative treatment strategy) over periods of 2 and five years would be necessary to achieve an ICER of CHF 50,000 or 100,000 per QALY gained.

For an estimated cost difference of CHF 6,992 at two years, a QALY difference of 0.140 and 0.070 would be needed in order to obtain an ICER of CHF 50,000 and CHF 100,000, respectively. At five years, the estimated cost difference of CHF 7,063 would require a similar QALY difference (0.141 and 0.071).

Based on a simplifying assumption of constant utility differences across the 2-year or 5-year time horizons, a utility difference of 0.070 and 0.035 would be required over a 2-year time horizon to meet an ICER threshold of CHF 50,000 and CHF 100,000, respectively. For a 5-year time horizon, a utility difference of 0.028 and 0.014 would be necessary to meet an ICER threshold of CHF 50,000 and CHF 100,000, respectively.

In comparison, the UK HTA by Carr et al. reported total QALYs over two years of 1.34 after arthroscopic repair and of 1.35 after conservative repair, in ITT analysis. The conservative treatment group of the UK HTA was closed prematurely. In the surgery group, mean EQ-5D values at baseline were relatively low at 0.535 across both surgery groups. The mean EQ-5D values after two years rose up to 0.750 in ITT analysis. Given the high increase from 0.535 at baseline to 0.750 at two years in the initial surgery group in the UK trial, a utility difference of 0.035 or even 0.07 might be considered potentially achievable. Further studies investigating the quality of life of full-thickness rotator cuff tear patients after surgery or conservative treatment are needed, especially since, between six months and five years, no significant difference in the mean changes from baseline between the treatment strategies were found for the physical component summary scale of the SF-36, in the small-to medium size full-thickness rotator cuff tear population of the Moosmayer trial.[52,53]

10.4 Budget impact analysis

Budget impact was calculated over a time period of five years (from 2018 to 2022) using a health insurance system perspective. A first BIA considered 6-month treatment costs per patient, for patients initiating treatment over a 5-year time period, from 2018 until 2022. In a second BIA we anticipated 5-year treatment costs per patient over the same time period of five years.

We estimated both the number of rotator cuff tear cases undergoing surgery between 2018 and 2022, and the number of cases who underwent surgery up to four years before 2018 but who still required follow-up treatment between 2018 and 2022, according to our assumptions in the *de novo* cost model. It was not possible to derive the exact number of full-thickness rotator cuff tear repair surgeries based on SwissDRG, ICD-10, and CHOP codes since these codes do not distinguish between rotator cuff tears and full-thickness rotator cuff tears. This means that the reported number of cases represent an upper limit for full-thickness rotator cuff tear surgeries. It was also not possible to estimate the number of patients undergoing conservative treatment in Switzerland because the Tarmed system does not report the specific indication (i.e. diagnosis) of reported physician visits and physiotherapies. There were also no other suitable sources. Therefore, our BIA provided information on the actual costs of surgery and standard follow-up physiotherapy for full-thickness rotator cuff tears in Switzerland, on the cost difference between initial surgery and conservative treatment strategy, but not on the total cost of conservative treatment.

A comparison between the SwissDRG codes in 2016 and 2017 showed important discrepancies in the distribution of cases across different SwissDRG codes. For this reason, an analytical approach of selecting cases according to ICD-10 and CHOP codes only (but no SwissDRG codes) was used as basis for this BIA.

The results suggested that total costs for the initial surgery strategy between 2018 and 2022 would reach CHF 659.4 million when only 6-month treatment costs were considered for each patient. In contrast, in case of use of an initially conservative treatment strategy, the total costs would be CHF 64.2 million (i.e. approximatively one tenth if compared to surgery). The resulting budget impact would be CHF 595.2 million over five years, and about CHF 120 million per year. It would increase or decrease linearly if the number of patients treated surgically instead of conservatively increased or decreased

When applying 5-year treatment costs for each patient, total costs for the initial surgery strategy between 2018 and 2022 may reach CHF 672.4 million (assuming 63,051 cases undergoing surgery between 2018 and 2022, and 896 (1.9% out of 47,148) cases who underwent surgery before 2018 but still required follow-up treatment between 2018 and 2022). The initial conservative treatment strategy for the same number of cases would cost CHF 227.2 million (i.e. approximatively one third if compared to surgery). The resulting budget impact would be CHF 445.2 million over five years, and about CHF 90 million per year. It would again increase or decrease linearly if the number of patients treated surgically instead of conservatively increased or decreased.

10.5 Strengths and Limitations

One strength of the *de novo* cost analysis was the use of the clinical systematic review part of this HTA as the basis for estimating clinical effectiveness outcomes with implications for medical resource use and costs. Unfortunately, not all required outcome parameters could be reported by the clinical systematic review team, due to lack of data.

Another strength, relevant for the BIA part, was the use of high-quality, national statistical data and two different approaches for the identification of eligible cases undergoing full-thickness rotator cuff tear surgery: i) combining relevant SwissDRG codes with ICD-10 codes and CHOP codes, which turned out to be potentially misleading due to limited suitability of SwissDRG codes for the purpose of patient identification; ii) focussing on a combination of ICD-10 codes and CHOP codes which permitted a slighlty broader but probably more accurate selection of patients, resulting in a more realistic cost estimation.

This economic assessment report has several limitations.

The lack of a high-quality data basis for health economic assessment is striking. Long-term clinical data were largely missing. No cost-effectiveness studies for the underlying PICO were available. Follow-up/additional treatment after surgery was not always clearly described in the literature. In addition, only one of the three available RCTs cited in the clinical systematic review part had a follow-up of five years[52,53], whereas the remaining two trials had follow-up periods of only two years.[51,93,94] Furthermore, the sample size of the 5-year trial was rather small: 52 patients in the surgery and 51 patients in the physiotherapy group. Moreover, the patient population with traumatic multiple tendon tears is greatly underrepresented in the currently available RCTs and may need different model assumptions. Health economic statements on this patient group cannot be made.

The PICO was broad and left open if full-thickness rotator cuff tear patients would be pre-treated or not. Not all of the three trials identified in the clinical systematic review part included patients at the time point of full-thickness rotator cuff tear. None of the three trials included patients straight after full-thickness rotator cuff tear was diagnosed. The mean symptom duration before enrollment across the trials varied between one and 2.5 years. All three trials included many patients who were already pre-treated with conservative treatment (physiotherapy and/or pain medication), but who had not received previous surgery.

A further challenge was the fact that the patient groups under investigation got mixed, because e.g. patients starting with a conservative treatment could crossover to repair surgery.[52,53,93,94]

In the base case of the *de novo* cost model, we assumed that all full-thickness rotator cuff tear repair surgeries were performed during an inpatient hospital stay, based on expert advice on current practice in Switzerland. However, in the USA and the Nordic countries, rotator cuff tear surgeries are also performed in an outpatient setting.[107] In Switzerland, there may be financial incentives for both the hospitals and the surgeons for an inpatient setting. Related patient preferences are unknown.

Our economic analyses required a substantial amount of assumptions, including on a plausible treatment scheme over five years and its relevance to full-thickness rotator cuff tear treatment in Switzerland. Alternative surgical interventions next to repair surgery, like e.g. total reverse shoulder arthroplasty or InSpace™, were not in the scope of the assessment. Also, the approximated costs for full-thickness rotator cuff tear repair were based on SwissDRG costs from 2014, projected to the year 2018. Another limitation of the present assessment is the identification of eligible patients. Three different coding systems (SwissDRG, ICD-10, and CHOP) were used. The analyses suggested that many patients classified with a relevant SwissDRG code or a relevant ICD-10 diagnosis did not receive any relevant treatment (CHOP code). Inversely, some patients undergoing relevant treatment were not classified or diagnosed accordingly. It could be interesting to investigate whether additional selection strategies might be possible, beyond the two strategies discussed above.

As a further limitation, it was not possible to determine the yearly number of cases that undergo conservative treatment in Switzerland.

Moreover, we did not include re-tear rates in the present cost model although re-tears after repair surgery are frequent. The functional outcome for patients with a re-rupture is not well known.[97] Also, there are ongoing discussions if clinical and anatomic outcome are correlated or not.[98] No correlation between structural findings (i.e. re-tear or re-tear size) after full-thickness rotator cuff tear repair surgery and functional outcomes could be demonstrated in a prospective study performed in South Korea.[98] The clinical expert group involved in this assessment confirmed that patients with re-tears are mostly asymptomatic and do not require any additional surgery nor treatment.[99,97] In fact, the high frequency of re-tears reported in the clinical trials may be driven by pre-planned follow-up investigations of the participating patients, independent from their health status or symptoms.

End-stage costs of the disease like e.g. the need for a prosthesis were not included in our model because of the selected 5-year time horizon which equaled the longest available follow-up in a RCT.[53]

Finally, the available information did not allow us to investigate total annual costs from a societal perspective. Total costs from a societal perspective could be expected to be much higher than direct medical costs alone: patients may be unable to work due to symptoms; patients undergoing surgery interventions are often unable to work for several weeks. Similarly, patients requiring periodical physiotherapy may temporarily be absent from work. Therefore, indirect costs related to loss of productivity are potentially high, and there impact on the (now societal) costs of the treatment strategies compared would be difficult to predict.

10.6 Personal clinical expert feedback

It is the personal view of clinical experts consulted for this HTA that for small degenerative tears the difference in clinical outcomes between repair surgery and conservative physiotherapy may be small. In day-to-day practice, treatment of degenerative full-thickness rotator cuff tears

usually starts with conservative physiotherapy treatment for patients with single tendon tears. This statement is underpinned by the patient populations of the three available RCTs who had a mean symptom duration of at least one year and were mostly pre-treated. Also, Seida et al.[16] mentioned that most patients first undergo non-operative treatment for six weeks to three months and move to operative treatment if shoulder pain does not improve with nonsurgical treatments for a certain period of time.[108] However, in the personal view of the experts, repair surgery can be of an advantage for patients with multiple tendon-tears. Also, these patients do suffer more pain and arm mobility restrictions. Especially for patients with traumatic multiple tendon tears, a prompt surgery may in their opinion have advantages for clinical outcomes. This statement is underpinned by several authors (Guo et al.[108], Habermeyer et al.[109], Spross et al.[110], Mall et al.[111]).

10.7 Conclusion of the health economic assessment part

The systematic review of the economic literature suggested that there is currently no cost-effectiveness study for the predefined PICO.

Our own analytical options were also substantially restricted given very sparse data. The *de novo* cost analysis suggested that in the management of full-thickness rotator cuff tears, an initial surgery strategy is much more expensive than an initially conservative treatment strategy, in the short-term and mid-term. For the BIA, the available data allowed the investigation of the costs of an initial surgery strategy for full-thickness rotator cuff tears in Switzerland, based on the current number of surgeries performed, as well as a cost comparison between an initial surgery strategy and a conservative treatment strategy on the same basis. Considering estimated 5-year treatment costs per patient, BIA results indicated that the current use of full-thickness rotator cuff tear surgery in Switzerland may lead to additional costs in the range of CHF 90 million per year, in comparison with an initially conservative treatment strategy. It was impossible to estimate the total costs of conservative treatment since there is currently no information concerning the utilisation of conservative full-thickness rotator cuff tears treatment.

Our economic results need to be carefully related to the clinical performance of the treatment strategies under investigation, as reported in the clinical systematic review part of this HTA. The overall conclusion of the clinical systematic review part is that *"surgery may be more effective than conservative treatment to improve shoulder function and reduce pain. However, the clinical relevance of these differences is questionable. For other patient-relevant outcomes such as shoulder range of motion, muscle strength, quality of life, and adverse events, only very limited data were available, showing no differences between the groups."*

Given the paucity of high-quality and long-term data on clinical outcomes and health related quality of life, it remains unclear whether an analysis over a longer period of observation or including indirect costs related to productivity losses might lead to different health economic results. Ultimately, it is not possible to judge on the basis of currently available data if the initial surgery strategy might meet frequently assumed cost-effectiveness thresholds (e.g. CHF 50,000 or CHF 100,000 per QALY gained). In this optic, long-term studies investigating treatment

effectiveness and the quality of life of full-thickness rotator cuff tear patients after surgery or conservative treatment, are needed. Long-term studies investigating the difference in outcomes for patients with traumatic vs. atraumatic full-thickness rotator cuff tears as well as for single vs. multiple tendon tears would also be important for refined analyses.

In the near future, the 10-year results of the RCT by Moosmayer are expected. These results will be the first trial-based data after 10 years follow-up for patients with small to medium sized full-thickness rotator cuff tears.

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Appendix A: List of included studies

Randomised controlled studies (3 studies, 5 publications [records, references])

Table 45: References of included RCTs.

Kukkonen 2014 and 2015

Kukkonen J, Joukainen A, Lehtinen J, et al. Treatment of non-traumatic rotator cuff tears: A randomised controlled trial with one-year clinical results. Bone Joint J 2014;96-B(1):75-81.

Kukkonen J, Joukainen A, Lehtinen J, et al. Treatment of non-traumatic rotator cuff tears: A randomised controlled trial with two-years of clinical and imaging follow-up. J Bone Joint Surg Am 2015;97(21):1729-37.

Lambers Heerspink 2015

Lambers Heerspink FO, van Raay JJ, Koorevaar RC, et al. Comparing surgical repair with conservative treatment for degenerative rotator cuff tears: a randomised controlled trial. J Shoulder Elbow Surg 2015;24(8):1274-81.

Moosmayer 2010 and 2014

Moosmayer S, Lund G, Seljom U, et al. Comparison between surgery and physiotherapy in the treatment of small and medium-sized tears of the rotator cuff: A randomised controlled study of 103 patients with one-year follow-up. J Bone Joint Surg Br 2010;92(1):83-91.

Moosmayer S, Lund G, Seljom US, et al. Tendon repair compared with physiotherapy in the treatment of rotator cuff tears: a randomised controlled study in 103 cases with a five-year follow-up. J Bone Joint Surg Am 2014;96(18):1504-14.

Non-randomised studies (7 studies, 8 publications [records, references])

Table 46: References of included NRSs.

Boorman 2014 and 2018

Boorman RS, More KD, Hollinshead RM, et al. The rotator cuff quality-of-life index predicts the outcome of non-operative treatment of patients with a chronic rotator cuff tear. J Bone Joint Surg Am 2014;22(96)1883-8.

Boorman RS, More KD, Hollinshead RM, et al. What happens to patients when we do not repair their cuff tears? Five-year rotator cuff quality-of-life index outcomes following non-operative treatment of patients with full-thickness rotator cuff tears. J Shoulder Elbow Surg 2018;27(3):444-8.

De Carli 2017

De Carli A, Fabbri M, Lanzetti RM, et al. Functional treatment in rotator cuff tears: is it safe and effective? A retrospective comparison with surgical treatment. Muscles Ligaments Tendons J 2017;7(1):40-5.

Fabbri 2016

Fabbri M, Ciompi A, Lanzetti RM, et al. Muscle atrophy and fatty infiltration in rotator cuff tears: Can surgery stop muscular degenerative changes? J Orthop Sci 2016;21(5):614-8.

Lee 2016

Lee WH, Do HK, Lee JH, et al. Clinical Outcomes of Conservative Treatment and Arthroscopic Repair of Rotator Cuff Tears: A Retrospective Observational Study. Annals of rehabilitation medicine 2016;40(2):252-62.

Vad 2002

Vad VB, Warren RF, Altchek DW, et al. Negative prognostic factors in managing massive rotator cuff tears. Clin J Sport Med 2002;12(3):151-7.

Yamada 2000

Yamada N, Hamada K, Nakajima T, et al. Comparison of conservative and operative treatments of massive rotator cuff tears. Tokai J Exp Clin Med 2000;25(4-6):151-63.

Yoo 2018

Yoo JC, Lim TK, Kim DH, et al. Comparison between the patients with surgery and without surgery after recommendation of surgical repair for symptomatic rotator cuff tear. J Orthop Sci 2018;23(1):64-9.

Registered (ongoing or completed but not yet published) studies

Table 47: Registered (ongoing or completed but not yet published) studies.

Study ID	Title	Study type	Country	Target N (patient)	Estimated completion date	Record last updated; recruitment status	Link
NCT00695981	Operative vs. Non-operative Management of Rotator Cuff Tear	RCT	Finland	100	06/2023	09/2018; not yet recruiting	https://clinicaltrials.gov/ct2/show/NCT00695981
NCT02885714	ACCURATE Trial Operative Treatment of Acute Rotator Cuff Tear Related to Trauma	RCT	Finland	200	01/2029	10/2017; recruiting	https://clinicaltrials.gov/ct2/show/NCT02885714
NCT02059473	Treatment of Small Acute Cuff Tears	RCT	Sweden	50	unknown *	02/2014; unknown status	https://clinicaltrials.gov/ct2/show/NCT02059473
NCT03295994	Operative vs. Non-Operative Treatment for Atraumatic Rotator Cuff Tears	RCT	USA	700	12/2022	11/2018; recruiting	https://clinicaltrials.gov/ct2/show/NCT03295994

NTR5700	BITE: Cutting the long biceps tendon as a treatment for elderly patients with a shoulder tendon rupture	RCT	Netherlands	120	no information	04/2016; unknown status	http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=5700
NCT03021733	A Pilot Cohort Study of Surgical and Non-surgical Management of Rotator Cuff Tears	NRS	USA	222	11/2016	09/2017; completed	https://clinicaltrials.gov/ct2/show/NCT03021733

ID = Identifier; N = Number of patients; NCT = Number (identifier) in ClinicalTrials.gov; NRS = Non-randomised Study; NTR = Netherlands Trial register; RCT = Randomised Controlled Trial.
*Results are not yet published (2018/11/02), and registry entry has not been updated since 02/2014.

Appendix B: Other systematic reviews

Table 48: Overview of other systematic reviews.

Reference	Currentness (latest search)	N included studies	Relevant included studies	Review authors' key conclusions
Kim et al.[75]	12/2017	overall: 15 relevant: 2	Based on RCTs	'Comparison between surgical treatment and physiotherapy alone for pain showed that physiotherapy alone reduced pain less than surgical treatment did. [...]. Although there was a statistically significant difference in pain, it is not clear whether it was related to clinical effectiveness [...].'
Piper et al.[74]	10/2016	3	Based on RCTs	'[...] there is a statistically significant advantage in both objective and subjective outcomes for patients treated with surgery for a full-thickness rotator cuff tear. However, this statistical advantage is not a clinically significant one. The most remarkable finding of this study is the paucity of high-level evidence available to guide treatment of full-thickness rotator cuff tears. Both operative management and non-operative management reliably improve functional outcome and pain scores and are reasonable initial treatment choices. [...].'
Ryösä et al.[35]	06/2015	3	Based on RCTs	'There is limited evidence that surgery is not more effective in treating symptomatic rotator cuff tear than conservative treatment alone. Thus, a conservative approach is advocated as the initial treatment modality.'
Seida et al.[16]	09/2009	overall: 137 relevant: 5	Based on RCTs and comparative NRSs	'All but 1 study [...] showed statistically significant differences in function that favoured operative repair. One study [...] showed that patients who had arthroscopic debridement had a statistically significant shorter time to maximum range of motion (3.2 months) than did those in the non-operative and open repair groups (6.8 months each). In general, the evidence was too limited to make conclusions regarding comparative effectiveness.'

N = Number of included research; NRS = Non-randomised Study; RCT = Randomised Controlled Trial.

Appendix C: List of excluded studies

Ineligible study design

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Ineligible study population

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Ineligible intervention

No excluded studies

Ineligible comparison

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Ineligible outcome

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Fulltext not retrievable

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Irrelevant ongoing study

1. Workers Compensation Board: Rotator Cuff Tear Management. https://ClinicalTrials.gov/show/NCT01498198; 2012.

2. A Pilot Cohort Study of Surgical and Non-surgical Management of Rotator Cuff Tears. https://ClinicalTrials.gov/show/NCT03021733; 2012.

3. Assessment of Muscle Function and Size in Older Adults With Rotator Cuff Tear. https://ClinicalTrials.gov/show/NCT01459536; 2011.

Appendix D: Clinical assessment search strategies

Ovid MEDLINE(R) 1946 to May Week 3 2018, Ovid MEDLINE(R) Epub Ahead of Print May 25, 2018, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations May 25, 2018, Ovid MEDLINE(R) Daily Update May 25, 2018			
	#	Searches	Results
A. Rotator cuff tear	1	Rotator Cuff Injuries/	4586
	2	Shoulder Impingement Syndrome/	1592
	3	((rotator cuff* or supraspinatus or infraspinatus or teres minor or subscapularis) adj3 (tear? or rupture* or injur* or disease or impingement)).ti,ab.	5864
	4	((shoulder or subacromial) adj impingement).ti,ab.	1105
	5	or/1-4	8711
B. surgery	6	Rotator Cuff/su [Surgery]	3134
	7	Rotator Cuff Injuries/su	384
	8	Arthroscopy/	20721
	9	(arthroscop* or acrom?oplast*).ti,ab.	26810
	10	((rotator cuff* or supraspinatus or infraspinatus or teres minor or subscapularis or tendon?) adj3 (surg* or repair or fixation or refixation or suture? or reconstruct* or reinsertion or open)).ti,ab.	10824
	11	or/6-10	40277
A+B	12	5 and 11	4758
Humans only	13	exp animals/ not exp humans/	4464699
	14	12 not 13	4519
no editorials	15	editorial/	458893
	16	14 not 15	4468

Embase.com, 29 May 2018		
No.	Query	Results
#1	'rotator cuff injury'/de	1899
#2	'rotator cuff rupture'/exp	5789
#3	'shoulder impingement syndrome'/exp	2454
#4	(('rotator cuff*' OR supraspinatus OR infraspinatus OR 'teres minor' OR subscapularis) NEAR/3 (tear OR tears OR rupture* OR injur* OR disease OR impingement)):ti,ab	6800
#5	((shoulder OR subacromial) NEXT/1 impingement):ti,ab	1355
#6	#1 OR #2 OR #3 OR #4 OR #5	11620
#7	'rotator cuff rupture'/exp/dm_su	2555
#8	'shoulder impingement syndrome'/exp/dm_su	490
#9	'shoulder surgery'/de OR 'shoulder arthroscopy'/de	3930
#10	arthroscop*:ti,ab OR acrom*oplast*:ti,ab	32534
#11	(('rotator cuff*' OR supraspinatus OR infraspinatus OR 'teres minor' OR subscapularis OR tendon*) NEAR/3 (surg* OR repair OR fixation OR refixation OR suture* OR reconstruct* OR reinsertion OR open)):ti,ab	12282

#12	#7 OR #8 OR #9 OR #10 OR #11	44749
#13	#6 AND #12	5804
#14	'animal'/exp NOT 'human'/exp	5044538
#15	#13 NOT #14	5526
#16	#15 AND [embase]/lim	4682
#17	#16 NOT 'editorial'/it	4590

Cochrane Library, 29 May 2018		
ID	Search	Results
#1	[mh "Rotator Cuff Injuries"]	201
#2	[mh "Shoulder Impingement Syndrome"]	232
#3	(("rotator cuff*" or supraspinatus or infraspinatus or "teres minor" or subscapularis) near/3 (tear or tears or rupture* or injur* or disease or impingement)):ti,ab,kw	547
#4	((shoulder or subacromial) next impingement):ti,ab,kw	403
#5	or 1 to 3	734
#6	[mh "Rotator Cuff"/su]	207
#7	[mh "Rotator Cuff Injuries"/su]	34
#8	(arthroscop* or acrom*oplast*):ti,ab,kw	3176
#9	(("rotator cuff*" or supraspinatus or infraspinatus or "teres minor" or subscapularis or tendon*) near/3 (surg* or repair or fixation or refixation or suture* or reconstruct* or reinsertion or open)):ti,ab,kw	1122
#10	or 6 to 9	3843
#11	#5 and #10	388

Science Citation Index Expanded (1900-present) (Web of Science), 29 May 2018		
Set	Results	Query
# 1	5689	TOPIC: (("rotator cuff*" OR supraspinatus OR infraspinatus OR "teres minor" OR subscapularis) NEAR/3 (tear OR tears OR rupture* OR injur* OR disease OR impingement))
# 2	1483	TOPIC: ("shoulder impingement" OR "subacromial impingement")
# 3	6740	#2 OR #1
# 4	11179	TOPIC: ((("rotator cuff*" OR supraspinatus OR infraspinatus OR "teres minor" OR subscapularis OR tendon*) NEAR/3 (surg* OR repair OR fixation OR refixation OR suture* OR reconstruct* OR reinsertion OR open)))
# 5	24915	TOPIC: (arthroscop* OR acrom?oplast*)
# 6	33575	#5 OR #4
# 7	3243	#6 AND #3
# 8	3167	#6 AND #3 Refined by: [excluding] DOCUMENT TYPES: (EDITORIAL MATERIAL)

Conference Proceedings Citation Index- Science (1990-present) (Web of Science), 29 May 2018

Set	Results	Query
# 1	229	TOPIC: (("rotator cuff*" OR supraspinatus OR infraspinatus OR "teres minor" OR subscapularis) NEAR/3 (tear OR tears OR rupture* OR injur* OR disease OR impingement))
# 2	54	TOPIC: ("shoulder impingement" OR "subacromial impingement")
# 3	265	#2 OR #1
# 4	512	TOPIC: (("rotator cuff*" OR supraspinatus OR infraspinatus OR "teres minor" OR subscapularis OR tendon*) NEAR/3 (surg* OR repair OR fixation OR refixation OR suture* OR reconstruct* OR reinsertion OR open))
# 5	1171	TOPIC: (arthroscop* OR acrom?oplast*)
# 6	1607	#5 OR #4
# 7	98	#6 AND #3

BIOSIS Citation Index (1926-present) (Web of Science), 29 May 2018		
	Results	
# 1	2075	TOPIC: (("rotator cuff*" OR supraspinatus OR infraspinatus OR "teres minor" OR subscapularis) NEAR/3 (tear OR tears OR rupture* OR injur* OR disease OR impingement))
# 2	357	TOPIC: ("shoulder impingement" OR "subacromial impingement")
# 3	2352	#2 OR #1
# 4	4819	TOPIC: (("rotator cuff*" OR supraspinatus OR infraspinatus OR "teres minor" OR subscapularis OR tendon*) NEAR/3 (surg* OR repair OR fixation OR refixation OR suture* OR reconstruct* OR reinsertion OR open))
# 5	11636	TOPIC: (arthroscop* OR acrom?oplast*)
# 6	15447	#5 OR #4
# 7	1201	#6 AND #3
# 8	1196	#6 AND #3 Refined by: [excluding] LITERATURE TYPES: (EDITORIAL)
# 9	1187	#6 AND #3 Refined by: [excluding] LITERATURE TYPES: (EDITORIAL) AND [excluding] DOCUMENT TYPES: (PATENT OR LETTER)

SportDiscus (Ebsco), 29 May 2018			
#	Query	Limiters/ Expanders	Results
S1	"ROTATOR cuff -- Wounds & injuries"	Search modes - Boolean/Phrase	618
S2	(rotator cuff* OR supraspinatus OR infraspinatus OR teres minor OR subscapularis) N2 (tear OR tears OR rupture* OR injur* OR disease OR impingement)	Search modes - Boolean/Phrase	1723
S3	(shoulder OR subacromial) W1 impingement	Search modes - Boolean/Phrase	550
S4	S1 OR S2 OR S3	Search modes - Boolean/Phrase	2155
S5	((DE "OPERATIVE surgery" OR DE "SURGICAL operations") OR (DE "SURGERY")) OR (DE "ARTHROSCOPY")	Search modes - Boolean/Phrase	13717

S6	arthroscop* or acrom*oplast*	Search modes - Boolean/Phrase	12449
S7	(rotator cuff* OR supraspinatus OR infraspinatus OR teres minor OR subscapularis OR tendon OR tendons) N2 (surg* OR repair OR fixation OR refixation OR suture* OR reconstruct* OR reinsertion OR open)	Search modes - Boolean/Phrase	2710
S8	S5 OR S6 OR S7	Search modes - Boolean/Phrase	21749
S9	S4 AND S8	Search modes - Boolean/Phrase	1070

ClinicalTrials.gov, 29 May 2018	
Query	Results
Rotator Cuff Tear|surgery OR repair OR arthroscopy OR suture OR sutures OR Arthroscopic OR acromioplasty	159

ICTRP, 29 May 2018		
Query		Results
surgery AND Rotator Cuff Tear OR repair AND Rotator Cuff Tear OR arthroscopy AND Rotator Cuff Tear OR suture AND Rotator Cuff Tear OR sutures AND Rotator Cuff Tear OR Arthroscopic AND Rotator Cuff Tear OR acromioplasty		281
PubMed similar articles search, 29 May 2018		
First 100 linked citations for each article were used		
Search	Query	Results
#1	Search 24395315[uid] Sort by: Best Match	1
#2	Similar articles for PubMed (Select 24395315)	154
#3	Search 26189808[uid] Sort by: Best Match	1
#4	Similar articles for PubMed (Select 26189808)	322
#5	Search 20044684[uid] Sort by: Best Match	1
#6	Similar articles for PubMed (Select 20044684)	52
#7	Search 26537160 25540295 25232074 22261136 26188786 9655101 15930537 25306517 14960664 11205861 23515988 16376229 24733157 24630958 19940295 22048089 26337247 18413680 17588838 25442645 24553881 28495574 21269421 17629505 22552669 16002486 18354140 23937927 23206691 18760204 10024034 23937927 16002486 25232074 25790835 11451975 17768188 26015443 15346112 18354140 26463717 12966383 26189808 26646515 20194317 21873021 21885298 18539948 25193889 25622985 19482895 28131687 23580030 19801287 21460068 24845686 17545428 25527081 24553881 12522399 24196461 20655763 15925934 18762651 24430409 16376228 16399460 23351978 19752204 21990030 20607465 17113319 25622985 22854988 18827245 21411687 20516311 11060430 23515988 24647511 20194334 9768891 10761941 17266840 23965698 22154313 12951309 22074913 22056325 12671621 23079878 21533643 12098132 7746922 28427872 20522833 18978411 26912284 16391256 24493188 20040768 19501286 19171279 23850308 12124536 21411681 11060430 14574601 11451975 21778071 26337247 10761941 24043432 15634822 10901312 27184542 15925933 21434791 23040553 25622985 21350064 19434410 18762651 9655101 25457783 26189808 2303503 21098196 18760207 7782358 24395315 16194734 20632922 25177461 17606793 25306517 28296750 17011216 24845686 16459854 16510819 21444007 20392649 17768188 11928909 22836229 22052627 17974879 25232074 25775342 19487518	212

	25776185 28669465 20392649 17588838 25512665 21258779 23512014 23523306 12124536 19499278 21048173 23276410 23850308 25760511 25389369 15494338 20056453 23104609 25002218 20056453 11182734 27660800 17606793 28495574 21737830 29505742 16093533 24733104 22000411 27049184 24318610 22014698 20194317 22543221 22595255 16510819 23423315 19052931 24630958 18850322 16459854 18591587 20621524 25137495 19651947 19714274 22014477 23523073 23580030 17513136 15378320 19685265 8444920 15129028 24680303 27988164 16757756 15106069 19434410 10546622 25547273 9698005 23906268 27900700 22584619 26475640 25442645 23924298 18827245 27876086 23369479 15111896 22095705 20554492 17088752 22036541 21600793 26537160 15346112 14574601 25540295 17148619 10804410 8643842 21798838 10750001 25117727 16422233 23996071 26614931 23163623 7746922 11912097 12579145 21481615 17768186 8665284 11155303 16252125 23760681[uid]	
#8	Search "Animals"[Mesh] NOT "Humans"[Mesh]	4456827
#9	Search (#7 NOT #8)	212
#11	Search "Editorial" [Publication Type] Sort by: Best Match	458229
#12	Search (#9 NOT #11)	211

Web of Science Core Collection - Forward citation tracking, 29 May 2018	
Article	Cited by
Kukkonen, J. et al. 2014. Treatment of non-traumatic rotator cuff tears: A randomised controlled trial with one-year clinical results. Bone Joint J, 96 B(1), pp.75–81.	42
Lambers Heerspink, F.O. et al. 2015. Comparing surgical repair with conservative treatment for degenerative rotator cuff tears: a randomised controlled trial. J Shoulder Elbow Surg / American Shoulder and Elbow Surgeons ... [et al.], 24(8), pp.1274–81.	16
Moosmayer, S. et al. 2010. Comparison between surgery and physiotherapy in the treatment of small and medium-sized tears of the rotator cuff: A randomised controlled study of 103 patients with one-year follow-up. J Bone Joint Surg, 92(1), pp.83–91.	40

Appendix E: Health economic assessment search strategies

Table 49: Clinical search strategy in Medline using OvidSP for full-thickness rotator cuff tear

Search performed on 27 November 2018

Ovid MEDLINE(R) 1946 to November Week 3 2018, Ovid MEDLINE(R) Epub Ahead of Print November 26, 2018, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations November 26, 2018, Ovid MEDLINE(R) Daily Update November 26, 2018			
	#	Searches	Results
A. Rotator cuff tear	1	Rotator Cuff Injuries/	4799
	2	Shoulder Impingement Syndrome/	1643
	3	((rotator cuff* or supraspinatus or infraspinatus or teres minor or subscapularis) adj3 (tear? or rupture* or injur* or disease or impingement)).ti,ab.	6151
	4	((shoulder or subacromial) adj impingement).ti,ab.	1137
	5	or/1-4	9109
B. Surgery	6	Rotator Cuff/su [Surgery]	3204
	7	Rotator Cuff Injuries/su	509
	8	Arthroscopy/	21341
	9	(arthroscop* or acrom?oplast*).ti,ab.	27813
	10	((rotator cuff* or supraspinatus or infraspinatus or teres minor or subscapularis or tendon?) adj3 (surg* or repair or fixation or refixation or suture? or reconstruct* or reinsertion or open)).ti,ab.	11245
	11	or/6-10	41698
A+B	12	5 and 11	4979
Humans only	13	exp animals/ not exp humans/	4518028
	14	12 not 13	4728
Exclude Editorials	15	editorial/	474028
	16	14 not 15	4661
NHS EED MEDLINE using OvidSP	17	Economics/	26977
	18	exp "costs and cost analysis"/	219804
	19	Economics, Dental/	1901
	20	exp economics, hospital/	23187
	21	Economics, Medical/	8984
	22	Economics, Nursing/	3982
	23	Economics, Pharmaceutical/	2821

	24	(economic$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab.	692359
	25	(expenditure$ not energy).ti,ab.	26528
	26	value for money.ti,ab.	1491
	27	budget$.ti,ab.	26431
	28	or/17-27	836982
	29	((energy or oxygen) adj cost).ti,ab.	3773
	30	(metabolic adj cost).ti,ab.	1270
	31	((energy or oxygen) adj expenditure).ti,ab.	22882
	32	or/29-31	27000
	33	28 not 32	830777
	34	letter.pt.	1007383
	35	editorial.pt.	474028
	36	historical article.pt.	348338
	37	or/34-36	1811733
	38	33 not 37	797030
	39	exp animals/ not humans/	4518028
	40	38 not 39	747392
	41	bmj.jn.	75200
	42	"cochrane database of systematic reviews".jn.	13907
	43	health technology assessment winchester england.jn.	1209
	44	or/41-43	90316
	45	40 not 44	741528
	46	limit 45 to yr="2010 -Current"	353967
	47	16 and 46	90

Table 50: Clinical search strategy in Embase using OvidSP for full-thickness rotator cuff tear

Search performed on 27 November 2018

Embase 1974 to 2018 November 21			
	No.	Query	Results
Clinical search strategy	1	exp rotator cuff injury/	9904
	2	exp rotator cuff rupture/	6163
	3	exp shoulder impingement syndrome/	2541
	4	((rotator cuff* or supraspinatus or infraspinatus or teres minor or subscapularis) adj3 (tear? or rupture* or injur* or disease or impingement)).ti,ab.	7218
	5	((shoulder or subacromial) adj impingement).ti,ab.	1415
	6	1 OR 2 OR 3 OR 4 OR 5	12 291
	7	exp rotator cuff rupture/su	518
	8	exp shoulder impingement syndrome/su	438
	9	Arthroscopy/	17890
	10	(arthroscop* or acrom?oplast*).ti,ab.	34250
	11	((rotator cuff* or supraspinatus or infraspinatus or teres minor or subscapularis or tendon?) adj3 (surg* or repair or fixation or refixation or suture? or reconstruct* or reinsertion or open)).ti,ab.	12687
	12	7 OR 8 OR 9 OR 10 OR 11	49087
	13	6 AND 12	5697
	14	exp animals/ not exp humans/	4343810
	15	13 NOT 14	5443
	16	editorial/	598528
	17	15 NOT 16	5368

NHS EED EMBASE using OvidSP	18	Health Economics/	31469
	19	exp Economic Evaluation/	281353
	20	exp Health Care Cost/	269384
	21	pharmacoeconomics/	6872
	22	18 or 19 or 20 or 21	495444
	23	(econom$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab.	917921
	24	(expenditure$ not energy).ti,ab.	35508
	25	(value adj2 money).ti,ab.	2160
	26	budget$.ti,ab.	34044
	27	23 or 24 or 25 or 26	950266
	28	22 or 27	1163216

	29	letter.pt.	1047199
	30	editorial.pt.	587932
	31	note.pt.	733301
	32	29 or 30 or 31	2368432
	33	28 not 32	1067621
	34	(metabolic adj cost).ti,ab.	1337
	35	((energy or oxygen) adj cost).ti,ab.	3914
	36	((energy or oxygen) adj expenditure).ti,ab.	28863
	37	34 or 35 or 36	33085
	38	33 not 37	1060941
	39	animal/	1386611
	40	exp animal experiment/	2305738
	41	nonhuman/	5624981
	42	(rat or rats or mouse or mice or hamster or hamsters or animal or animals or dog or dogs or cat or cats or bovine or sheep).ti,ab,sh.	5343470
	43	39 or 40 or 41 or 42	8220267
	44	exp human/	19084332
	45	human experiment/	426867
	46	44 or 45	19085740
	47	43 not (43 and 46)	6089255
	48	38 not 47	965924
	49	0959-8146.is.	58642
	50	(1469-493X or 1366-5278).is.	22059
	51	1756-1833.en.	26872
	52	49 or 50 or 51	99169
	53	48 not 52	959178
	54	conference abstract.pt.	3221049
	55	53 not 54	791991
	56	limit 55 to yr="2010 -Current"	355388
	57	17 AND 56	116

Table 51: Clinical search strategy in the Cochrane Library

Search performed on 27 November 2018

	Cochrane Library, 27 November 2018		
	ID	**Search**	**Hits**
Clinical search strategy	#1	[mh "Rotator Cuff Injuries"]	287
	#2	[mh "Shoulder Impingement Syndrome"]	265
	#3	(("rotator cuff*" or supraspinatus or infraspinatus or "teres minor" or subscapularis) near/3 (tear or tears or rupture* or injur* or disease or impingement)):ti,ab,kw	673
	#4	((shoulder or subacromial) next impingement):ti,ab,kw	451
	#5	#1-#4	1030
	#6	[mh "Rotator Cuff"/su]	189
	#7	[mh "Rotator Cuff Injuries"/su]	41
	#8	(arthroscop* or acrom*oplast*):ti,ab,kw	3371
	#9	(("rotator cuff*" or supraspinatus or infraspinatus or "teres minor" or subscapularis or tendon*) near/3 (surg* or repair or fixation or refixation or suture* or reconstruct* or reinsertion or open)):ti,ab,kw	1255
	#10	#6-#9	4113
	#11	#5 and #10	485
NHS EED economic Medline strategy translated into Cochrane (based on http://crebp-sra.com)	#12	([mh ^Economics])	43
	#13	([mh "costs and cost analysis"])	9552
	#14	([mh ^"Economics, Dental"])	1
	#15	([mh "economics, hospital"])	661
	#16	([mh ^"Economics, Medical"])	25
	#17	([mh ^"Economics, Nursing"])	12
	#18	([mh ^"Economics, Pharmaceutical"])	69
	#19	((economic* OR cost OR costs OR costly OR costing OR price OR prices OR pricing OR) (pharmacoeconomic*):ti,ab)	560
	#20	((expenditure* NOT energy):ti,ab)	1317
	#21	value for money.ti,ab.	15
	#22	(budget*:ti,ab)	687
	#23	#12-#22	11690
	#24	(((energy OR oxygen) NEXT cost):ti,ab)	374
	#25	(metabolic NEXT cost):ti,ab	96
	#26	(((energy OR oxygen) NEXT expenditure):ti,ab)	3063
	#27	or #24-#26	3420
	#28	(#23 NOT #27)	11668
	#29	(letter:pt)	8030

	#30	(editorial:pt)	709
	#31	("historical article":pt)	93
	#32	OR #29-#31	8828
	#33	(#28 NOT #32)	11597
	#34	(bmj.jn.)	3
	#35	("cochrane database of systematic reviews.jn.")	69
	#36	("health technology assessment winchester england.jn.")	2
	#37	OR #34-#35	69
	#38	(#33 NOT #37)	11588
		#11(clincal) and #38(economic)	6
		Filtered additionally to >=year 2000	4

12 Postscript

Background

The results of the 10-year follow-up of the RCT conducted by Moosmayer et al. (Comparison of Surgical Treatment by Tendon Repair and Physiotherapy in the Treatment of Small and Medium-sized Tears of the Rotator Cuff; ClinicalTrials.gov: NCT00852657) have been recently published.[1] Although the results were published too late for being incorporated in the clinical systematic review and the economic assessment, we decided to briefly illustrate and discuss them in this post-scriptum.

As already mentioned in the main report, Moosmayer et al. recruited 103 patients with a rotator cuff tear not exceeding 3 cm, and randomly assigned them to primary tendon repair or physiotherapy with optional secondary repair (tendon repair n=52; physiotherapy n=52; secondary surgery 14 cross-overs after 10 years).[1] Ninety-one of 103 patients attended the last follow-up after 10 years.

Results

Treatment effects

The authors reported that *"the results were better for primary tendon repair, by 9.6 points on the Constant score (p = 0.002), 15.7 points on the American Shoulder and Elbow Surgeons score (p < 0.001), 1.8 cm on a 10-cm visual analog scale for pain (p < 0.001), 19.6° for pain-free abduction (p = 0.007), and 14.3° for pain-free flexion (p = 0.01). Fourteen patients had crossed over from physiotherapy to secondary surgery and had an outcome on the Constant score that was 10.0 points inferior compared with that of the primary tendon repair group (p = 0.03)."* Based on these findings, Moosmayer et al. concluded that the long-term *"differences in outcome between primary tendon repair and physiotherapy for small and medium-sized rotator cuff tears had increased, with better results for primary tendon repair"*.[1]

For comparison, Moosmayer et al. reported the following outcomes differences at six months, one year, two years, five years, and ten years follow-up: [1]

- Shoulder function measured with the CMS (points):
  - at six months: 2.8; 95%-CI -4.5; 10.1
  - at 1 year: 8.5; 95%-CI 1.9; 15.0
  - at 2 years: 2.6; 95%-CI -3.1; 8.3
  - at 5 years: 6.5; 95%-CI -0.7; 13.6
  - at 10 years: 9.6; 95%-CI 3.6; 15.7

- Shoulder function measured with the ASES score (points):
  - at six months: 10.6; 95%-CI 3.8; 17.5
  - at 1 year: 10.8; 95%-CI 4.6; 17.0
  - at 2 years: 5.5; 95%-CI -0.3; 11.4

  - at 5 years: 8.3; 95%-CI 1.2; 15.3
  - at 10 years: 15.7; 95%-CI 9.3; 22.1

- Shoulder pain with the VAS (cm):
  - at six month: 2.8; 95%-CI -4.5; 10.1
  - at 1 year: 8.5; 95%-CI 1.9; 15.0
  - at 2 years: 2.6; 95%-CI -3.1; 8.3
  - at 5 years: 6.5; 95%-CI -0.7; 13.6
  - at 10 years: 9.6; 95%-CI 3.6; 15.7

- Pain-free abduction (degree):
  - at six month: 2.2; 95%-CI -15.8; 20.3
  - at 1 year: 16.8; 95%-CI 1.2; 32.4
  - at 2 years: -0.5; 95%-CI -13.3; 12.2
  - at 5 years: 14.7; 95%-CI 0.1; 29.4
  - at 10 years: 19.6; 95%-CI 5.6; 33.6

- Pain-free flection (degree):
  - at six month: 2.1; 95%-CI -13.9; 18.1
  - at 1 year: 10.3; 95%-CI -3.1; 23.6
  - at 2 years: -1.0; 95%-CI -10.8; 8.7
  - at 5 years: 8.3; 95%-CI -4.4; 21.0
  - at 10 years: 14.3; 95%-CI 3.3; 25.3

A comparison of treatment efficacy between the study groups over 10 years showed better results for primary tendon repair at all follow-ups. Both groups improved during the first two years. Thereafter, shoulder function remained stable in the surgical group but declined in the physiotherapy group. Furthermore, the authors reported that 41% of tears that were still unrepaired after 10 years showed a tear enlargement of at least 10 mm. Risk factors leading to tear progression, however, could not be idenfied in this study. The difference at 10 years was statistically significant for the majority of reported outcome scores, but their clinical importance is questionable (considering a published estimate for the minimal clinically important difference for a shoulder function of 10.4 points [measured with the CMS] and for pain of 1.4 cm [measured with the VAS]).[2,3]

Retears rate after primary repair

Among the patients who were treated by primary repair, Moosmayer et al. found increasing full-thickness retear rates, with 21% after 1 year, 28% after 5 years, and 35% after 10 years.[1] If compared to patients undergoing surgery but with an intact repair, patients with retears had a significantly lower CMS (76.9 vs. 82.9 points after 10 years, p=0.04).

Subgroup tendon repair

Fourteen patients (27%) in the physiotherapy group reported an insufficient treatment result from physiotherapy and crossed over to secondary surgery (12 patients within the first two years and two patients between five and ten years). Using the primary repair group as the reference, the authors found significantly inferior results for the CMS in the secondary surgery group by 10 points (95%-CI 0.9; 19.2) after ten years.

Conclusion

Overall, these findings don't interfere with the results of the current report suggesting that surgery may be more effective than conservative treatment to improve shoulder function and reduce pain.

Whether the long-term benefits are relevant from a patient and economic perspective remains unclear. Mossmayer et al. reported that, despite the above-mentioned differences in favour of surgery, the SF-36 scores for quality of life after 10 years follow-up showed only small, non-significant between-group differences. [1] This suggests that the lower CMS, ASES score, VAS for shoulder pain, pain-free abduction and flection in patients undergoing physiotherapy had no effect on the quality of life.

It could be argued that in the long-term patients undergoing physiotherapy may require additional treatments (i.e. additional physiotherapy sessions) or may be less productives (i.e. workdays lost) if compared to patients undergoing surgery. Unfortunately, ressource use or productivity losses were not reported in the 10-year follow-up.

References

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