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Sektion Health Technology Assessment

Health Technology Assessment (HTA)

HTA Scoping Report

Title	Scoping Report for the Evaluation of the Removal of Osteosynthesis Materials in Switzerland
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Technology	Removal of osteosynthetic material
Date	29.01.2019
Type of Technology	Medical procedures
Keywords	Extremity fractures, osteosynthetic material, internal fixations, removal

Executive Summary:

Medical Background

Osteosynthesis is the internal fixation of fractures by mechanical devices. After bone and soft tissue healing there is either the option to remove the osteosynthetic material or to leave it in place. In case the internal fixation causes symptoms such as pain or reduced physical functioning removal of the device is indicated. In contrast, elective removal of the osteosynthetic material in asymptomatic patients is a controversial surgical intervention.

Methods

A systematic literature search was performed in Pubmed, Embase, EconLit, Cinahl and CENTRAL (10/2018).

Central research question

Is removal of osteosynthesis material in patients without medical indication (elective removal) effective in terms of complication rates, clinical/functional outcomes, health-related quality of life and cost effectiveness outcomes compared to retaining of the osteosynthesis material?

Results

The systematic literature search identified ten eligible studies (1 RCT, 4 cohort studies, 5 before-after studies). No eligible studies containing economic, legal, social, ethical or organizational aspects associated with the technology were identified.

All studies compared elective removal versus non-removal of osteosynthetic material. The implants regarded plates, screws, nails and/or staples. Implants were removed between 6 weeks and 27 months after surgery. The studies included a total of 410 patients. Primary and secondary efficacy and safety outcomes included functional mobility and pain scores, surgery related complications, quality of life, osteoarthritis and return to work. Follow-up ranged from 9 weeks to 31 months.

Feasibility HTA

Contractor: The contractor proposes to adapt the literature search strategy by removing the WHO

strata and language limitations and excluding before-after studies. In order to refine the research question, the contractor proposes to include an additional research question that addresses the prognostic and predictive factors affecting the effectiveness of elective removal of the osteosynthetic material. Acknowledging these proposed changes, the contractor considers it possibly feasible to conduct a full HTA report on this topic.

FOPH: The decision to conduct an HTA is predominantly based on quantity and quality of available evidence and cost saving potential. The overall body of evidence, as presented by the contractor, is considered small. The quality of the presented evidence appears moderate to low and the individual studies show large heterogeneity. Nonetheless, the presented evidence does not exclude that a more sensitive (e.g., on ankle fractures only) search strategy may detect sufficient evidence to conduct a meta-analysis and subsequent HTA. However, the relatively small potential budget impact per indication does not seem to justify conducting a full HTA.

Zusammenfassung:

Hintergrund

Osteosynthese bezeichnet die interne Fixierung von Knochenbrüchen (-segmenten) mit stabilisierendem Material. Sobald die Fraktur und das umliegende Gewebe abgeheilt sind, kann das Osteosynthesematerial entweder operativ entfernt oder am Knochen belassen werden. Falls die Fixierung Symptome wie Schmerzen oder physische Einschränkungen verursacht, ist eine Entfernung des Materials indiziert. Im Gegensatz dazu wird die Notwendigkeit einer elektiven Entfernung des Materials bei asymptomatischen Patienten kontrovers diskutiert.

Methoden

Eine systematische Literaturrecherche in Pubmed, Embase, EconLit, Cinahl and CENTRAL (10/2018) wurde durchgeführt.

Zentrale Fragestellung

Ist eine Entfernung des Osteosynthesematerials bei Patienten ohne medizinische Indikation (elektive Entfernung) im Vergleich zum Belassen des Osteosynthesematerials effektiv bezogen auf Komplikationen, klinische/funktionelle Endpunkte, gesundheitsbezogene Lebensqualität und Kosteneffektivität?

Ergebnisse

Die systematische Literaturrecherche erbrachte 10 geeignete Studien (1 RCT, 4 Kohorten Studien, 5 Vorher-Nachher Studien) Keine der Studien untersuchte ökonomische, rechtliche, soziale, ethische oder organisatorische Aspekte, die mit der Technologie verbunden sind.

Alle Studien verglichen die elektive Entfernung mit dem Belassen des Osteosynthesematerials. Platten, Schrauben, Nägel und Klammern wurden untersucht. Die Fixierung wurde zwischen 6 Wochen und 27 Monaten nach der Implantierung entfernt. Die Studien schlossen insgesamt 410

Patienten ein. Primäre und sekundäre Endpunkte (Wirksamkeit und Sicherheit) waren funktionale Mobilität, Schmerzskalen, eingriffsbezogene Komplikationen, Lebensqualität, Osteoarthritis und Rückkehr zur Arbeit. Die Nachbeobachtung erfolgte zwischen 9 Wochen und 31 Monaten.

Machbarkeit eines HTA

Auftragnehmer: Der Auftragnehmer schlägt vor die Literaturrecherche anzupassen und die WHO Strata, Sprachlimitationen und Vorher-Nachher Studien zu entfernen. Um die zentrale Fragestellung zu erweitern, schlägt der Auftragnehmer vor eine Fragestellung zu prognostischen und prädiktiven Faktoren, die die Wirksamkeit von der elektiven Entfernung von Osteosynthesematerial beeinflussen, zu ergänzen. Bei Anwendung dieser Vorschläge erachtet der Auftragnehmer eine Durchführung eines Voll-HTAs für wahrscheinlich machbar.

BAG: Die Entscheidung für oder wider einen Voll-HTA durchzuführen ist abhängig von der Quantität und Qualität der verfügbaren Evidenz und dem Kosteneinsparpotential. Der body of evidence, der vom Auftragnehmer dargestellt wird, wird als klein eingeschätzt. Die Qualität der präsentierten Evidenz wird als moderat bis niedrig betrachtet und die individuellen Studien zeigen hohe Heterogenität. Nichtdestotrotz, die vorhandene Evidenz schließt nicht aus, dass eine sensitivere Recherche (z.B. Sprunggelenksfrakturen) möglicherweise ausreichend Evidenz für eine Metaanalyse und einen nachfolgenden HTA liefern könnte. Jedoch scheint das relativ kleine Budget-Impact Potential pro Indikation die Durchführung eines Voll-HTAs nicht zu rechtfertigen.

Table of contents:

Objective of the HTA Scoping Report

In the scoping phase, a health technology is examined and a central research question is presented with additional operational key questions, in order to determine the full scope of the HTA report. The target population, the appropriate comparator and the relevant health outcomes are defined. Based on the quality and quantity of the available evidence to answer the central research questions, as presented in the scoping report, it is decided whether a full HTA report is commissioned.

1. Medical Background

Osteosynthesis is the internal fixation of fractures or osteotomy by mechanical devices. After bone and soft tissue healing there is either the option to remove the osteosynthetic material or to leave it in place. In case the internal fixation causes symptoms such as pain, reduced physical functioning, spatial limitation, negative body sensation, pseudo arthrosis, wound infection, or device failure removal of the device is indicated. In contrast, elective removal of the osteosynthetic material in asymptomatic patients is a controversial surgical intervention.[1] Reasons for elective removals often remain unstated or poorly defined (e.g. "patient preference") or are due to hospital policy ("routine").

In Switzerland 11'124 inpatient osteosynthetic material removals and 8'926 outpatient osteosynthetic material removals were recorded in 2016 (based on MedStat and TARMED data). The three most frequent removals regard the lower leg (5’414), followed by foot/ankle joints (4’156) and lower arm (3'164).

The total costs for the inpatient and outpatient removals are calculated at approximately 85 million per year (69 for outpatient removals and 16 million for inpatient removals, based on SwissDRG and reported outpatient data). In Switzerland it can be estimated that possibly more than 25% of these interventions are elective.[2] [3] This corresponds with a potential cost saving of approximately CHF 20 million, if coverage of elective device removal were to be restricted.

Despite the fact that removal of osteosynthetic material is a common surgical procedure, at this time there is no uniform recommendation regarding these procedures.

2. Technology

2.1 Technology Description

Removal of osteosynthetic material is the removal of hardware (plates, nails, pins, rods, wires or screws) after complete bone and soft tissue healing. Most (>90%) of the internal fixations are removed within 24 months after the initial surgery. The time-point of removal depends mainly on the time-point of bone healing. Bone healing depends on many factors including localization, type and severity of the fracture, type of fixation device/s used and patient characteristics.

2.2 Alternative Technologies

No removal.

3. PICO

The **central research question** of the report: Is removal of osteosynthesis material in patients without medical indication (elective removal) effective in terms of complication rates, clinical/functional outcomes, health-related quality of life and cost effectiveness outcomes compared to retaining of the osteosynthesis material?

A protocol was developed in reconciliation with the Swiss FOPH. It was written following the structure of PROSPERO (International prospective register of systematic reviews) and finalized on the 30th of April 2018.

3.1 Patients

Asymptomatic patients with an internal fixation in the extremities. Spinal implants are not considered within the scope of this report.

3.2 Intervention

Elective (without medical indication) removal of osteosynthetic material.

3.3 Comparator

Non-removal of osteosynthetic material.

3.4 Outcomes

Health and functional outcomes such as morbidity, mobility, mortality, health-related quality of life and adverse events/complications.

3.5 Study Types

Comparative study designs were considered.

Systematic reviews were hand searched for potential additional studies of interest.

To address the economic aspects of the central research question economic evaluations and budget impact analyses were considered.

To address legal, social, ethical and organisational aspects of the central research question all types of studies were considered.

3.6 PICO Box

P:	Asymptomatic patients with an internal fixation in the extremities
I:	Elective (without medical indication) removal of osteosynthetic material
C:	Non-removal of osteosynthetic material
O:	Health and functional outcomes such as morbidity, mobility, mortality, health-related quality of life, adverse events/complications

4. Research Methodology

4.1 Databases

A systematic literature search in Pubmed, Embase, EconLit, CINAHL and CENTRAL was conducted in October 2018. The search strategy for Pubmed is displayed in *Box 1*. The search strategies for the other databases are presented in **Appendix I**. The search strategy was developed by an information specialist and checked by another reviewer by consulting the Peer Review of Electronic Search Strategies (PRESS) criteria.[4]

Box 1: Search Strategy for Pubmed

osteosynthesis[tiab] OR osteosyntheses[tiab] OR osteosynthetic[tiab] OR orthopedic[tiab] OR orthopaedic[tiab] OR osteotomy[tiab] OR osteotomies[tiab] OR "Fractures, Bone"[Mesh] OR fracture[tiab] OR fractures[tiab]

AND ("Fracture Fixation, Intramedullary"[Mesh] OR "Fracture Fixation, Internal"[Mesh] OR "Fracture Fixation"[Mesh] OR "Surgical Fixation Devices"[Mesh] OR "Orthopedic Fixation Devices"[Mesh] OR "Internal Fixators"[Mesh] OR "Bone Nails"[Mesh] OR "Bone Plates"[Mesh] OR "Bone Screws"[Mesh] OR "Bone Wires"[Mesh] OR material[tiab] OR materials[tiab] OR implant[tiab] OR implants[tiab] OR implantation[tiab] OR implantations[tiab] OR internal fixator*[tiab] OR intramedullary nail*[tiab] OR intramedullary fixation[tiab] OR internal fixation[tiab] OR hardware[tiab] OR plate[tiab] OR plates[tiab] OR nail[tiab] OR nails[tiab] OR screw[tiab] OR screws[tiab] OR wire[tiab] OR wires[tiab] OR pin[tiab] OR pins[tiab])

AND ("Device Removal"[Mesh] OR remov*[tiab])

NOT ("Comment" [Publication Type] OR "Letter" [Publication Type] OR "Editorial" [Publication Type])

NOT (animals[mh] NOT humans[mh])

All titles/abstracts identified in the electronic databases were screened by one reviewer and a second reviewer screened all excluded titles/abstracts (liberal acceleration). The literature search was limited to English- and German-language articles, without publication date limitations. Only studies performed in the WHO-Mortality-Stratum A were included to ensure applicability of results to the Swiss health care system. Comments, editorials, letters and research on animals were excluded. Systematic reviews and meta-analyses were hand searched for relevant articles. Following the title/abstract search and selection, studies were full-text analysed by two independent reviewers.

4.2 Other Sources

There were no other sources considered for the preparation of this scoping review.

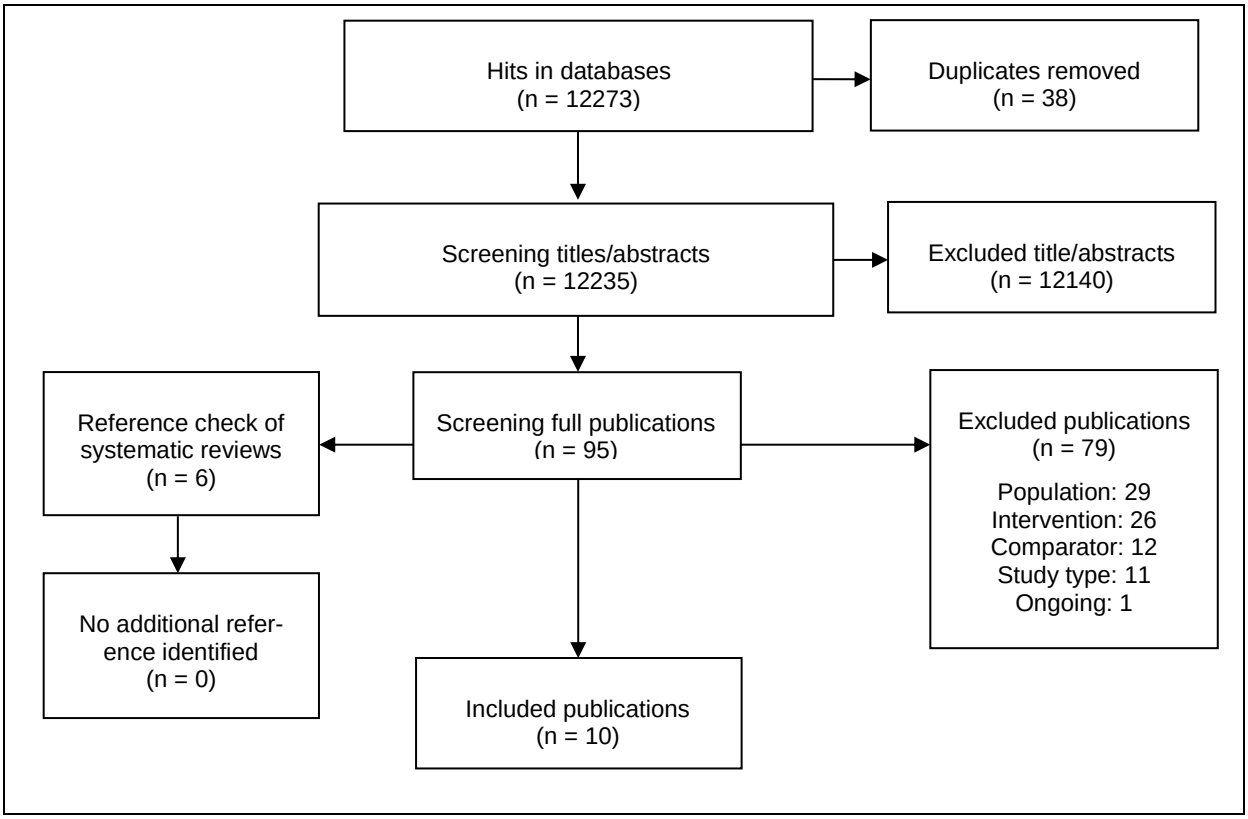
For a full HTA report, the peer-reviewed literature search will be expanded by including more publication languages, trial registries and conference abstracts. Experts and scientific societies may be consulted for additional relevant publications and data (e.g. registry data).

Data for economic analysis are to be extracted from Swiss data sources (e.g. MedStat, TARMED, SwissDRG).

4.3 PRISMA Flow Diagram

Figure 1 shows the study selection process. The literature search identified 10 eligible studies (one RCT, four cohort studies, five before-after studies).[5-15] Eight studies assessed the effectiveness and safety of removal/non-removal of the osteosynthetic material at the lower extremities (four ankle, three fibular/tibiofibular and one femoral fracture) and one study investigated the effectiveness and safety of removal/non-removal in the proximal humerus.[5-14] One study analysed the effectiveness of osteosynthetic material removal in children in all body parts.[15] The studies were conducted in Germany,[9-11] the USA,[12 13 15] Switzerland,[5] Singapore,[6] New Zealand[7] and the UK.[14]

Figure 1: Study selection flow-diagram for the literature search on all indications



5. Clinical Effectiveness and Safety

The studies included adults (nine studies) and children (one study). All studies compared elective removal versus non-removal of osteosynthetic material. The implants regarded plates, screws, nails and staples. Sometimes a combination of implants was used. Implants were removed between 6 weeks and 27 months after surgery. Ankle screws were typically removed before weight bearing (6-12 weeks) whereas plates and nails were removed after longer periods of bone healing. The studies included a total of 410 patients. Primary efficacy and safety outcomes included functional mobility scores (e.g., Olerud-Molander ankle or American Orthopaedic Foot and Ankle Society ankle-hind foot scores) and pain scores (e.g., VAS). Secondary outcomes included surgery related complications, quality of life, osteoarthritis and return to work. Follow-up ranged from 9 weeks to 31 months.

5.1 Clinical Effectiveness

A first inspection of the selected studies showed that four studies showed a functional benefit (typically expressed in mobility scores) in elective patients after removal of the osteosynthetic material, one study showed the opposite and two studies did not show a difference between the removal and non-removal study groups. A clinical benefit (most often expressed as decrease in or no pain) was shown in one study. Two studies showed an increase of clinical complaints after removal of the osteosynthetic material in patients who had been asymptomatic before the procedure. One study showed no difference between the study groups.

5.2 Safety

The selected studies showed no major complications after removal or non-removal of the osteosynthetic material. Complications related to removal were generally breakage or malpositioning of the device and superficial wound infection. The complications were typically treated and temporary, respectively.

6. Costs, Budget Impact, Cost-Effectiveness

No economic evaluations and budget impact analyses were identified in the screened literature.

7. Legal, Social and Ethical Issues

No studies on legal, social and ethical aspects were identified in the screened literature.

8. Organisational Changes

No studies on organisational aspects were identified in the screened literature.

9. Feasibility HTA

9.1 Feasibility according to the contractor

Short study follow-up times and small patient groups hinder drawing conclusions regarding effectiveness and safety of elective removal of osteosynthetic material in extremities, according to the contractor. Moreover, the contractor questions the quality of the evidence retrieved from before-and-after studies. Excluding this study design when conducting a full HTA is proposed.

In order to increase the quantity of evidence for a full HTA analysis the contractor proposes to expand the search strategy by removing the WHO strata and language limitations. The contractor also proposes to include an additional research question that addresses the prognostic and predictive factors affecting the effectiveness of removal of the osteosynthetic material. It is proposed to apply subgroup analyses to identify such factors (e.g. age, gender, comorbidity, implant features or location of the fracture). Within study subgroup analyses are to be considered based on interaction/homogeneity test outcomes and at a minimum of 10 events observed per subgroup. A subgroup analysis using meta-regression (between study analyses) is to be performed if at least 5 studies are available per specific subgroup. Along with diagnostic information, prognosis factors could guide clinical decision making, concludes the contractor.

The contractor states that a health economic evaluation is feasible for those indications where sufficient reliable evidence is identified. Since no evidence of economic evaluations in the field of osteosynthetic material removal was identified in the literature, only a specific analysis for the Swiss context

is proposed. Resource use and prices for the economic domain will be estimated using Swiss utilization statistics (e.g. MedStat-Data, TARMED-Statistics) and price lists (e.g. SwissDRGs). The economic analysis will be performed from the perspective of the Swiss health care system. The economic data will distinguish inpatient and outpatient care data and direct medical and non-medical costs.

A full HTA report will require a budget impact and cost utility analyses. Considering the diversity in fracture locations and osteosynthetic materials applied, it seems not feasible to assess the economic aspects for all possible indications. Most efficacy evidence exists for syndesmotic screws used in ankle fractures. This indication is therefore considered as indication with a sufficient body of evidence on effectiveness data (quantity and quality) for an economic evaluation. Because high quality effectiveness data seems to be sparse in general, valid estimation of quality adjusted life years might not be possible. If the lack of evidence hinders conducting a cost-utility analysis, a cost-consequence and budget impact analysis is proposed.

A potential limitation/restriction of coverage of elective osteosynthetic material removal has likely legal, social and ethical implications, according to the contractor. Restriction/limitation of the procedure for specific patient groups may promote discrimination between patient groups in favour of those who can afford to pay the intervention “out-of-the-pocket”. A full HTA will focus on these aspects.

Overall, considering the so far identified body of evidence and expanding the research question as suggested above, the contractor considers it possibly feasible to conduct a full HTA report on this topic.

9.2 Feasibility according to the FOPH

The decision to conduct an HTA is predominantly based on quantity and quality of available evidence and cost saving potential. The overall body of evidence, as presented by the contractor, is considered small. The quality of the presented evidence appears moderate to low and the individual studies show large heterogeneity. Nonetheless, the presented evidence does not exclude that a more sensitive search strategy may detect sufficient evidence to conduct a meta-analysis. However, the relatively small potential budget impact per indication does not seem to justify conducting a full HTA.

10. References

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11. Appendices

Appendix I: Search strategies

Embase search strategy

(('osteosynthesis'/exp OR 'orthopedic surgery'/exp OR 'osteotomy'/exp OR 'fracture'/exp OR (osteosynthesis OR osteosyntheses OR osteosynthetic OR orthopedic OR orthopaedic OR osteotomy OR osteotomies OR fracture OR fractures):ti,ab,kw AND ('fracture fixation'/exp OR 'intramedullary nailing'/exp OR 'orthopedic fixation device'/exp OR 'orthopedic implant'/exp OR 'internal fixator'/exp OR 'plate fixation'/exp OR 'splinting'/exp OR 'volar plate fixation'/exp OR 'wire fixation'/exp OR 'bone nail'/exp OR 'bone plate'/exp OR 'bone screw'/exp OR 'bone wire'/exp OR 'bone pin'/exp OR (material OR materials OR implant OR implants OR implantation OR implantations OR 'internal fixator*' OR 'intramedullary nail*' OR 'intramedullary fixation' OR 'internal fixation' OR hardware OR plate OR plates OR nail OR nails OR screw OR screws OR wire OR wires OR pin OR pins):ti,ab,kw) AND ('implant removal'/exp OR remov*:ti,ab,kw) AND ([embase]/lim)) NOT (('comment' OR 'letter' OR 'editorial'):it)) AND (embase NOT (embase AND medline))

EconLit search strategy

TI (osteosynthesis OR osteosyntheses OR osteosynthetic OR orthopedic OR orthopaedic OR osteotomy OR osteotomies OR fracture OR fractures) OR AB (osteosynthesis OR osteosyntheses OR osteosynthetic OR orthopedic OR orthopaedic OR osteotomy OR osteotomies OR fracture OR fractures) AND (TI (material OR materials OR implant OR implants OR implantation OR implantations OR “internal fixator*” OR “intramedullary nail*” OR “intramedullary fixation” OR “internal fixation” OR hardware OR plate OR plates OR nail OR nails OR screw OR screws OR wire OR wires OR pin OR pins) OR AB (material OR materials OR implant OR implants OR implantation OR implantations OR “internal fixator*” OR “intramedullary nail*” OR “intramedullary fixation” OR “internal fixation” OR hardware OR plate OR plates OR nail OR nails OR screw OR screws OR wire OR wires OR pin OR pins)) AND (TI remov* OR AB remov*)

CINAHL search strategy

MH "Osteotomy" OR MH "Orthopedic Surgery" OR MH "Fractures" OR TI (osteosynthesis OR osteosyntheses OR osteosynthetic OR orthopedic OR orthopaedic OR osteotomy OR osteotomies OR fracture OR fractures) OR AB (osteosynthesis OR osteosyntheses OR osteosynthetic OR orthopedic OR orthopaedic OR osteotomy OR osteotomies OR fracture OR fractures) AND (MH "Fracture Fixation" OR MH "Orthopedic Fixation Devices" OR MH "Internal Fixators" OR MH "Bone Screws" OR TI (material OR materials OR implant OR implants OR implantation OR implantations OR “internal fixator*” OR “intramedullary nail*” OR “intramedullary fixation” OR “internal fixation” OR hardware OR plate OR plates OR nail OR nails OR screw OR screws OR wire OR wires OR pin OR pins) OR AB (material OR materials OR implant OR implants OR implantation OR implantations OR “internal fixator*” OR “intramedullary nail*” OR “intramedullary fixation” OR “internal fixation” OR hardware OR plate OR plates OR nail OR nails OR screw OR screws OR wire OR wires OR pin OR pins)) AND (MH "Device Removal" OR TI remov* OR AB remov*) NOT (PT ("Comment" OR "Letter" OR "Editorial"))

CENTRAL search strategy

#1 MeSH descriptor: [Fractures, Bone] explode all trees
#2 (osteosynthesis OR osteosyntheses OR osteosynthetic OR orthopedic OR orthopaedic OR osteotomy OR osteotomies OR fracture OR fractures):ti,ab,kw
#3 MeSH descriptor: [Fracture Fixation, Intramedullary] explode all trees
#4 MeSH descriptor: [Fracture Fixation, Internal] explode all trees
#5 MeSH descriptor: [Fracture Fixation] explode all trees
#6 MeSH descriptor: [Surgical Fixation Devices] explode all trees
#7 MeSH descriptor: [Orthopedic Fixation Devices] explode all trees
#8 MeSH descriptor: [Internal Fixators] explode all trees
#9 MeSH descriptor: [Bone Nails] explode all trees
#10 MeSH descriptor: [Bone Plates] explode all trees
#11 MeSH descriptor: [Bone Screws] explode all trees
#12 MeSH descriptor: [Bone Wires] explode all trees
#13 (material OR materials OR implant OR implants OR implantation OR implantations OR internal fixator* OR intramedullary nail* OR intramedullary fixation OR internal fixation OR hardware OR plate OR plates OR nail OR nails OR screw OR screws OR wire OR wires OR pin OR pins):ti,ab,kw
#14 MeSH descriptor: [Device Removal] explode all trees
#15 (remov*):ti,ab,kw
#16 #1 OR #2
#17 #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13
#18 #14 OR #15
#19 #16 AND #17 AND #18

Appendix II: data extraction tables

Study	Patients (IG/CG)	Intervention	Comparison	Outcomes (IG/CG or before/after)	Study type	Country/setting
Acklin 2016	**Inclusion** - Proximal humerus fracture - Removal of a locking plate after minimal invasive plate osteosynthesis - Patients ≥18 years **Exclusion** - Hemiplegia/relevant neurologic disorders - nonunion - primary or secondary intra-articular screw perforation, implant breakage, infection or avascular necrosis of the humeral head - polytrauma with an Injury Severity Score greater than 16, posttraumatic brachial plexus injury or peripheral nerve palsy. **Characteristics** Male n(%): 8 (40) Age [y] mean ± SD: 56 ± 12 Dominant arm n: 5 Mechanism of injury n(%): Ski 8 (40) Fall at home 4 (20) Pedestrian 4 (20) Miscellaneous 4 (20) Operation room time [min] mean ± SD: Fracture fixation 86 ± 26 Implant removal 35 ± 10	N=20 Removal after 13 ± 5 months (mean ± SD) postoperatively	-	Constant-Murley score of the at 9 ± 4 weeks follow up (mean, mean difference, CI): 70.8/75.6, 4.8, 95% CI 1.8–7.8	Before-After Study	Switzerland, NR

Bell 2006	**Inclusion** - Weber type C ankle fracture with syndesmotic disruption treated with syndesmotic screws **Exclusion** - Fractures resulting from direct crushing injuries - open fractures - no syndesmotic diastasis on intraoperative testing **Characteristics** <u>Age [y] mean (range):</u> 36 (18-67) / 32 (18-45) <u>Fracture pattern n(%):</u> Unimalleolar 5 (22) / 2 (29) Bimalleolar 14 (61) / 4 (57) Trimalleolar 3 (13) / 1 (14) Maisonneuve 1 (4) / 0 <u>Mechanism of injury n(%):</u> Misstep 10 (43) / 3 (43) Sports 7 (30) / 2 (29) Fall from height 4 (17) / 0 Traffic accident 1 (4) / 2 (29) Hit over leg 1 (4) / 0 <u>Complications n(%):</u> Superficial wound infection 1 (4)/ 1 (14) Screw malposition 1 (4) / 0 Screw breakage 0 / 2 (29)	N=23 Removal of syndesmotic screws before weight bearing	N=7 Retaining of syndesmotic screws before weight bearing	Baird and Jackson ankle score after 15/16 months follow up (mean, p): 88 / 86, p=0.79 Pain free walking (n(%), p): 11 (48) / 2 (29), p > 0.05 Return to work (n(%), p): 13 (57) / 4 (57), p > 0.05 ***Ankle range of motion (mean motion deficit in degrees compared to normal ankle, p)*** Flexion: 11.5 / 12.1, p > 0.05 Inversion: 10.4 / 10.0, p > 0.05 Osteoarthritis: 0/0	Cohort Study	Singapore, General Hospital 01.2001-12.2002

Boyle 2014	**Inclusion** - displaced distal fibular fracture with associated tibiofibular diastasis (Orthopaedic Trauma Association (OTA) type 44-B1, 44-B2, 44-C1 or 44-C217), occurred < 48 hours prior to presentation to hospital - 16 – 65 years **Exclusion** - open fracture - pre-existing abnormality of the ankle, neurovascular injury, posterior malleolar fracture involving > 10% of the tibial articular surface on lateral radiographs - tibial plafond fracture (although those with a medial malleolar fracture and/or a posterior malleolar fracture were included), diaphyseal tibial fracture, pathological fracture, polytrauma - cognitive impairment, pregnancy **Characteristics** <u>Male n(%):</u> 19 (73) / 16 (64) <u>Age [y] mean ± SD:</u> 30.8 ± 12.8 / 36.2 ± 14.1 <u>BMI [kg/m²] mean ± SD:</u> 30.6 ± 4.6 / 31.9 ± 5.5 <u>Smoker n(%):</u>	N=26 Removal of syndesmotic screws before weight bearing, Removal after 3 months postoperatively	N=25 Retaining of syndesmotic screws	Olerud–Molander ankle score after 12 months postoperatively (mean, mean difference, CI): 86.7 / 82.4, 4.3, 95% CI -5.2–13.9 American Orthopaedic Foot and Ankle Society ankle-hind foot score after 12 months postoperatively (mean, mean difference, CI): 90.1 / 88.6, 1.5, 95% CI -6.0–9.1 American Academy of Orthopaedic Surgeons foot and ankle score after 12 months postoperatively (mean, mean difference, CI): 91.8 / 87.0, 4.8, 95% CI -3.5–13.2 Pain measured with VAS after 12 months postoperatively (mean, mean difference, CI): 0.66 / 1.03, -0.38, 95% CI -1.01–0.26 Ankle dorsiflexion after 12	RCT	New Zealand, University of Otago 07.2011-11.2012

	9 (35) / 8 (32) Diabetes n(%): 0 / 1 (4) Ethnicity n(%): European 14 (54) / 11 (44) Maori 4 (15) / 2 (8) Pacific 6 (23) / 7 (28) Asian 2 (8) / 5 (20) Mechanism of injury n(%): Collision sport 9 (35) / 6 (24) Non-collision sport 2 (8) / 4 (16) Simple fall 12 (46) / 13 (52) Other 3 (11) / 2 (8) Time from injury to surgery [d] mean ± SD: 4.8 ± 4.7 / 4.0 ± 3.2 Surgical duration [min] mean ± SD): 86.3 ± 31.4 / 77.7 ± 23.5 Surgeon seniority n(%): Surgeon 1 (4) / 0 Fellow 1 (4) / 0 Senior registrar 14 (54) / 13 (52) Junior registrar 10 (38) / 12 (48) Syndesmosis screw location from tibial plafond[mm] mean ± SD: 16.4 ± 8.4 / 19.3 ± 8.3			months postoperatively [degree] (mean, mean difference, CI): 13.0 / 10.2, 2.7, 95% CI -1.4–6.9 Ankle plantar flexion after 12 months postoperatively [degree] (mean, mean difference, CI): 31.2 / 33.6, -2.3, 95% CI -9.3–4.6 Calf girth loss after 12 months postoperatively [cm] (mean, mean difference, CI): 0.04 / 0.07, -0.21, 95% CI -0.69–0.26 Tibiofibular clear space after 12 months postoperatively [mm] (mean, mean difference, CI): 5.3 / 5.0, 0.34, 95% CI -0.28–0.95		

Chu 2009	**Inclusion** - Children between 2-18 years - removal of osteosynthesis material **Characteristics** <u>Male n(%):</u> 16 (64) <u>Age [y] mean(range):</u> 11.6 (3-18) <u>Flexible nail n(%):</u> Both bone forearm 5 (50) Elbow 3 (30) Wrist 1 (10) Tibia 1 (10) <u>Plates/Screws n(%):</u> Legg-Calve-Perthes 4 (57) Both bone forearm 1 (14) Development dysplasia of the hip 1 (14) Femur 1 (14) <u>Screws n(%):</u> Ankle 2 (50) Development dysplasia of the hip 1 (25) Tibia 1 (25) <u>Staples n(%):</u> Cavus 1 (50) Genu valgum 1 (50) <u>Screws/rod n(%):</u> Ankle 1 (100) <u>Staples/Steinmann pin n(%):</u> Cavus 1 (100)	N=25 Removal after 8.3 (2-31) months (mean, range) postop-eratively	-	Pain (n(%)): 7 (28) / 3 (12) ***Pediatric Outcomes Data Collection Instrument (follow-up NR)*** Upper extremity: p=0.033 Transfer/basic mobility: p=0.014 Sports and physical function-ing: p=0.017 Global functioning: p=0.012 Pain/Comfort: p > 0.05 Happiness: p > 0.05	Before-After Study	USA, NR 11.2005-05.2007

Garner 2015	**Inclusion** - Patients ≥18 years - Osteosynthesis of tibial plateau fractures with Synthes 3.5 or 4.5 Locking Compression Plates **Exclusion** - Deep infection - Concurrent ipsilateral lower extr. injuries - Isolated coronal shear fractures of the medial tibial plateau **Characteristics** Male n(%): 22 (53) / 13 (37) Age [y] mean (range): 49 (44.5-58.5) / 68 (59.5-75.3) BMI [kg/m²] mean(range): 25.0 (22.6-28.7) / 25.7 (21.4-33.1) Comorbidities n(%): Diabetes 1 (3) / 1 (3) Hypertension 5 (13) / 7 (19) Hyperlipidemia 3 (8) / 2 (6) Peripheral vascular disease 0 / 0 Smoking History 3 (8) / 1 (3) EtOH abuse 5 (13) / 3 (8) Time from index procedure until final follow-up [months] mean(range): 15.4 (13.6-26.5) / 40.6 (13.6-57.7) Schatzker n(%): 1–2 29 (74) / 22 (61) 5–6 10 (26) / 14 (39)	N=39 Removal of implants in median at 7.3 months	N=36 Retaining of implants	Knee Outcome Survey at 15.4 / 40.6 (mean) months follow-up (median, p): 85 / 78.8, p=0.12 Lower Extremity Functional Scale at 15.4 / 40.6 (mean) months follow-up (median, p): 80 / 66.3, p< 0.05 ***Short Form-36 Survey at 15.4 / 40.6 (mean) months follow-up (median, p)*** Mental Component Summary: 57.6 / 55.6, p=0.78 Physical Component: 50.9 / 44.9, p<0.05 VAS: 0.6 / 0.5, p=0.64	Cohort Study	Germany, Trauma Center 06.2009-06.2014

Gosling 2005	**Inclusion** - Osteosynthesis of tibial fractures with an intramedullary nail in patients who were symptoms-free before removal **Exclusion** - Additional surgery to removal of intramedullary nail	N=18 Removal of intramedullary nail after 21 months (mean)	-	Complaints recorded in 17% of patients after nail removal No change in symptoms in 83% of patients after nail removal	Before-After Study	Germany, NR 01.1987-12.1999
Gosling 2004	**Inclusion** - Osteosynthesis of femoral fractures with an intramedullary nail in patients who were symptoms-free before removal	N=51 Removal of intramedullary nail after 27 months (mean)	-	Complaints recorded in 20% of patients after nail removal No change in symptoms in 80% pf patients after nail removal	Before-After Study	Germany, level I trauma center 1.1990-3.1999

Hamid 2009	**Inclusion** - ankle fracture with syndesmotic disruption treated with syndesmotic screws **Exclusion** - Patients ≥ 18 years - syndesmosis screw placed for reasons other than disruption of the syndesmosis - chronic injury (>one month) of the syndesmosis, postoperative infection, postoperative hardware failure prior to bone healing, post-operative complications requiring additional surgery, placement of a bio absorbable syndesmosis screw **Characteristics** <u>Male n(%):</u> 8 (53) / 20 (54) <u>Age [y] mean(range):</u> 47 (21-72) <u>Weber-classification n(%):</u> Weber-B 3 (20) / 12 (32) Weber-C 12 (80) / 25 (68)	N=15 Removal of implants after 13.1 weeks (mean)	N=37 Retaining of implants	American Orthopaedic Foot and Ankle Society ankle-hind foot score after 30 months (mean)/ postoperatively (mean): 85.8 / 85.59, p=0.714 VAS after 30 months (mean)/ postoperatively (mean): 0.074 / 2.02, p=0.268	Cohort Study	USA, NR 2001-2005

Miller 2010	**Inclusion** - ankle fracture with syndesmotic disruption treated with syndesmotic screws and plates - injuries resulting from a twisting mechanism **Exclusion** - fractures resulting from direct crush injuries, open fractures, patients with stable Syndesmoses **Characteristics** <u>Male n(%):</u> 11 (44) <u>Age [y] mean(range):</u> 40 (17-78)	N=25 Removal of implants after 4.3 months (mean)	-	***Foot and Ankle Outcome at 2 weeks follow up (mean, p)*** Symptoms: 58 / 71, p=0.0003 Pain: 65 / 77, p=0.001 Activities of daily living: 74 / 86, p=0.002 Sports and recreation: 49 / 68, p=0.001 Quality of life: 40 / 53, p=0.0008 Olerud-Molander Ankle Score at 2 weeks follow up (mean, p): 42 / 65, p=0.003 ***Average range of motion at 2 weeks follow up [degree] (mean, p)*** Dorsiflexion: 10 / 20, p<0.05 Plantarflexion: 35 / 45, p<0.05	Before-After Study	USA, NR 07.2007-01.2008

Tucker 2013	**Inclusion** - syndesmotic screw fixations performed at a single hospital site by any consultant surgeon Exclusion - any ankle fixation not involving a syndesmosis screw and no available address or contact details on clinical records **Characteristics** <u>Male n(%):</u> 26 (60.5) / 9 (45) <u>Age [y] mean(range):</u> 41.84 (16-80) / 45.3 (19-78) <u>Time of follow-up [months] mean(range):</u> 31.45 (10-43) / 28.57 (26-43) <u>Time of follow-up [d] mean, (range):</u> 83.44 (47–178) / NA	N=43 Removal of implants after 83.44 days (mean)	N=20 Retaining of implants	Olerud-Molander Ankle Score at 31 months follow up (mean, p): 75.0 / 81.5, p=0.107 Excellent overall functional outcome grouping at 31 months follow up (%, mean adjusted difference, CI): 23.26 / 25, –9.3, 95% CI -18.5 – -0.2	Cohort Study	UK, level 1 trauma center practice 01.2008-12.2010

IG=intervention group, CG= control group, SD= standard deviation, NR= not reported, CI= confidence interval, VAS= visual analogue scale, RCT= randomized controlled trial, BMI= body mass index, EtOH= ethanol, NA= not available, UK= United Kingdom