Musculoskeletal Tumor Society

MANAGEMENT OF METASTATIC HUMERAL DISEASE

Clinical Practice Guideline

Adopted by:
The Musculoskeletal Tumor Society Executive Committee
April 12, 2023

This Clinical Practice Guideline has been endorsed by:

AAOS
American Academy of Orthopaedic Surgeons

Disclaimer

This clinical practice guideline (CPG) was developed by the clinical practice guideline development group composed of volunteer physicians based on a formal systematic review of the available scientific and clinical information and accepted approaches to treatment and/or diagnosis. This clinical practice guideline is not intended to be a fixed protocol, as some patients may require more or less treatment or different means of diagnosis. Clinical patients may not necessarily be the same as those found in a clinical trial. Patient care and treatment should always be based on a clinician's independent medical judgment, given the individual patient's specific clinical circumstances.

Disclosure Requirement

In accordance with Musculoskeletal Tumor Society (MSTS) and American Academy of Orthopedic Surgeons (AAOS) policy, all individuals whose names appear as authors or contributors to the clinical practice guideline filed a disclosure statement as part of the submission process. All panel members provided full disclosure of potential conflicts of interest prior to voting on the recommendations contained within this clinical practice guideline.

Funding Source

This clinical practice guideline was funded exclusively by the Musculoskeletal Tumor Society who received no funding from outside commercial sources to support the development of this document.

FDA Clearance

Some drugs or medical devices referenced or described in this clinical practice guideline may not have been cleared by the Food and Drug Administration (FDA) or may have been cleared for a specific use only. The FDA has stated that it is the responsibility of the physician to determine the FDA clearance status of each drug or device he or she wishes to use in clinical practice.

Published 2023 by the Musculoskeletal Tumor Society
1515 E. Woodfield Rd, Suite 345
Schaumburg, IL 60173 First Edition

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1. Plating/Internal Fixation, Intramedullary Fixation, and/or Photodynamic Polymer

When treating pathologic diaphyseal humerus fractures, clinicians can consider either the use of plating/internal fixation, intramedullary fixation, and/or photodynamic polymer, as there does not appear to be a significant difference in clinical outcomes or reoperation rate between these constructs based on limited available evidence.

- Combined Strength of Recommendation = **Limited**

2. En Bloc Resection, Curettage, Internal Fixation, Or Intramedullary Nailing

No studies met inclusion criteria comparing survivorship or other oncologic outcomes between en bloc resection, curettage, internal fixation, or intramedullary nailing. Based on the lack of evidence, no recommendations can be made for or against en bloc resection pertaining to metastatic disease of the humerus.

- Combined Strength of Recommendation = **N/A**

3. Patient Selection for Nonsurgical Techniques Versus Surgical Techniques

No studies met inclusion criteria to compare nonoperative vs operative treatment in the setting of metastatic disease of the humerus. Based on the lack of definitive evidence, no recommendations can be made for or against patient selection or indication for nonoperative vs. operative treatment pertaining to metastatic disease of the humerus.

- Combined Strength of Recommendation = **N/A**

4. Cementation Vs No Cementation

In patients undergoing surgical fixation of the humerus for metastatic bone disease, clinicians may consider cement augmentation. Two low quality studies meeting inclusion criteria suggested the addition of cement to surgical fixation of pathologic fractures of the humerus may provide short-term improvements in pain relief and functional mobility, however no difference in surgical complications were observed.

- Combined Strength of Recommendation = **Limited**

5. Reconstruction Approach

In patients undergoing arthroplasty to reconstruct the proximal humerus for metastatic bone disease, clinicians may consider reverse total shoulder

arthroplasty over conventional shoulder arthroplasty and hemiarthroplasty in order to decrease shoulder instability and improve range-of-motion.

- Combined Strength of Recommendation = **Limited**

6. Prognostic Markers

Based on low levels of evidence, clinicians should consider the following potential negative socioeconomic prognostic markers when caring for patients with metastatic malignancy of the humerus:

- **Age > 60 years**
- **Have Medicaid insurance compared to commercial insurance**
- **Black race compared to white race**
- **Lower income status**
- **Lower initial performance status**
- **Male sex**
- **Rapidly growing tumor histologies versus slow growing**

- Combined Strength of Recommendation = **Limited**

7. VTE Prophylaxis

There is no available evidence to make an Action Statement on VTE prophylaxis for metastatic bone disease of the humerus. In the absence of direct evidence, we refer clinicians to the ASCO, ASH, and ICM-VTE guidelines which indicate that oncology patients are at a higher risk for VTE, and prophylaxis should be considered during the peri-operative period.

- Combined Strength of Recommendation = **N/A**

GUIDELINE DEVELOPMENT GROUP ROSTER

Nate Mesko, MD, Co-Chair
Co-Director of the Sarcoma Center in the Taussig Cancer Institute, and Assistant Professorship at the Cleveland Clinic Lerner College of Medicine

Nicholas Tedesco, DO, Co-Chair,
Good Samaritan Regional Medical Center and Pastega Regional Cancer Center, Corvallis, OR, Clinical Assistant Professor, Western University College of Osteopathic Medicine of the Pacific Northwest
Cecilia Belzarena, MD
Department of Orthopedic Surgery, University of Missouri, Columbia, MO.

Alexander B. Christ, MD
Assistant Professor in Residence of Orthopaedic Surgery Department of Orthopaedic Surgery, David Geffen School of Medicine at UCLA
Matthew Colman, MD
Spine Surgery & Musculoskeletal Oncology, Associate Professor, Rush University Medical Center
Yee-Cheen Doung, MD
Associate Professor, Oregon Health and Science University, Portland, OR
Michelle Ghert, MD, FRCSC
Professor Department of Surgery, Division of Orthopaedic Surgery, McMaster University
Trey Gurich, MD
Department of Orthopedic Surgery, Prisma Health-Upstate, Greenville, South Carolina, Assistant Professor, University of South Carolina School of Medicine-Greenville
Matthew T. Houdek, MD
Associate Professor Orthopedic Surgery, Fellowship Director Orthopedic Oncology, Mayo Clinic
Dipak B. Ramkumar, MD, MS
The Lahey Clinic and Boston Children's Hospital, Boston, MA
Geoffrey W. Siegel, MD
Assistant Professor, Division of Orthopaedic Oncology, Department of Orthopaedic Surgery, University of Michigan School of Medicine
Steve Thorpe, MD, FACS
Associate Professor, University of California, Davis
Matthew T. Wallace, MD, MBA
Assistant Professor, Department of Surgery and Perioperative Care, The University of Texas at Austin Dell Medical School

MSTS AND AAOS STAFF

Felasfa Wodajo, MD
GDG Oversight chair
Virginia Cancer Specialists and Professor of Medical Education, University of Virginia School of Medicine, Inova Campus
Jayson Murray, MA
Managing Director, Clinical Quality and Value, AAOS
Danielle Schulte, MS, EMBA
Manager, Clinical Quality and Value, AAOS

Elizabeth Weintraub, MPH
Research Analyst, Clinical Quality and Value, AAOS
Tyler Verity
Medical Research Librarian, Clinical Quality and Value, AAOS
Kerri L. Mink
Executive Director, Musculoskeletal Tumor Society

INTRODUCTION

Overview

This clinical practice guideline for the surgical management of metastatic humeral disease is based on a systematic review of published studies surrounding the management of metastatic disease, multiple myeloma, and lymphoma limited to the humerus. In addition to providing practice recommendations, this guideline also highlights both limitations in the literature and consequent areas that should be the focus of future research collaborations.

This guideline is intended to be used by all qualified and appropriately trained physicians and surgeons involved in the surgical management of metastatic disease of the humerus. It is also intended to serve as an information resource for decision makers, researchers, and developers of practice guidelines.

Goals and Rationale

The purpose of this clinical practice guideline is to help improve treatment based on the current best evidence available. Practicing evidence-based medicine (EBM) demands that physicians use the best available evidence in their clinical decision making. The systematic review detailed herein was conducted between January 2022 and August 2022. These guidelines demonstrate where there is good evidence, where evidence is lacking, and what topics future research must target in order to improve the management of bony metastatic humeral disease burden. AAOS staff and the physician work group systematically reviewed the available literature and subsequently wrote the following recommendations using a rigorous, standardized process. Musculoskeletal oncology care in the setting of metastatic disease is provided in many different settings by many different providers. We created this guideline as an educational tool to guide qualified physicians through a series of treatment decisions in an effort to improve the quality and efficiency of care. Providers that may be impacted by the guideline include both surgical and non-surgical specialists. This guideline should not be construed as including all proper methods of care or excluding methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific procedure or treatment must be made in light of all circumstances presented by the patient and the needs and resources particular to the locality or institution.

Intended Users

This guideline is intended to be used by orthopaedic surgeons and physicians managing metastatic bony disease of the humerus. While a fellowship-trained orthopaedic oncologist is considered a target audience for these guidelines, the rising burden of skeletal related events (SREs) due to metastatic disease means that management of metastatic bony disease will be increasingly shared burden amongst a variety of providers. This guideline addresses prognostic implications, peri-operative management, and operative vs. non-operative decision making that can help guide decision making for general/non-oncology orthopaedic specialty trained surgeons. Insurance payers, governmental bodies, and health-policy decision-makers may also find this guideline useful as both a foundation of evolving standard of evidence regarding management, as well as opportunities for future funded research surrounding management of humerus metastatic disease burden. Adult primary care physicians, medical oncologists, radiation oncologists, geriatricians, palliative medicine specialists, hospice providers, hospital based adult medicine specialists, physical therapists, occupational therapists, nurse practitioners, physician assistants, emergency physicians, and other healthcare professionals who routinely see this type of patient in various practice settings may also benefit from this guideline.

Management of metastatic disease in the bony humerus is based on the assumption that decisions are predicated on communication between the patient and/or the patient's qualified heath care advocate and their physician regarding available treatments and procedures applicable to the individual patient. Once the patient and or their advocate have been informed of available therapies and have discussed these options with his/her physician, an informed decision can be made. Clinician input that balances their experience with conservative management and the clinician's surgical experience and skill set increases the probability of identifying patients who will benefit from specific treatment options. Because of the prognostic implications of metastatic (Stage 4) cancer, the decision-making process should weigh the goals of improved function and pain versus the recovery required and potential complications from a chosen intervention. Shared decision making with a multi-disciplinary team of surgeon providers, cancer providers, and ancillary rehabilitation specialists creates the best opportunity in determining the correct treatment for each patient.

Patient Population

This document addresses the management of metastatic disease of the humerus. Multiple myeloma and lymphoma skeletal involvement can be considered as equivalent to metastatic malignancy. This guideline is not intended to address management of primary sarcomas involving the skeletal anatomy of the humerus or aggressive benign tumors of the humerus. This guideline also does not address metastatic disease of the peri-scapular location around the glenohumeral joint outside of the humerus. While all age groups were considered, the adult population was the primary focus given the predilection for metastatic disease of the skeleton in non-pediatric age groups.

Burden of Disease, Incidence & Prevalence

The incidence of Metastatic Bone Disease (MBD) in the United States continues to climb, with estimates that 22 million Americans will have an active cancer diagnosis by 2030. Behind the lungs and liver, bone is the 3rd most commonly affected organ by metastatic cancer. As the incidence of cancer rises, so does the incidence of MBD – and subsequently skeletal related events (SREs). SREs can present in the form of impending or realized pathologic fracture, hypercalcemia, severe bone pain from malignancy, or spinal cord compression. It is estimated that there are now between 600,000 to 800,000 SREs in the United States annually. Additionally, the presentation of one SRE commonly is a harbinger for additional SREs that can occur in increasing frequency. Up to 1 in 5 patients can present with an SRE at the first initial presentation of bony involvement, and autopsy reports have suggested that up to 70% of patients with cancer history have involvement of the skeleton.[1] Additionally, the presence of a SRE has been correlated with worse survival.[2]

The economic burden of cancer care in the United States in 2030 is estimated to approach $246 billion.[3] Nearly one-fifth of this cost is attributed to the treatment of MBD.[1] Current spending on MBD per patient in the United States is approximately $18,000 per year, with overall cost expenditures over a lifetime of cancer treatment more than double in patients with MBD as compared to those without MBD.[1] Financial and Societal costs to be considered include:

1. Direct medical cost
2. Long-term medical and end-of-life cost
3. Balancing pain relief and functional improvement anticipated, the

required recovery anticipated, and overall anticipated prognosis.

4. Time off work, disability payments, and family members assisting in care utilizing resources and Family Medical Leave Act (FMLA) assistance

It is also important to note that, with rare exceptions of oligometastatic disease in the setting of breast, thyroid, or renal cancer, the diagnosis of MBD involvement portends an incurable diagnosis. Therefore, the possibility of multiple interventions in a patient over their remaining lifetime of treatment is very real.

The most common sites for MBD involvement are the spine, pelvis, ribs, and proximal femur. Approximately 20% of MBD occurs in the upper extremity, with half of that occurring in the humerus. Additionally, metastatic disease in the humerus accounts for 16-39% of all impending or completed pathologic fractures in long bones.[4] This can dramatically affect the ability to perform activities of daily living (ADLs) and necessary feeding or personal hygiene activity.

Etiology

Metastatic disease is the result of a primary malignancy arising from a distant organ (breast, colon, prostate, lung, skin, etc.) that spreads to a distant site, such as the skeletal system. This may present incidentally during routine cancer staging/surveillance or in the setting of worsening symptoms. Multiple Myeloma presents as a primary malignancy of the bone marrow and affects the entire skeletal system. Lymphoma can primarily arise in the bone or, more commonly, arise in the lymphatic system (spleen, lymph nodes, etc.) and concurrently involve the bone.

Several steps are involved in the development of metastatic disease. First, tumor cell intravasation needs to occur. This is typically mediated by the E Cadherin cell adhesion molecule on tumor cells. Then, the tumor cells within the blood or lymphatic system must avoid immune surveillance. Next, target tissue localization occurs, and the tumor cells attach to target organ endothelium via Integrin cell adhesion molecules that are expressed on tumor cells. The tumor cells then must extravasate into the target tissue and induce angiogenesis via Vasculoendothelial Growth Factor (VEGF). Finally, genomic instability must be present to allow for unchecked growth and decreased apoptosis.

These tumors, when localized to bone, can then induce osteolysis via upregulation of Receptor Activator of Nuclear Factor Kappa-B Ligand (RANK-L) or blastic disease via Endothelin I. Additionally, bone pain in the setting of BMD may occur from frank bony destruction by tumor grown or tumor-mediated release of cytokines, substance P, or pro-inflammatory molecules, such as the Tumor Necrosis Factor (TNF) superfamily.

Risk Factors

Risk factors for development of a pathologic fracture of the humerus in the setting of multiple myeloma, lymphoma, or metastatic cancer include, but are not limited to, advanced stages of disease, poor disease control with systemic hormonal or chemotherapy agents, tumor size, faster tumor growth rate, lytic (as opposed to blastic disease), specific tumor location (i.e. tensile portion of the involved bone), continued pain following localized radiation therapy, nonuse of bone modifying drugs (ex. RANK-L inhibitors, bisphosphonates), female sex, advanced age, underlying osteoporosis, patient noncompliance with medications or weightbearing restrictions, impaired balance, localized trauma, and inadequate home safety or supervision.

Potential Benefits, Harms, and Contraindications

Most treatments are associated with some known risks, especially invasive and operative treatments. Even conservative non-operative management is not without potential risks to the patient. Contraindications vary widely based on the treatment administered, the performance status of the patient, expected prognosis, and medical comorbidities. A particular concern when managing impending or realized pathologic fractures in the humerus is the potential for the overall fracture treatment to result in increased patient mortality or decreased level of mobility and independence (compared to status prior to the presence of humeral disease). Additional factors may affect the choice of treatment including, but not limited to: associated injuries, mass-effect of the presenting tumor, or disease burden the patient may present with, the individual's age and medical co-morbidities, specific patient characteristics including low bone mass and presence of adjacent joint tumor involvement or pre-existing osteoarthritis, performance status of the patient, patient and family desires and expectations, dominant vs. nondominant extremity, overall prognosis and current or expected response to systemic treatment, radiosensitivity of the specific tumor pathology, or barriers to appropriate follow-up, rehabilitation, and compliance of the patient.

Clinician input based on previous experience increases the probability of identifying patients who will likely benefit from specific treatment options. The individual patient and/or their decision surrogate dynamic will also influence treatment decisions. Therefore, discussion of available treatments and procedures applicable to the individual patient rely on mutual communication between the patient and/or decision surrogate and physician, weighing the potential risks and benefits for that patient. Once the patient and/or their decision surrogate have been informed of available therapies and have discussed these options with the patient's physician via a thorough PARQ conference, an informed decision can be made.

Future Research

Consideration for future research is provided for each recommendation within this document. In general, we found little high-quality evidence regarding surgical management of humerus metastatic disease. This is not surprising given the rarity of the diseases that orthopedic oncologists treat, and the paucity of data reported for musculoskeletal oncology pathologies as specific as humeral metastatic disease. Historically, single center case series have been the mainstay for orthopedic oncology clinical research and literature, with very few comparative or randomized studies available. The goal for any CPG is to provide evidence-based recommendations, but also importantly to drive future research that will help answer these questions more definitively and improve care and outcomes for the patients involved.[5]

METHODS

The methods used to perform this systematic review were employed to minimize bias and enhance transparency in the selection, appraisal, and analysis of the available evidence. These processes are vital to the development of reliable, transparent, and accurate clinical recommendations. To view the full MSTS clinical practice guideline methodology please visit http://msts.org/index.php/education/evidence-based-medicine
This clinical practice guideline evaluates the management of metastatic humeral disease. The MSTS approach incorporates practicing physicians (clinical experts) and methodologists who are free of potential conflicts of interest relevant to the topic under study, as recommended by clinical practice guideline development experts.

This clinical practice guideline was prepared by the MSTS Metastatic Humeral Disease Guideline physician development group (clinical experts) with the assistance of the AAOS Clinical Quality and Value (CQV) Department (methodologists). To develop this clinical practice guideline, the clinical practice guideline development group held an introductory meeting on January 15th, 2022, to establish the scope of the clinical practice guideline. As physician experts, the clinical practice guideline development group defined the scope of the clinical practice guideline by creating PICO Questions (i.e., population, intervention, comparison, and outcome) that directed the literature search. The AAOS Medical Librarian created and executed the search (see Appendix III for search strategy).

Literature Searches

The systematic review begins with a comprehensive search of the literature. Articles we consider must be published prior to the start date of the search in a minimum of three electronic databases; PubMed, EMBASE, and the Cochrane Central Register of Controlled Trials. The medical librarian conducts the search using key terms determined from the guideline development group's PICO questions. The initial literature search was conducted Feb 3rd, 2022, and a final literature search as conducted on May 9th, 2022.

A methodologist reviewed/included primary literature and evaluated all recalled, full-text articles for possible inclusion based on the study selection criteria and summarized the evidence for the guideline development group of who assisted with reconciling possible errors and omissions.

A study attrition diagram is provided in the appendix of each document that details the numbers of identified abstracts, recalled and selected studies, and excluded studies that were evaluated in the CPG. The search strategies used to identify the abstracts is also included in the appendix of the CPG document.

Defining the Strength of Recommendation

Judging the quality of evidence is only a steppingstone towards arriving at the strength of a CPG recommendation. The strength of recommendation also takes into account the quality, quantity, and the trade-off between the benefits and harms of a treatment, the magnitude of a treatment's effect, and whether data exists on critical outcomes.

Strength of recommendation expresses the degree of confidence one can have in a recommendation. As such, the strength expresses how possible it is that a recommendation will be overturned by future evidence. It is very difficult for future evidence to overturn a recommendation that is based on many high quality randomized controlled trials that show a large effect. It is much more feasible that future evidence could overturn recommendations derived from a few small retrospective comparative studies. Consequently, statements based on the former kind of evidence are given a "strong" strength of recommendation and statements based on the latter kind of evidence are given a "limited" strength. In the event there is no supporting evidence, the strength is unassigned (Table I). The recommendations can be further downgraded or upgraded based on the consensus of the GDG, utilizing the GRADE Evidence to Decision framework criteria. Physician workgroup members utilized an EtD form with numerical scores associated with the individual items. The scores were summed and predetermined score thresholds were used to suggest whether a recommendation should be upgraded or downgraded (Table II).

Voting on the Action Statements

The action statements and their strength were voted on by the guideline development group members before and after the final meeting. If disagreement between the guideline development group occurred during the meeting, there was further

discussion to see whether the disagreement(s) could be resolved. Approval and adoption of action statements during the development of clinical practice guidelines requires, at minimum, a supermajority (i.e. two-thirds or 67%). GDGs may choose to continue revising a recommendation even if supermajority is reached to refine the statement with the aim of achieving consensus of the entire GDG. All approvals and scores are recorded in the final guideline document to ensure transparency to the end user.

Peer and Public Review Period

Following the final meeting, the CPG draft undergoes a 3-week review period for additional input from external content experts. Written comments are provided on the structured review form. All reviewers are required to disclose their conflicts of interest.

To guide who participates, the CPG work group identifies specialty societies at the introductory meeting. Organizations, not individuals, are specified. The specialty societies are solicited for nominations of individual reviewers approximately six weeks before the final meeting. The review period is announced as it approaches, and others interested can volunteer to review the draft. The chairs of the guideline work group review the draft of the guideline prior to dissemination.

Some specialty societies (both orthopaedic and non-orthopaedic) ask their evidence-based practice (EBP) committee or equivalent to provide review of the guideline. The organization is responsible for coordinating the distribution of our materials and consolidating their comments onto one form. The chair of the external EBP committees provides disclosure of their conflicts of interest (COI) and manages the potential conflicts of their members.

The MSTS asks for comments to be assembled into a single response form by the specialty society and for the individual submitting the review to provide disclosure of potentially conflicting interests. The review stage gives external stakeholders an opportunity to provide evidence-based direction for modifications that they believe have been overlooked. Since the draft is subject to revisions until its approval by the MSTS Executive Committee as the final step in the guideline development process, confidentiality of all working drafts is essential.

The CPG is also provided to members of the MSTS Executive Committee, relevant external medical organizations, and the broader MSTS membership for review. Based on these bodies, over 200 commentators should have the opportunity to provide input into each CPG.

The chairs of the guideline work group and the methodologists draft the initial responses to comments that address methodology and the chair and co-chair, also organize initial responses to questions concerning clinical practice and techniques. All comments received and the initial drafts of the responses are also reviewed by all members of the guideline development group. All proposed changes to recommendation language as a result of the review period must be based on the evidence and must be approved by the GDG. Final revisions are summarized in a report that is provided alongside the guideline document throughout the remainder of the approval processes and final publication.

The MSTS believes in the importance of demonstrating responsiveness to input received during the review process and welcomes the critiques of external specialty societies. Following final approval of the guideline, all individual responses are posted on our website http:/www.MSTS.org/guidelines with a point-by-point reply to each non-editorial comment. Reviewers who wish to remain anonymous notify the MSTS to have their names de-identified; their comments, our responses, and their COI disclosures are still posted.

The MSTS Approval Process

This final CPG draft must be approved by the MSTS Committee on Guidelines and Evidence Based Medicine and the MSTS Executive Committee. These decision-making bodies are described in the Appendix of each guideline. Their charge is to approve or reject its publication by majority vote, not suggest modifications to the content of the documents.

Revision Plans

CPGs represent a cross-sectional view of current treatment and may become outdated as new evidence becomes available. They will be revised in accordance with new evidence, changing practice, rapidly emerging treatment options, and new technology. Additionally, they will be updated or withdrawn in five years.

CPG Dissemination Plans

The primary purpose of CPGs is to provide interested readers with full documentation about not only our recommendations, but also about how we arrived at those recommendations.
To view all MSTS published CPG recommendations, please visit http://www.MSTS.org/guidelines.
Shorter versions of the CPGs are available in other venues. Publication of most CPGs is announced by an MSTS press release, articles authored by the CPG work group and published in the appropriate journals. Other dissemination efforts outside of the MSTS will include submitting the CPGs to the ECRI Guidelines Trust, Guidelines International Network Library, and distributing the guideline at other medical specialty societies' meetings.

INTERPRETING THE STRENGTH OF EVIDENCE

Table I. Level of Evidence Descriptions

Combined Strength of Recommendation	Aggregate Strength of Evidence	Description of Evidence Quality
Strong	Strong or Moderate	Evidence from two or more "High" quality studies with consistent findings for recommending for or against the intervention. Or Rec is upgrade from Moderate using the EtD framework.
Moderate	Strong, Moderate or Limited	Evidence from two or more "Moderate" quality studies with consistent findings, or evidence from a single "High" quality study for recommending for or against the intervention. Or Rec is upgraded or downgraded from Limited or Strong using the EtD framework.
Limited	Limited or Moderate	Evidence from two or more "Low" quality studies with consistent findings or evidence from a single "Moderate" quality study recommending for or against the intervention. Or Rec is downgraded from Strong or Moderate using the EtD Framework.
N/A	No Evidence	There is no supporting evidence, or higher quality evidence was downgraded due to major concerns addressed in the EtD framework. In the absence of reliable evidence, the guideline work group is making a recommendation based on their clinical opinion.

Evidence to Decision Framework

The Evidence to Decision Framework (EtDF) utilized by the MSTS is a novel scoring rubric developed by the Guidelines and Evidence Based Medicine (GEBM) Committee. Some form of EtDF is used in any clinical practice guideline to leverage clinical experience with the quality of the literature to determine recommendation strength. The MSTS GEBM developed the scoring system as a means to quantify the quality of the literature more objectively, such that any recommendations would be more consistent, transparent, and reproducible across panelists. It is a series of categories with weighted numeric scaling that incorporates aggregate methodological critique and perceptions of importance, risks, benefits, consistency with other literature on the subject, and cost of the intervention studied to answer a particular PICO question (see Appendix VI). The scoring is used to determine where the strength of recommendation should ultimately fall.

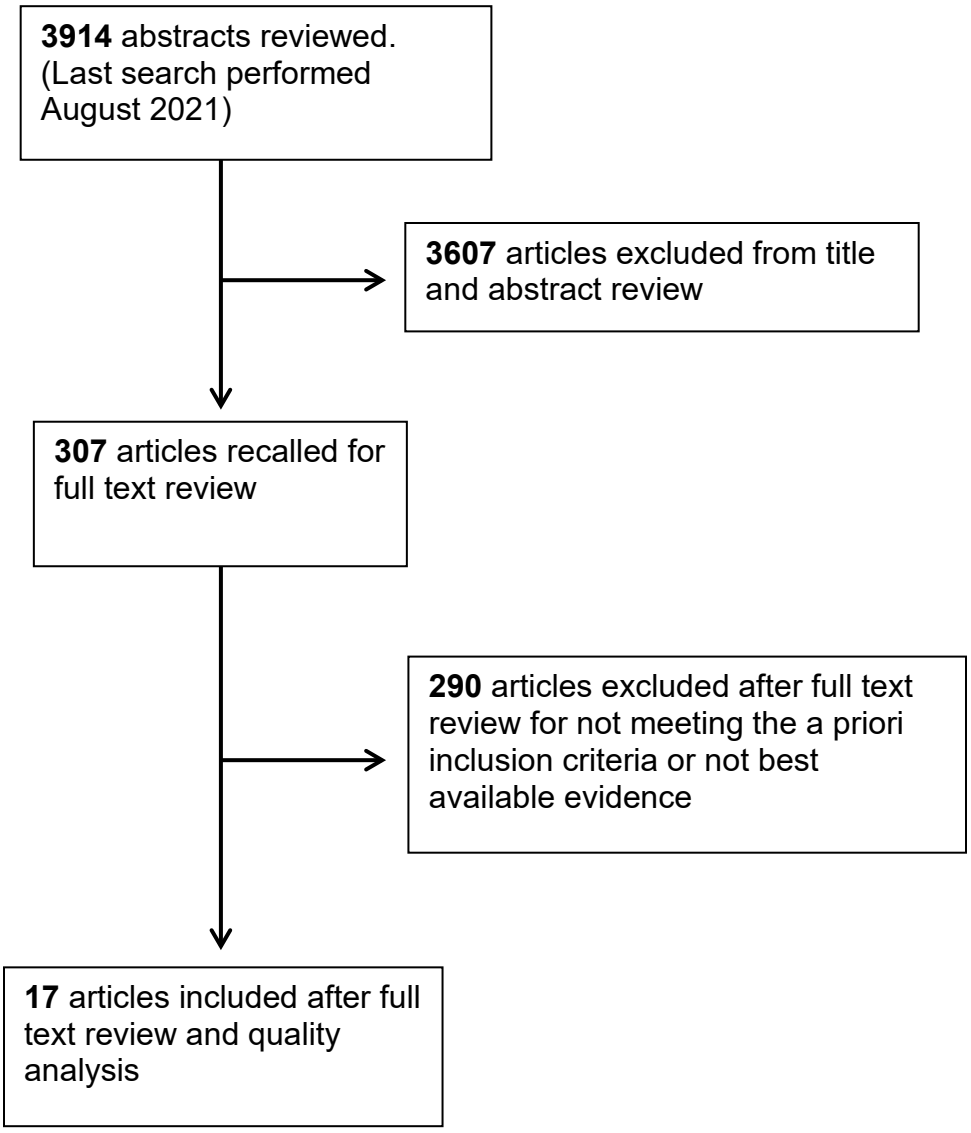
The study methodology and design incorporated into the level of evidence (ex. I-V) is first used to initially determine the strength of recommendation. Then, the EtDF scoring rubric is used to determine if that alone is enough to determine the strength of recommendation or if the risk-to-benefit profile, effect on the patients or society, or overall cost of implementing the intervention is so importantly skewed that the strength of the recommendation should be increased or decreased as appropriate (see Table II below). An example of this would be downgrading a recommendation based on Level I evidence that showed a benefit to an intervention, but had a tremendous amount of treatment crossover, protocol deviations, and patient attrition with an

intervention so expensive it would be largely unattainable for most institutions. So, while it might be level I evidence in favor of a specific intervention, there are too many variables, issues, and implementation pragmatics that make it a low overall recommendation that ultimately needs further research.

Table II. Evidence to Decision Framework Score Thresholds

Upgrade/Downgrade Thresholds	EtDF Score
Increase recommendation strength +2	38-42
Increase recommendation strength +1	31-37
No change in recommendation strength	18-30
Decrease recommendation strength -1	13-17
Decrease recommendation strength -2	3-12

STUDY ATTRITION FLOWCHART



ACTION STATEMENTS

1. Plating/Internal Fixation, Intramedullary Fixation, and/or Photodynamic Polymer

When treating pathologic diaphyseal humerus fractures, clinicians can consider either the use of plating/internal fixation, intramedullary fixation, and/or photodynamic polymer, as there does not appear to be a significant difference in clinical outcomes or reoperation rate between these constructs based on limited available evidence.

Strength of Recommendation

- Aggregate Evidence = **Limited** (3 Low quality Studies)
- EtD Framework Score = **21**
- Combined Strength of Recommendation = **Limited**

Rationale

Three lower quality studies were included and examined for this portion of the clinical practice guideline. These studies were retrospective and included low numbers of patients. Further, these studies included varied outcomes measured in terms of surgical complications and clinical function.

When treating pathologic diaphyseal humerus fractures in the setting of metastatic disease, the available evidence does not appear to show a significant difference in clinical outcomes (pain relief, upper extremity function, complication rates) between these constructs. However, with the low numbers available there was noted an increased failure rate with photodynamic polymer fixation compared to intramedullary nail fixation. Despite this potential difference, there does not appear to be a significant difference in reoperation rate between plating/internal fixation, intramedullary fixation, and photodynamic polymer.

Based on the low-level evidence of the articles analyzed, any of the constructs, including intramedullary nailing, photodynamic polymer, or plating/internal fixation, constitutes a reasonable and safe option when treating realized or impending pathologic diaphyseal humerus fractures. However, caution is advised regarding the use of photodynamic polymer fixation until further evidence is available due to the potential higher failure rates with this construct.

Further research is needed to better elucidate any potentially undetected outcome difference among the various constructs. The best study design to help determine this would be a collaborative, multicenter, randomized controlled trial.

Included Evidence:

1. Dijkstra, S., Stapert, J., Boxma, H., Wiggers, T. Treatment of pathological fractures of the humeral shaft due to bone metastases: a comparison of intramedullary locking nail and plate osteosynthesis with adjunctive bone cement. *European Journal of Surgical Oncology* 1996; 6: 621-6
2. Hoellwarth, J. S., Weiss, K., Goodman, M., Heyl, A., Hankins, M. L., McGough, R., 3rd Evaluating the reoperation rate and hardware durability of three stabilizing implants for 105 malignant pathologic humerus fractures. *Injury* 2020; 4: 947-954
3. Sarahrudi, K., Wolf, H., Funovics, P., Pajenda, G., Hausmann, J. T., Vecsei, V. Surgical treatment of pathological fractures of the shaft of the humerus. *Journal of Trauma-Injury Infection & Critical Care* 2009; 3: 789-94

Evidence to Decision Framework Scoring

Criteria	Detailed considerations	Judgements (points)	Score
What is the baseline quality/strength of the evidence? See above.	Baseline strength of recommendation is listed above	No evidence (0) Low (3) Moderate (4) High (5)	3
What is the value and importance of the outcomes to clinical practice?	Are the outcomes assessed by the studies impactful (e.g., pain reduction, functional improvement, etc.)?	None (0) Low (2) Moderate (3) High (5)	3
What is the magnitude of the desired effect?		None (0) Low (2) Moderate (3) High (5)	3
What is the magnitude of undesirable effects/complications?		High (0) Moderate (1) Low (2) None (3)	2
Do the benefits outweigh the risks?	Do the benefits clearly outweigh the risks or is there a balance of benefits and harms?	No (0) Probably No (1) Uncertain (2) Probably Yes (3) Yes (5)	2
What amount of resources are required to produce the desired effect?	What is the estimated equipment need, space, time, and ability of any institution to provide these needs?	Prohibitive (0) High (1) Moderate (2) Minimal (3) None (5)	2
What is the cost to produce the desired effect?	What is the estimated monetary cost?	Prohibitive (0) High (1) Moderate (2) Minimal (3) None (4)	1
Is the intervention/outcomes acceptable to key stakeholders?	-Are there any stakeholders who wouldn't accept risk to benefit ratio, the costs, the importance of outcomes? -Would anyone morally object to intervention (in regard to ethical principles such as no maleficence, beneficence, or justice)? -Would intervention effect people's autonomy?	No (0) Probably No (1) Uncertain (2) Probably Yes (4) Yes (5)	1
Is the intervention feasible to implement?	-Is intervention sustainable? -Any barriers limiting the feasibility of implementing recommendation?	No (0) Probably No (1) Uncertain (2) Probably Yes (4) Yes (5)	4
Total Score			**21**

2. En Bloc Resection, Curettage, Internal Fixation, or Intramedullary Nailing

No studies met inclusion criteria comparing survivorship or other oncologic outcomes between en bloc resection, curettage, internal fixation, or intramedullary nailing. Based on the lack of evidence, no recommendations can be made for or against en bloc resection pertaining to metastatic disease of the humerus.

Strength of Recommendation

- Aggregate Evidence = **N/A (**No Included Literature)
- EtD Framework Score = **15** (strength cannot be designated lower than N/A)
- Combined Strength of Recommendation = **N/A**

Rationale

No studies met inclusion criteria to compare en bloc resection and internal fixation in terms of disease control or clinical outcomes. Based on the lack of definitive evidence, no recommendations can be made for or against specific surgical treatments for metastatic disease of the humerus. While supporting literature is lacking, it is appropriate for the surgeon to consider en bloc resection based on the clinical circumstances and/or the reconstructive needs of the patient. The histologic subtype of metastatic bone disease, oligometastatic disease state, condition of the adjacent joint, available bone stock, and other patient-centric factors may indicate resection as an appropriate treatment.

Future studies should compare internal fixation versus intramedullary nailing versus en bloc resection for functional outcomes, failure and/or reoperation rates, pain relief, and oncologic outcomes. Comparisons between histologic primaries and number of bony metastases should be considered in these studies.

Included Evidence:

No evidence met inclusion criteria

Evidence to Decision Framework Scoring

Criteria	Detailed considerations	Judgements (points)	Score
What is the baseline quality/strength of the evidence? See above.	Baseline strength of recommendation is listed above	No evidence (0) Low (3) Moderate (4) High (5)	0
What is the value and importance of the outcomes to clinical practice?	Are the outcomes assessed by the studies impactful (e.g., pain reduction, functional improvement, etc.)?	None (0) Low (2) Moderate (3) High (5)	0
What is the magnitude of the desired effect?		None (0) Low (2) Moderate (3) High (5)	2
What is the magnitude of undesirable effects/complications?		High (0) Moderate (1) Low (2) None (3)	2
Do the benefits outweigh the risks?	Do the benefits clearly outweigh the risks or is there a balance of benefits and harms?	No (0) Probably No (1) Uncertain (2) Probably Yes (3) Yes (5)	2
What amount of resources are required to produce the desired effect?	What is the estimated equipment need, space, time, and ability of any institution to provide these needs?	Prohibitive (0) High (1) Moderate (2) Minimal (3) None (5)	2
What is the cost to produce the desired effect?	What is the estimated monetary cost?	Prohibitive (0) High (1) Moderate (2) Minimal (3) None (4)	2
Is the intervention/outcomes acceptable to key stakeholders?	-Are there any stakeholders who wouldn't accept risk to benefit ratio, the costs, the importance of outcomes? -Would anyone morally object to intervention (in regard to ethical principles such as no maleficence, beneficence, or justice)? -Would intervention effect people's autonomy?	No (0) Probably No (1) Uncertain (2) Probably Yes (4) Yes (5)	1
Is the intervention feasible to implement?	-Is intervention sustainable? -Any barriers limiting the feasibility of implementing recommendation?	No (0) Probably No (1) Uncertain (2) Probably Yes (4) Yes (5)	4
Total Score			**15**

3. Patient Selection for Nonoperative Techniques Versus Operative Techniques

No studies met inclusion criteria to compare nonoperative vs operative treatment in the setting of metastatic disease of the humerus. Based on the lack of definitive evidence, no recommendations can be made for or against patient selection or indication for nonoperative vs. operative treatment pertaining to metastatic disease of the humerus.

Strength of Recommendation

- Aggregate Evidence = **N/A** (No Included Literature)
- EtD Framework Score = **26**
- Combined Strength of Recommendation = **N/A**

Rationale

While specific literature is lacking, the group recommends that both nonoperative treatment and operative treatment can be considered based on the clinical circumstances of the patient, active comorbidities, metastatic disease burden and prognosis, location of the lesion, histologic subtype, presence of displacement or angulation, expected responsiveness to radiation and/or chemotherapy, and patient goals and expectations.

Future research such as prospective cohort studies could help elucidate the clinical scenarios in which patients can be treated successfully with nonoperative management for metastatic disease of the humerus.

Included Evidence:

No evidence met inclusion criteria

Evidence to Decision Framework Scoring

Criteria	Detailed considerations	Judgements (points)	Score
What is the baseline quality/strength of the evidence? See above.	Baseline strength of recommendation is listed above	No evidence (0) Low (3) Moderate (4) High (5)	0
What is the value and importance of the outcomes to clinical practice?	Are the outcomes assessed by the studies impactful (e.g., pain reduction, functional improvement, etc.)?	None (0) Low (2) Moderate (3) High (5)	0
What is the magnitude of the desired effect?		None (0) Low (2) Moderate (3) High (5)	2
What is the magnitude of undesirable effects/complications?		High (0) Moderate (1) Low (2) None (3)	3
Do the benefits outweigh the risks?	Do the benefits clearly outweigh the risks or is there a balance of benefits and harms?	No (0) Probably No (1) Uncertain (2) Probably Yes (3) Yes (5)	3
What amount of resources are required to produce the desired effect?	What is the estimated equipment need, space, time, and ability of any institution to provide these needs?	Prohibitive (0) High (1) Moderate (2) Minimal (3) None (5)	5
What is the cost to produce the desired effect?	What is the estimated monetary cost?	Prohibitive (0) High (1) Moderate (2) Minimal (3) None (4)	4
Is the intervention/outcomes acceptable to key stakeholders?	-Are there any stakeholders who wouldn't accept risk to benefit ratio, the costs, the importance of outcomes? -Would anyone morally object to intervention (in regard to ethical principles such as no maleficence, beneficence, or justice)? -Would intervention effect people's autonomy?	No (0) Probably No (1) Uncertain (2) Probably Yes (4) Yes (5)	4
Is the intervention feasible to implement?	-Is intervention sustainable? -Any barriers limiting the feasibility of implementing recommendation?	No (0) Probably No (1) Uncertain (2) Probably Yes (4) Yes (5)	5
Total Score			**26**

4. Cementation Vs No Cementation

In patients undergoing surgical fixation of the humerus for metastatic bone disease, clinicians may consider cement augmentation. One low quality study meeting inclusion criterion suggested the addition of cement to surgical fixation of pathologic fractures of the humerus may provide short-term improvements in pain relief and functional mobility, however no difference in surgical complications were observed when compared to fixation alone.

Strength of Recommendation

- Aggregate Evidence = **Limited** (2 Low quality Study)
- EtD Framework Score (from below) = **23**
- Combined Strength of Recommendation = **Limited**

Rationale

A single small, retrospective comparison study demonstrated improved postoperative pain relief and functional outcomes at 1 and 6 weeks postoperatively with the addition of cement to intramedullary nailing of pathologic humeral shaft fractures. These results were compared to a historical cohort of uncemented intramedullary nails. There was no difference in perioperative complications, and no difference in pain or functional outcomes at 6 months postoperatively. Two other studies included in the review were also retrospective studies, one of which included 39 patients and the other 208 patients. These both appeared to include lesions at the proximal, diaphyseal, and distal humerus. In the larger study (excluding endoprosthetic reconstruction), plate fixation (as compared to intramedullary fixation), had a higher failure rate. The other included study did not note a difference between these constructs.

Future studies should compare cemented and cementless constructs for fixation of pathologic humerus fractures, and evaluate pain, location of the lesion, functional outcomes, and mechanical failure rates of each construct.

Included Evidence:

1. Laitinen, M., Nieminen, J., Pakarinen, T. K. Treatment of pathological humerus shaft fractures with intramedullary nails with or without cement fixation. *Archives of Orthopaedic & Trauma Surgery* 2011; 4: 503-8
2. Sarahudi K., Wolf H., Funovics H., Pajenda G., Hausman J., Vecsei V. Surgical treatment of pathological fractures of the shaft of the humerus. J Trauma. 2009 Mar; 66(3):789-94.

Additional References:

1. Wedin R., Hansen B., Laitinen M., Trovik C., Zaikova O., Bergh P., Kalen A., Schwarz-Lausten G., von Steyern G., Walloe A., Keller J., Weiss R. Complications and survival after surgical treatment of 214 metastatic lesions of the humerus. *J Shoulder Elbow Surg*. 2012. Aug;21(8):1049-55.

Evidence to Decision Framework Scoring

Criteria	Detailed considerations	Judgements (points)	Score
What is the baseline quality/strength of the evidence? See above.	Baseline strength of recommendation is listed above	No evidence (0) Low (3) Moderate (4) High (5)	3
What is the value and importance of the outcomes to clinical practice?	Are the outcomes assessed by the studies impactful (e.g., pain reduction, functional improvement, etc.)?	None (0) Low (2) Moderate (3) High (5)	2
What is the magnitude of the desired effect?		None (0) Low (2) Moderate (3) High (5)	2
What is the magnitude of undesirable effects/complications?		High (0) Moderate (1) Low (2) None (3)	2
Do the benefits outweigh the risks?	Do the benefits clearly outweigh the risks or is there a balance of benefits and harms?	No (0) Probably No (1) Uncertain (2) Probably Yes (3) Yes (5)	3
What amount of resources are required to produce the desired effect?	What is the estimated equipment need, space, time, and ability of any institution to provide these needs?	Prohibitive (0) High (1) Moderate (2) Minimal (3) None (5)	2
What is the cost to produce the desired effect?	What is the estimated monetary cost?	Prohibitive (0) High (1) Moderate (2) Minimal (3) None (4)	3
Is the intervention/outcomes acceptable to key stakeholders?	-Are there any stakeholders who wouldn't accept risk to benefit ratio, the costs, the importance of outcomes? -Would anyone morally object to intervention (in regard to ethical principles such as no maleficence, beneficence, or justice)? -Would intervention effect people's autonomy?	No (0) Probably No (1) Uncertain (2) Probably Yes (4) Yes (5)	1
Is the intervention feasible to implement?	-Is intervention sustainable? -Any barriers limiting the feasibility of implementing recommendation?	No (0) Probably No (1) Uncertain (2) Probably Yes (4) Yes (5)	5
Total Score			**23**

5. Reconstruction Approach

In patients undergoing arthroplasty to reconstruct the proximal humerus for metastatic bone disease, clinicians may consider reverse total shoulder arthroplasty over conventional shoulder arthroplasty and hemiarthroplasty in order to decrease shoulder instability and improve range-of-motion.

Strength of Recommendation

- Aggregate Evidence = **Limited** (2 Low quality Studies)
- EtD Framework Score = **25**
- Combined Strength of Recommendation = **Limited**

Rationale

Two retrospective comparative studies demonstrate a decreased rate of dislocation/subluxation, improved shoulder range-of-motion, and decreased reoperation rates with reverse total shoulder arthroplasty compared to hemiarthroplasty. One study demonstrated decreased local tumor recurrence in the reverse arthroplasty group as well. Careful consideration of anatomy involved in resection and harboring metastatic disease (glenoid, deltoid insertion/muscle, axillary nerve) as well as patient-centric factors should be used to guide appropriate selection of technique.

Future research should involve cohort or randomized studies between hemiarthroplasty and reverse total shoulder arthroplasty in comparable patient populations to evaluate range-of-motion, instability, reoperation rates, and pain between the two reconstructive techniques.

Included Evidence:

1. Houdek, M. T., Bukowski, B. R., Athey, A. G., Elhassan, B. T., Barlow, J. D., Morrey, M. E., Rose, P. S., Wagner, E. R., Sanchez-Sotelo, J. Comparison of reconstructive techniques following oncologic intraarticular resection of proximal humerus. *Journal of Surgical Oncology* 2021; 1: 133-140
2. Grosel, T. W., Plummer, D. R., Everhart, J. S., Kirven, J. C., Ziegler, C. L., Mayerson, J. L., Scharschmidt, T. J., Barlow, J. D. Reverse total shoulder arthroplasty provides stability and better function than hemiarthroplasty following resection of proximal humerus tumors. *Journal of Shoulder & Elbow Surgery* 2019; 11: 2147-2152

Evidence to Decision Framework Scoring

Criteria	Detailed considerations	Judgements (points)	Score
What is the baseline quality/strength of the evidence? See above.	Baseline strength of recommendation is listed above	No evidence (0) Low (3) Moderate (4) High (5)	3
What is the value and importance of the outcomes to clinical practice?	Are the outcomes assessed by the studies impactful (e.g., pain reduction, functional improvement, etc.)?	None (0) Low (2) Moderate (3) High (5)	3
What is the magnitude of the desired effect?		None (0) Low (2) Moderate (3) High (5)	3
What is the magnitude of undesirable effects/complications?		High (0) Moderate (1) Low (2) None (3)	2
Do the benefits outweigh the risks?	Do the benefits clearly outweigh the risks or is there a balance of benefits and harms?	No (0) Probably No (1) Uncertain (2) Probably Yes (3) Yes (5)	3
What amount of resources are required to produce the desired effect?	What is the estimated equipment need, space, time, and ability of any institution to provide these needs?	Prohibitive (0) High (1) Moderate (2) Minimal (3) None (5)	3
What is the cost to produce the desired effect?	What is the estimated monetary cost?	Prohibitive (0) High (1) Moderate (2) Minimal (3) None (4)	2
Is the intervention/outcomes acceptable to key stakeholders?	-Are there any stakeholders who wouldn't accept risk to benefit ratio, the costs, the importance of outcomes? -Would anyone morally object to intervention (in regard to ethical principles such as no maleficence, beneficence, or justice)? -Would intervention effect people's autonomy?	No (0) Probably No (1) Uncertain (2) Probably Yes (4) Yes (5)	1
Is the intervention feasible to implement?	-Is intervention sustainable? -Any barriers limiting the feasibility of implementing recommendation?	No (0) Probably No (1) Uncertain (2) Probably Yes (4) Yes (5)	5
Total Score			**25**

6. Prognostic Markers

Based on low levels of evidence, clinicians should consider the following potential negative socioeconomic prognostic markers when caring for patients with metastatic malignancy of the humerus:

- **Age > 60 years**
- **Have Medicaid insurance compared to commercial insurance**
- **Black race compared to white race**
- **Lower income status**
- **Lower initial performance status**
- **Male sex**
- **Rapidly growing tumor histologies versus slow growing**

Strength of Recommendation

- Aggregate Evidence = **Limited** (11 Low quality Studies)
- EtD Framework Score = **21**
- Combined Strength of Recommendation = **Limited**

Rationale

There is a lack of data examining the socioeconomic impact of race, gender, and insurance status on the outcome of patients with non-primary malignancies. Current data is limited to small series of patients and a low-quality of evidence. Similar to studies in other types of cancers, lack of insurance or having Medicaid, lower household income and black race were associated with a poor outcome. The studies reviewed showed rapidly growing histologies to be most often lung, gastrointestinal, and renal. The slower growing histologies were most often breast, prostate and thyroid. There were no studies describing the type of lesion (lytic vs blastic) as a predictor. There is likely no way to improve the quality of evidence for these studies as it would be near impossible to maintain equipoise while performing a prospective randomized study on this topic, however future studies on the use of prospectively collected data from multicenter or international collaborations may shed insight into the impact of these socioeconomic factors.

Included Evidence:

1. Herget, G., Saravi, B., Schwarzkopf, E., Wigand, M., Sudkamp, N., Schmal, H., Uhl, M., Lang, G. Clinicopathologic characteristics, metastasis-free survival, and skeletal-related events in 628 patients with skeletal metastases in a tertiary orthopedic and trauma center. *World Journal of Surgical Oncology* 2021; 1: 62
2. Huang, Z., Du, Y., Zhang, X., Liu, H., Liu, S., Xu, T. Clear cell renal cell carcinoma bone metastasis: What should be considered in prognostic evaluation. *European Journal of Surgical Oncology* 2019; 7: 1246-1252
3. Hung, B., Pennington, Z., Hersh, A. M., Schilling, A., Ehresman, J., Patel, J., Antar, A., Porras, J. L., Elsamadicy, A. A., Sciubba, D. M. Impact of race on nonroutine discharge, length of stay, and postoperative complications after surgery for spinal metastases. *Journal of Neurosurgery Spine* 2021; 0: 1-8
4. Rades, D., Haus, R., Janssen, S., Schild, S. E. An easy-to-use scoring system to estimate the survival of patients irradiated for bone metastases from lung cancer. *Translational Lung Cancer Research* 2020; 4: 1067-1073
5. Rades, D., Haus, R., Janssen, S., Schild, S. E. Interval Between Cancer Diagnosis and Radiotherapy - An Independent Prognostic Factor of Survival in Patients Irradiated for Bone Metastases from Kidney Cancer. *In Vivo* 2020; 2: 767-770
6. Rades, D., Haus, R., Schild, S. E., Janssen, S. Prognostic factors and a new scoring system for survival of patients irradiated for bone metastases. *BMC Cancer* 2019; 1: 1156
7. Scott, E., Klement, M. R., Brigman, B. E., Eward, W. C. Beyond Mirels: Factors Influencing Surgical Outcome of Metastasis to the Extremities in the Modern Era. *Journal of Surgical Orthopaedic Advances* 2018; 3: 178-186
8. Vos, M., Ho, V. K. Y., Oosten, A. W., Verhoef, C., Sleijfer, S. Minimal Increase in Survival Throughout the Years in Patients with Soft Tissue Sarcoma with Synchronous Metastases: Results of a Population-Based Study. *Oncologist* 2019; 7: e526-e535
9. Wisanuyotin, T., Sirichativapee, W., Sumnanoont, C., Paholpak, P., Laupattarakasem, P., Sukhonthamarn, K., Kosuwon, W. Prognostic and risk factors in patients with metastatic bone disease of an upper extremity. *Journal of Bone Oncology* 2018; 0: 71-75
10. Wong, E., Chow, E., Zhang, L., Bedard, G., Lam, K., Fairchild, A., Vassiliou, V., Alm El-Din, M. A., Jesus-Garcia, R., Kumar, A., Forges, F., Tseng, L. M., Hou, M. F., Chie, W. C., Bottomley, A. Factors influencing health related quality of life in cancer patients with bone metastases. *Journal of Palliative Medicine* 2013; 8: 915-21
11. Yanamandra, U., Sharma, R., Shankar, S., Yadav, S., Kapoor, R., Pramanik, S., Ahuja, A., Kumar, R., Sharma, S., Das, S., Chatterjee, T., Somasundaram, V., Verma, T., Mishra, K., Singh, J., Sharma, A., Nair, V. Survival Outcomes of Newly Diagnosed Multiple Myeloma at a Tertiary Care Center in North India (IMAGe: 001A Study). *JCO Global Oncology* 2021; 0: 704-715

Evidence to Decision Framework Scoring

Criteria	Detailed considerations	Judgements (points)	Score
What is the baseline quality/strength of the evidence? See above.	Baseline strength of recommendation is listed above	No evidence (0) Low (3) Moderate (4) High (5)	3
What is the value and importance of the outcomes to clinical practice?	Are the outcomes assessed by the studies impactful (e.g., pain reduction, functional improvement, etc.)?	None (0) Low (2) Moderate (3) High (5)	5
What is the magnitude of the desired effect?		None (0) Low (2) Moderate (3) High (5)	5
What is the magnitude of undesirable effects/complications?		High (0) Moderate (1) Low (2) None (3)	0
Do the benefits outweigh the risks?	Do the benefits clearly outweigh the risks or is there a balance of benefits and harms?	No (0) Probably No (1) Uncertain (2) Probably Yes (3) Yes (5)	5
What amount of resources are required to produce the desired effect?	What is the estimated equipment need, space, time, and ability of any institution to provide these needs?	Prohibitive (0) High (1) Moderate (2) Minimal (3) None (5)	1
What is the cost to produce the desired effect?	What is the estimated monetary cost?	Prohibitive (0) High (1) Moderate (2) Minimal (3) None (4)	1
Is the intervention/outcomes acceptable to key stakeholders?	-Are there any stakeholders who wouldn't accept risk to benefit ratio, the costs, the importance of outcomes? -Would anyone morally object to intervention (in regard to ethical principles such as no maleficence, beneficence, or justice)? -Would intervention effect people's autonomy?	No (0) Probably No (1) Uncertain (2) Probably Yes (4) Yes (5)	1
Is the intervention feasible to implement?	-Is intervention sustainable? -Any barriers limiting the feasibility of implementing recommendation?	No (0) Probably No (1) Uncertain (2) Probably Yes (4) Yes (5)	1
Total Score			**21**

7. VTE prophylaxis

No studies met inclusion criteria to make a specific recommendation on VTE prophylaxis for metastatic bone disease of the humerus. In the absence of direct evidence, we refer clinicians to the ASCO, ASH, and ICM-VTE guidelines which indicate that oncology patients are at a higher risk for VTE, and prophylaxis should be considered during the peri-operative period.

Strength of Recommendation

- Aggregate Evidence = **N/A** (No Included Literature)
- EtD Framework Score = **19**
- Combined Strength of Recommendation = **N/A**

Rationale

Both the American Society of Clinical Oncology and the American Society of Hematology (ASCO and ASH) guidelines recommend that patients with cancer without a history of VTE undergoing a major surgical procedure should be offered pharmacologic prophylaxis with either unfractionated heparin or low molecular weight heparin (LMWH), unless contraindicated because of active bleeding or high bleeding risk. The highest risk period for patients is in the perioperative setting in which they are hospitalized and immobilized.

Recommendations from the International Consensus Meeting – Venous Thromboembolism (ICM-VTE) for Shoulder and Elbow state that VTE prophylaxis should be considered in patients undergoing osteosynthesis who are also at high risk of VTE, and those undergoing surgery under general anesthesia that lasts over 90 minutes. Regarding shoulder arthroplasty, in patients without substantial risk factors for VTE, they do not recommend LMWH or direct oral anticoagulants (DOAC). However, they do not comment on those with substantial risk factors for VTE.

The ICM-VTE for Oncology states that all patients with bone metastases undergoing major surgical intervention should be offered pharmacologic thromboprophylaxis unless contraindicated. They state that larger studies are needed to determine optimal pharmacologic thromboprophylaxis between low molecular weight heparin, direct oral anticoagulants, vitamin K antagonists, and aspirin. These would include large, prospective, randomized studies conducted in collaboration with hematology and medical oncology specialists.

Included Evidence:
No evidence met inclusion criteria

Evidence to Decision Framework Scoring

Criteria	Detailed considerations	Judgements (points)	Score
What is the baseline quality/strength of the evidence? See above.	Baseline strength of recommendation is listed above	No evidence (0) Low (3) Moderate (4) High (5)	0
What is the value and importance of the outcomes to clinical practice?	Are the outcomes assessed by the studies impactful (e.g., pain reduction, functional improvement, etc.)?	None (0) Low (2) Moderate (3) High (5)	3
What is the magnitude of the desired effect?		None (0) Low (2) Moderate (3) High (5)	3
What is the magnitude of undesirable effects/complications?		High (0) Moderate (1) Low (2) None (3)	1
Do the benefits outweigh the risks?	Do the benefits clearly outweigh the risks or is there a balance of benefits and harms?	No (0) Probably No (1) Uncertain (2) Probably Yes (3) Yes (5)	3
What amount of resources are required to produce the desired effect?	What is the estimated equipment need, space, time, and ability of any institution to provide these needs?	Prohibitive (0) High (1) Moderate (2) Minimal (3) None (5)	2
What is the cost to produce the desired effect?	What is the estimated monetary cost?	Prohibitive (0) High (1) Moderate (2) Minimal (3) None (4)	3
Is the intervention/outcomes acceptable to key stakeholders?	-Are there any stakeholders who wouldn't accept risk to benefit ratio, the costs, the importance of outcomes? -Would anyone morally object to intervention (in regard to ethical principles such as no maleficence, beneficence, or justice)? -Would intervention effect people's autonomy?	No (0) Probably No (1) Uncertain (2) Probably Yes (4) Yes (5)	0
Is the intervention feasible to implement?	-Is intervention sustainable? -Any barriers limiting the feasibility of implementing recommendation?	No (0) Probably No (1) Uncertain (2) Probably Yes (4) Yes (5)	4
Total Score			**19**

APPENDICES

Appendix I: References

Introduction References

1. DiCaprio MR, Murtaza H, Palmer B, Evangelist M. Narrative review of the epidemiology, economic burden, and societal impact of metastatic bone disease. *Annals of Joint*. 2022;7(0). doi:10.21037/aoj-20-97

2. Saad F, Lipton A, Cook R, Chen YM, Smith M, Coleman R. Pathologic fractures correlate with reduced survival in patients with malignant bone disease. *Cancer*. 2007;110(8):1860-1867. doi:10.1002/cncr.22991

3. Mariotto AB, Enewold L, Zhao J, Zeruto CA, Yabroff KR. Medical Care Costs Associated with Cancer Survivorship in the United States. *Cancer Epidemiology, Biomarkers & Prevention*. 2020;29(7):1304-1312. doi:10.1158/1055-9965.EPI-19-1534

4. Voskuil RT, Mayerson JL, Scharschmidt TJ. Management of Metastatic Disease of the Upper Extremity. *JAAOS - Journal of the American Academy of Orthopaedic Surgeons*. 2021;29(3):e116. doi:10.5435/JAAOS-D-20-00819

5. Jiang, Tracey A. Martin, Lin Ye, Andrew J. Sanders, Jane Lane, Wen G. “Cancer Invasion and Metastasis: Molecular and Cellular Perspective - Madame Curie Bioscience Database - NCBI Bookshelf.” *National Center for Biotechnology Information*, edited by Rahul Jandial, Landes Bioscienc, 2013, https://www.ncbi.nlm.nih.gov/books/NBK164700/.

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2. Grosel, T. W., Plummer, D. R., Everhart, J. S., Kirven, J. C., Ziegler, C. L., Mayerson, J. L., Scharschmidt, T. J., Barlow, J. D. Reverse total shoulder arthroplasty provides stability and better function than hemiarthroplasty following resection of proximal humerus tumors. *Journal of Shoulder & Elbow Surgery* 2019; 11: 2147-2152
3. Herget, G., Saravi, B., Schwarzkopf, E., Wigand, M., Sudkamp, N., Schmal, H., Uhl, M., Lang, G. Clinicopathologic characteristics, metastasis-free survival, and skeletal-related events in 628 patients with skeletal metastases in a tertiary orthopedic and trauma center. *World Journal of Surgical Oncology* 2021; 1: 62
4. Hoellwarth, J. S., Weiss, K., Goodman, M., Heyl, A., Hankins, M. L., McGough, R., 3rd Evaluating the reoperation rate and hardware durability of three stabilizing implants for 105 malignant pathologic humerus fractures. *Injury* 2020; 4: 947-954
5. Houdek, M. T., Bukowski, B. R., Athey, A. G., Elhassan, B. T., Barlow, J. D., Morrey, M. E., Rose, P. S., Wagner, E. R., Sanchez-Sotelo, J. Comparison of reconstructive techniques

following oncologic intraarticular resection of proximal humerus. *Journal of Surgical Oncology* 2021; 1: 133-140

6. Huang, Z., Du, Y., Zhang, X., Liu, H., Liu, S., Xu, T. Clear cell renal cell carcinoma bone metastasis: What should be considered in prognostic evaluation. *European Journal of Surgical Oncology* 2019; 7: 1246-1252
7. Hung, B., Pennington, Z., Hersh, A. M., Schilling, A., Ehresman, J., Patel, J., Antar, A., Porras, J. L., Elsamadicy, A. A., Sciubba, D. M. Impact of race on nonroutine discharge, length of stay, and postoperative complications after surgery for spinal metastases. *Journal of Neurosurgery Spine* 2021; 0: 1-8
8. Laitinen, M., Nieminen, J., Pakarinen, T. K. Treatment of pathological humerus shaft fractures with intramedullary nails with or without cement fixation. *Archives of Orthopaedic & Trauma Surgery* 2011; 4: 503-8
9. Rades, D., Haus, R., Janssen, S., Schild, S. E. An easy-to-use scoring system to estimate the survival of patients irradiated for bone metastases from lung cancer. *Translational Lung Cancer Research* 2020; 4: 1067-1073
10. Rades, D., Haus, R., Janssen, S., Schild, S. E. Interval Between Cancer Diagnosis and Radiotherapy - An Independent Prognostic Factor of Survival in Patients Irradiated for Bone Metastases from Kidney Cancer. *In Vivo* 2020; 2: 767-770
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14. Scott, E., Klement, M. R., Brigman, B. E., Eward, W. C. Beyond Mirels: Factors Influencing Surgical Outcome of Metastasis to the Extremities in the Modern Era. *Journal of Surgical Orthopaedic Advances* 2018; 3: 178-186
15. Vos, M., Ho, V. K. Y., Oosten, A. W., Verhoef, C., Sleijfer, S. Minimal Increase in Survival Throughout the Years in Patients with Soft Tissue Sarcoma with Synchronous Metastases: Results of a Population-Based Study. *Oncologist* 2019; 7: e526-e535
16. Wisanuyotin, T., Sirichativapee, W., Sumnanoont, C., Paholpak, P., Laupattarakasem, P., Sukhonthamarn, K., Kosuwon, W. Prognostic and risk factors in patients with metastatic bone disease of an upper extremity. *Journal of Bone Oncology* 2018; 0: 71-75
17. Wong, E., Chow, E., Zhang, L., Bedard, G., Lam, K., Fairchild, A., Vassiliou, V., Alm El-Din, M. A., Jesus-Garcia, R., Kumar, A., Forges, F., Tseng, L. M., Hou, M. F., Chie, W. C., Bottomley, A. Factors influencing health related quality of life in cancer patients with bone metastases. *Journal of Palliative Medicine* 2013; 8: 915-21

Appendix II: PICO Questions and Inclusion Criteria Used to Define Literature Search

PICO Questions

1. In patients undergoing surgical fixation of the humerus for metastatic bone disease, does plating/internal fixation, intramedullary fixation, and/or photodynamic polymer reduce local disease progression, revision rates, reoperations, time to union, pain, QoL and other relevant patient-reported outcomes?
2. In patients with metastatic bones disease undergoing surgical intervention of the humerus, is en bloc resection associated with better disease control/defined outcomes than curettage (intralesional resection), internal fixation, and/or intramedullary nailing?
3. In patients with metastatic disease of the humerus and a pathologic/impending/displaced humerus fracture (excluding osteoporotic fracture, fragility fracture) who have not undergone surgery, which patients are best served utilizing nonsurgical techniques versus surgical techniques?
4. In patients undergoing surgical fixation of the humerus for metastatic bone disease, does cementation vs no cementation reduce local disease progression, revision rates, reoperations, time to union, pain, QoL and other relevant patient-reported outcomes?
5. For patients with metastatic bone disease undergoing arthroplasty to reconstruct the proximal humerus for metastatic humeral bone disease, which reconstruction approach (conventional vs. reverse) is preferred in terms of resulting in better/improved patient-reported outcomes?
6. In patients with metastatic malignancies, disease, myeloma etc, which factors affect patient outcomes (disease burden, histology, socioeconomic, insurance status, race, sex, gender, medical co-morbidities, health literacy, etc.)?
7. In patients with metastatic bone disease undergoing surgical intervention, does type of VTE prophylaxis and/or use (vs. no use) of VTE prophylaxis affect postoperative complications?

Inclusion Criteria

Standard Criteria for all CPGs

1. Article must be a full article report of a clinical study.
2. Medical records review, meeting abstracts, historical articles, editorials, letters, and commentaries are excluded. Bibliographies of meta-analyses and systematic reviews will be examined to ensure inclusion of all relevant literature.
3. Confounded studies (i.e. studies that give patients the treatment of interest AND another treatment) are excluded.
4. Composite measures or outcomes are excluded even if they are patient-oriented.
5. Study must appear in a peer-reviewed publication
6. Study must be of humans
7. Study must be published in English
8. Study results must be quantitatively presented
9. Study must not be an in vitro study
10. Study must not be a biomechanical study
11. Study must not have been performed on cadavers
12. Surrogate outcomes are evaluated only when no patient-oriented outcomes are available.

Project Dependent Criteria
A priori article inclusion criteria are constructed for all CPGs. These criteria are our "rules of evidence" and articles that did not meet them are, for the purposes of this guideline, not evidence.
The following criteria may be adjusted by the GDG prior to beginning the systematic literature review, depending on the topic under study:

1. Study must be published in or after <**1990**>
2. Study should have < **5** > or more patients per group
3. For surgical treatment a minimum of: **no minimum**
4. For nonoperative treatment a minimum of: **no minimum**

Patient population definitions:

- Study must be of adults with Metastatic Disease of the Humerus (include myeloma, lymphoma, metastatic sarcoma)
  - Adults>= 18
  - Excluding osteoporotic and fragility Fxs; Excluding any pathologic Fxs related to genetics or other bone metabolism diseases, metastatic disease of other bones)
  - Mixed populations acceptable?: yes
- Authors must report specific stratifications of number of patient type (location of disease, indication for Tx, diagnosis)

Agreement Threshold for Voting on Final Recommendations:

- Supermajority (three-fourths; 75%)

Best Available Evidence
When examining primary studies, we will analyze the best available evidence regardless of study design. We will first consider randomized controlled trials identified by the search strategy. In the absence of two or more RCTs, we will sequentially search for prospective controlled trials, prospective comparative studies, retrospective comparative studies, and prospective case-series studies. Only studies of the highest level of available evidence are included, assuming that there were 2 or more studies of that higher level. For example, if there are two Level II studies that address the recommendation, Level III and IV studies are not included

Appendix III: Quality Appraisal

KEY:
High Risk of Bias = ○
Unclear Risk of Bias = ◑
No/Minimal Risk of Bias = ●

Study	Patient Spectrum	Participant Recruitment	Treatment recording	Confounding Variables	Outcome measurement bias	Incomplete Outcome Data	Adequate Reporting	Strength
Dijkstra, S., 1996	●	●	●	●	●	●	●	Low Quality
Grosel, T. W., 2019	●	◑	○	◑	●	●	●	Low Quality
Herget, G., 2021	●	○	○	○	●	●	●	Low Quality
Hoellwarth, J. S., 2020	●	●	●	●	●	●	●	Low Quality
Houdek, M. T., 2021	●	◑	○	○	●	●	●	Low Quality
Huang, Z., 2019	●	○	◑	○	●	●	●	Low Quality
Hung, B., 2021	●	○	○	○	●	●	●	Low Quality
Laitinen, M., 2011	●	○	○	○	●	●	●	Low Quality
Rades, D., 2019	●	○	○	○	●	●	●	Low Quality
Rades, D., 2020	●	○	○	○	●	●	●	Low Quality
Rades, D., 2020	●	○	○	○	●	●	●	Low Quality
Raschka, T., 2022	●	◑	○	○	●	●	●	Low Quality
Sarahrudi, K., 2009	●	◑	○	○	◑	●	●	Low Quality
Scott, E., 2018	●	◑	○	○	●	●	●	Low Quality

Study	Patient Spectrum	Participant Recruitment	Treatment recording	Confounding Variables	Outcome measurement bias	Incomplete Outcome Data	Adequate Reporting	Strength
Vos, M., 2019	●	◑	○	○	●	●	●	Low Quality
Wisanuyotin, T., 2018	●	◑	○	◑	○	●	●	Low Quality
Wong, E., 2013	●	◑	○	◑	○	●	●	Low Quality

Appendix IV: Literature Search Strategy

Literature Search Methods

The medical librarian conducted a comprehensive search of MEDLINE, Embase, and the Cochrane Library based on key terms and concepts from the workgroup-defined PICO questions. Bibliographies of relevant systematic reviews were hand searched for additional references. All databases were last searched on May 9, 2022 with limits for English-language publications with publication dates from 1990 to present.

PRISMA Diagram Data

Records identified through database searching: 5,449
Records after duplicates removed: 3,913
Additional records identified through other sources: 1
Records screened: 3,914

Literature Search Strategies by Database

Database: Ovid MEDLINE® and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions ® 1946 to May 8, 2022
Interface: Ovid (http://ovidsp.ovid.com/autologin)
Date Searched: 5/9/2022

Line	Search Strategy
1	English.lg.
2	(exp Animals/ NOT Humans/) OR exp Cadaver/ OR (animal? OR dog OR dogs OR sheepdog OR canine OR cats OR feline OR horse? OR equine OR mouse OR mice OR murine OR rat OR rats OR rabbit? OR sheep OR ovine OR porcine OR pig OR pigs OR rodent? OR monkey? OR hen OR hens OR veterinar* OR avian OR reindeer OR dolphin).ti. OR cadaver*.ti,ab. OR in-vitro.ti. OR ((comment OR editorial OR letter OR historical article) NOT clinical trial).pt. OR address.pt. OR news.pt. OR newspaper article.pt. OR pmcbook.af. OR case reports.pt. OR (case report? OR abstracts OR editorial OR reply OR comment? OR commentary OR letter).ti.
3	1 NOT 2
4	limit 3 to yr=1990-Current
5	exp Humerus/ OR Humeral-Fractures/ OR (humer* OR (long ADJ (bone? OR limb?))).ti,ab.
6	exp Neoplasms/sc OR exp Neoplasm-Metastasis/ OR (metasta* OR ((disseminat* OR spread*) ADJ2 (disease OR tumo?r* OR malignan* OR lesion?)) OR (lymphoma* NOT (primary ADJ4 lymphoma*)) OR myeloma* OR (tumo?r* ADJ3 lesion?) OR (pathologic* ADJ5 fracture?) OR (secondar* ADJ5 (tumo?r* OR neoplas* OR malignan* OR chondrosarcoma*)) OR (tumo?r* ADJ4 invad*)).ti,ab.
7	4 AND 5 AND 6
8	(exp Infant/ OR exp Child/ OR exp Adolescent/ OR (p?ediatric* OR child OR children OR childhood OR adolescen* OR juvenile? OR teen OR teens OR teenager? OR youth? OR infant*).ti.) NOT (exp Adult/ OR adult*.ti. OR (elderly OR geriatric? OR (older ADJ (adult? OR people OR person? OR women OR men OR patient?))).ti,ab. OR (mean-age ADJ3 18*).ab.)
9	7 NOT 8

10	exp Bone-and-Bones/ OR exp Bone-Neoplasms/ OR (bone? OR extremit* OR hip OR vertebra* OR spine OR spinal OR osteosarcoma* OR skelet*).ti,ab.
11	(10 AND 6 AND 4) NOT 8
12	Venous-Thrombosis/ OR Thrombophlebitis/ OR Venous-Thromboembolism/ OR (dvt OR vte OR thrombos* OR thrombotic OR thromboembol* OR thrombophlebitis).ti,ab.
13	exp Anticoagulants/ OR (anticoagul* OR anti-coagul*).ti,ab. OR exp Fibrinolytic-Agents/ OR exp Thrombolytic-Therapy/ OR (antithromb* OR thrombolytic* OR thromboprophyla* OR chemoprophyla*).ti,ab. OR exp Platelet Aggregation Inhibitors/ OR (antiplatelet* OR anti-platelet*).ti,ab. OR exp Heparin/ OR (heparin* OR dalteparin OR Fragmin OR tinzaparin OR Innohep OR enoxaparin OR Lovenox).ti,ab. OR Clopidogrel/ OR (Plavix OR clopidogrel).ti,ab. OR Warfarin/ OR (Coumadin OR Jantoven OR warfarin*).ti,ab. OR exp Antithrombins/ OR Fondaparinux/ OR Dabigatran/ OR (Arixtra OR factor-Xa-inhibitor* OR rivaroxaban OR Xarelto OR apixaban OR Eliquis OR edoxaban OR Savaysa OR betrixaban OR Bevyxxa OR bivalirudin OR Angiomax OR lepirudin OR Refludan OR dabigatran OR Pradaxa OR desirudin OR Iprivask).ti,ab. OR exp Aspirin/ OR aspirin.ti,ab.
14	Stockings-Compression/ OR (compression ADJ (stocking? OR device?)).ti,ab. OR Intermittent-Pneumatic-Compression-Devices/ OR (foot AND pump?).ti,ab. OR ((pneumatic OR leg OR calf) ADJ compression).ti,ab. OR (mechanical ADJ3 prophyla*).ti,ab.
15	(11 AND 12 AND (13 OR 14))
16	9 OR 15
17	Healthcare-Disparities/ OR Health-Status-Disparities/ OR exp Sociological-Factors/ OR exp Socioeconomic-Factors/ OR Race-Factors/ OR Sex-Factors/ OR exp Insurance-Coverage/ OR exp *Health-Facilities/ OR exp *Population/ OR exp Population-Groups/ OR ((race OR racial* OR sex OR sexual OR male OR female OR age OR gender OR transgender OR social OR socio* OR insurance OR insured OR uninsured OR ethnic* OR demographic* OR black OR disabilit* OR disabled OR handicap*) ADJ5 (difference? OR disparit* OR impact* OR outcome? OR effect? OR predict* OR factor? OR prognos* OR risk? OR correlat* OR related OR relationship? OR determinant*)).ti,ab. OR (exp Health-Facilities/ AND (facilit* OR center? OR hospital? OR clinic?).ti.)
18	exp Regression-Analysis/ OR exp Analysis-of-Variance/ OR (regression OR ((varia* OR univaria* OR multivaria* OR Cox) ADJ5 (analys* OR model* OR tests))).ti,ab.
19	11 AND 17 AND 18
20	19 OR 16
21	((exp *Bone Diseases, Metabolic/ OR *Osteoporotic-Fractures/ OR exp *Metabolic-Diseases/) NOT exp *Neoplasm-Metastasis/) OR (osteoporo* OR diabet* OR ((fragility OR insufficiency OR low-energy) ADJ4 fracture?)).ti.
22	20 NOT 21

Database: Embase

Interface: Elsevier (https://embase.com)
Date Searched: 5/9/2022

Line	Search Strategy
1	[english]/lim
2	abstract-report/de OR book/de OR editorial/de OR editorial:it OR note/de OR note:it OR letter/de OR letter:it OR case-study/de OR case-report/de OR chapter:it OR conference-paper/exp OR conference-paper:it OR conference-abstract:it OR conference-review:it OR (abstracts OR editorial OR reply OR comment$ OR commentary OR letter):ti OR cadaver/de OR in-vitro-study/exp OR cadaver*:ti,ab OR in-vitro:ti OR animal-experiment/exp OR (animal$ OR dog OR dogs OR sheepdog OR canine OR cats OR feline OR horse$ OR equine OR mouse OR mice OR murine OR rat OR rats OR rabbit$ OR sheep OR ovine OR porcine OR pig OR pigs OR rodent$ OR monkey$ OR hen OR hens OR veterinar* OR avian OR reindeer OR dolphin):ti
3	(#1 NOT #2) AND [1990-3000]/py
4	humerus/exp OR humerus-fracture/exp OR long-bone/de OR (humer* OR (long NEXT/1 (bone$ OR limb$))):ti,ab
5	metastasis/exp OR (metasta* OR ((disseminat* OR spread*) NEAR/2 (disease OR tumo$r* OR malignan* OR lesion$)) OR myeloma* OR (lymphoma* NOT (primary NEAR/4 lymphoma*)) OR (tumo$r* NEAR/3 lesion$) OR (pathologic* NEXT/5 fracture$) OR (secondar* NEXT/5 (tumo$r* OR neoplas* OR malignan* OR chondrosarcoma*)) OR (tumo$r* NEAR/4 invad*)):ti,ab
6	#3 AND #4 AND #5
7	(Juvenile/exp OR (p$ediatric* OR child OR children OR childhood OR adolescen* OR juvenile$ OR teen OR teens OR teenager$ OR youth$ OR infant*):ti) NOT (adult/exp OR adult*:ti OR (elderly OR geriatric$ OR (older NEXT/1 (adult$ OR people OR person$ OR women OR men OR patient$))):ti,ab OR (mean-age NEXT/3 18*):ab)
8	#6 NOT #7
9	bone/exp or bone-tumor/exp OR (bone$ OR extremit* OR hip OR vertebra* OR spine OR spinal OR osteosarcoma* OR skelet*):ti,ab
10	(#9 AND #5 AND #3) NOT #7
11	vein-thrombosis/exp OR thromboembolism/exp OR (dvt OR vte OR thrombos* OR thrombotic OR thromboembol* OR thrombophlebitis):ti,ab OR ((pulmonary OR lung$) AND (infarct* OR embol* OR clot*)):ti,ab
12	anticoagulant-agent/exp OR (anticoagul* OR anti-coagul*):ti,ab OR fibrinolytic-agent/exp OR fibrinolytic-therapy/exp OR chemoprophylaxis/de OR blood-clotting-inhibitor/exp OR antithrombocytic-agent/exp OR thrombocyte-aggregation-inhibition/de OR (antithromb* OR thrombolytic* OR thromboprophyla* OR chemoprophyla*):ti,ab OR (antiplatelet* OR anti-platelet*):ti,ab OR heparin/exp OR heparin-derivative/exp OR (heparin* OR dalteparin OR Fragmin OR tinzaparin OR Innohep OR enoxaparin OR Lovenox):ti,ab OR clopidogrel/exp OR (Plavix OR clopidogrel):ti,ab OR warfarin/exp OR (Coumadin OR Jantoven OR warfarin*):ti,ab OR dabigatran-etexilate/exp OR (Arixtra OR fondaparinux OR factor-Xa-inhibitor* OR rivaroxaban OR Xarelto OR apixaban OR Eliquis OR edoxaban OR Savaysa OR betrixaban OR Bevyxxa OR bivalirudin OR Angiomax OR lepirudin OR Refludan OR

	dabigatran OR Pradaxa OR desirudin OR desulfatohirudin OR Iprivask OR argatroban OR aspirin):ti,ab
13	compression-garment/exp OR (compression NEXT/1 (stocking$ OR device$)):ti,ab OR intermittent-pneumatic-compression-device/de OR (foot AND pump$):ti,ab OR ((pneumatic OR leg OR calf) NEXT/1 compression):ti,ab OR (mechanical NEXT/3 prophyla*):ti,ab
14	(#10 AND #11 AND (#12 OR #13))
15	#8 OR #14
16	health-care-disparity/de OR social-status/exp OR ethnic-or-racial-aspects/exp OR gender/exp OR sex-difference/exp OR sex/de OR population/exp OR demography/exp OR population-parameters/exp OR population-research/de OR population-group/exp OR health-insurance/exp OR ((race OR racial* OR sex OR sexual OR male OR female OR age OR gender OR transgender OR social OR socio* OR insurance OR insured OR uninsured OR ethnic* OR demographic* OR black OR disabilit* OR disabled or handicap*) NEAR/5 (difference$ OR disparit* OR impact* OR outcome$ OR effect$ OR predict* OR factor$ OR prognos* OR risk$ OR correlat* OR related OR relationship$ OR determinant*)):ti,ab OR (health-care-facilities-and-services/exp AND (facilit* OR center$ OR hospital$ OR clinic$):ti)
17	regression-analysis/exp OR analysis-of-variance/de OR (regression OR ((varia* OR univaria* OR multivaria* OR Cox) NEAR/5 (analys* OR model* OR tests))):ti,ab
18	#10 AND #16 AND #17
19	#18 OR #15
20	((metabolic-bone-disease/exp/mj OR fragility-fracture/mj OR metabolic-disorder/exp/mj) NOT metastasis/exp/mj) OR (osteoporo* OR diabet* OR ((fragility OR insufficiency OR low-energy) NEAR/4 fracture$)):ti
21	#19 NOT #20

Database: Cochrane Library
Interface: Wiley (https://www.cochranelibrary.com/central)
Date Searched: 5/9/2022

Line	Search Strategy
1	(humer* OR (long NEXT/1 (bone? OR limb?))):ti,ab
2	(metasta* OR ((disseminat* OR spread*) NEAR/2 (disease OR tumo?r* OR malignan* OR lesion?)) OR (lymphoma* NOT (primary NEAR/4 lymphoma*)) OR myeloma* OR (tumo?r* NEAR/3 lesion?) OR (pathologic* NEXT/5 fracture?) OR (secondar* NEXT/5 (tumo?r* OR neoplas* OR malignan* OR chondrosarcoma*)) OR (tumo?r* NEAR/4 invad*)):ti,ab
3	#1 AND #2
4	(bone? or extremit* or hip or vertebra* or spine or spinal OR osteosarcoma* OR skelet*):ti,ab

5	#4 AND #2
6	(dvt OR vte OR thrombos* OR thrombotic OR thromboembol* OR thrombophlebitis OR ((pulmonary OR lung?) AND (infarct* OR embol* OR clot*))):ti,ab
7	(anticoagul* OR "anti coagul*"):ti,ab OR (antithromb* OR thrombolytic* OR thromboprophyla* OR chemoprophyla*):ti,ab OR (antiplatelet* OR (anti NEXT/1 platelet*)):ti,ab OR (heparin* OR dalteparin OR Fragmin OR tinzaparin OR Innohep OR enoxaparin OR Lovenox):ti,ab OR (Plavix OR clopidogrel):ti,ab OR (Coumadin OR Jantoven OR warfarin*):ti,ab OR (Arixtra OR fondaparinux OR (factor NEXT/1 Xa NEXT/1 inhibitor*) OR rivaroxaban OR Xarelto OR apixaban OR Eliquis OR edoxaban OR Savaysa OR betrixaban OR Bevyxxa OR bivalirudin OR Angiomax OR lepirudin OR Refludan OR dabigatran OR Pradaxa OR desirudin OR desulfatohirudin OR Iprivask OR argatroban OR aspirin):ti,ab
8	(compression NEXT/1 (stocking? OR device?)):ti,ab OR (foot AND pump?):ti,ab OR ((pneumatic OR leg OR calf) NEXT/1 compression):ti,ab OR (mechanical NEXT/3 prophyla*):ti,ab
9	#5 AND #6 AND (#7 OR #8)
10	#3 OR #9
11	((race OR racial* OR sex OR sexual OR male OR female OR age OR gender OR transgender OR social OR socio* OR insurance OR insured OR uninsured OR ethnic* OR demographic* OR black OR disabilit* OR disabled OR handicap*) NEAR/5 (difference? OR disparit* OR impact* OR outcome? OR effect? OR predict* OR factor? OR prognos* OR risk? OR correlat* OR related OR relationship? OR determinant*)):ti,ab OR ([mh "Health Facilities"] AND (facilit* OR center? OR hospital? OR clinic?):ti)
12	(regression OR ((varia* OR univaria* OR multivaria* OR Cox) NEAR/5 (analys* OR model* OR tests))):ti,ab
13	#5 AND #11 AND #12
14	#10 OR #13
15	"conference abstract":pt OR (abstracts OR editorial OR reply OR comment? OR commentary OR letter):ti OR cadaver*:ti,ab OR "in vitro":ti OR (animal? OR dog OR dogs OR sheepdog OR canine OR cats OR feline OR horse? OR equine OR mouse OR mice OR murine OR rat OR rats OR rabbit? OR sheep OR ovine OR porcine OR pig OR pigs OR rodent? OR monkey? OR hen OR hens OR veterinar* OR avian OR reindeer OR dolphin):ti
16	([mh Infant] OR [mh Child] OR [mh Adolescent] OR (pediatric* OR paediatric* OR child OR children OR childhood OR adolescen* OR juvenile? OR teen OR teens OR teenager? OR youth? OR infant*):ti) NOT ([mh Adult] OR adult*:ti OR (elderly OR geriatric? OR (older NEXT/1 (adult? OR people OR person? OR women OR men OR patient?))):ti,ab OR (mean-age NEXT/3 18*):ab)
17	(osteoporo* OR diabet* OR ((fragility OR insufficiency OR "low energy") NEAR/4 fracture?)):ti
18	#14 NOT (#15 OR #16 OR #17) *with Publication Year from 1990 to 2022, in Trials*
19	#14 NOT (#15 OR #16 OR #17) *with Cochrane Library publication date from Jan 1990 to Feb 2022, in Cochrane Reviews*
20	#18 OR #19

Appendix V: Excluded literature not meeting inclusion criteria

Article Title	Authors	Year	Reason for Exclusion
Prevalence and countermeasures for venous thromboembolic diseases associated with spinal surgery: A follow-up study of an institutional protocol in 209 patients	Akeda, K.; Matsunaga, H.; Imanishi, T.; Hasegawa, M.; Sakakibara, T.; Kasai, Y.; Sudo, A.	2014	patient population, only 21 pts had metastatic bone disease
Extra-articular shoulder resections: outcomes of 54 patients	Angelini, A.; Mavrogenis, A. F.; Trovarelli, G.; Pala, E.; Arbelaez, P.; Casanova, J.; Berizzi, A.; Ruggieri, P.	2017	irrelevant topic; no metastatic bone disease
Risk factors of distant metastasis after surgery among different breast cancer subtypes: a hospital-based study in Indonesia	Anwar, S. L.; Avanti, W. S.; Nugroho, A. C.; Choridah, L.; Dwianingsih, E. K.; Harahap, W. A.; Aryandono, T.; Wulaningsih, W.	2020	irrelevant topic; risk of metastatic disease
What Factors Are Associated with Local Metastatic Lesion Progression After Intramedullary Nail Stabilization?	Arpornsuksant, P.; Morris, C. D.; Forsberg, J. A.; Levin, A. S.	2021	irrelevant comparison; no treatment comparison; pts <18 years old
Complications of Percutaneous Bone Tumor Cryoablation: A 10-year Experience	Auloge, P.; Cazzato, R. L.; Rousseau, C.; Caudrelier, J.; Koch, G.; Rao, P.; Chiang, J. B.; Garnon, J.; Gangi, A.	2019	irrelevant topic; no humerus
Predictors of short-term mortality in critically ill patients with solid malignancies	Azoulay, E.; Moreau, D.; Alberti, C.; Leleu, G.; Adrie, C.; Barboteu, M.; Cottu, P.; Levy, V.; Le Gall, J. R.; Schlemmer, B.	2000	Irrelevant topic; Non-metastatic cancer
Comparison of outcomes of 2 surgical treatments for proximal humerus giant cell tumors: a multicenter retrospective study	Bai, W. Z.; Guo, S. B.; Zhao, W.; Yu, X. C.; Xu, M.; Zheng, K.; Hu, Y. C.; Wang, F.; Zhang, G. C.	2019	irrelevant topic; no metastatic bone disease

Article Title	Authors	Year	Reason for Exclusion
Demographics, Pattern of Care, and Outcome Analysis of Malignant Melanomas - Experience From a Tertiary Cancer Centre in India	Bajpai, J.; Abraham, G.; Saklani, A. P.; Agarwal, A.; Das, S.; Chatterjee, A.; Kapoor, A.; Eaga, P.; Mondal, P. K.; Chandrasekharan, A.; Bhargava, P. G.; Srinivas, S.; Turkar, S.; Rekhi, B.; Khanna, N.; Janu, A. K.; Bal, M.; Ostwal, V. S.; Ramaswamy, A.; Rohila, J.; Desouza, A. L.; Guha, A.; Kumar, R.; Menon, N. S.; Rath, S.; Patil, V. M.; Noronha, V. M.; Joshi, A. P.; Laskar, S.; Rangarajan, V.; Prabhash, K.; Gupta, S.; Banavali, S.	2021	irrelevant comparison; metastatic vs non-metastatic
Pathological fractures; a consideration with metachondromatosis and differential diagnoses. Osteochondromatosis and Gauchers disease	Banks, R. J.	2002	irrelevant topic; Goucher's disease
Treatment of pathological fractures of the humerus with a locked intramedullary nail	Bauze, A. J.; Clayer, M. T.	2003	no comparison group
Prognostic factors affecting survival of patients with pathologic humerus shaft fractures treated with intramedullary nailing without tumor removal	Bayram, S.; Ozmen, E.; Birisik, F.; Kiral, D.; Salduz, A.; Ersen, A.	2019	no comparison group
Treatment of venous thromboembolism in cancer patients: The dark side of the moon	Becattini, C.; Di Nisio, M.; Franco, L.; Lee, A.; Agnelli, G.; Mandala, M.	2021	Irrelevant topic; Review article
Risk factors for same-admission mortality after pathologic fracture secondary to metastatic cancer	Behnke, N. K.; Baker, D. K.; Xu, S.; Niemeier, T. E.; Watson, S. L.; Ponce, B. A.	2017	irrelevant topic; spinal metastases
Humeral Nail: Comparison of the Antegrade and Retrograde Application	Bencic, I.; Cengic, T.; Prenc, J.; Bulatovic, N.; Matejcic, A.	2016	irrelevant comparison; fracture type, not treatment type
Inferior vena cava filters prevent pulmonary emboli in patients with metastatic pathologic fractures of the lower extremity	Benevenia, J.; Bibbo, C.; Patel, D. V.; Grossman, M. G.; Bahramipour, P. F.; Pappas, P. J.	2004	irrelevant topic; vena cava filters
Outcomes of a Modular Intercalary Endoprosthesis as Treatment for Segmental Defects of the Femur, Tibia, and Humerus	Benevenia, J.; Kirchner, R.; Patterson, F.; Beebe, K.; Wirtz, D. C.; Rivero, S.; Palma, M.; Friedrich, M. J.	2016	not all pts have metastatic bone disease

Article Title	Authors	Year	Reason for Exclusion
Supplemental Bone Grafting in Giant Cell Tumor of the Extremity Reduces Nononcologic Complications	Benevenia, J.; Rivero, S. M.; Moore, J.; Ippolito, J. A.; Siegerman, D. A.; Beebe, K. S.; Patterson, F. R.	2017	irrelevant topic; no humerus/metastatic bone disease
Economic burden of skeletal-related events in patients with multiple myeloma: analysis of US commercial claims database	Bhowmik, D.; Hines, D. M.; Intorcia, M.; Wade, R. L.	2018	irrelevant topic; skeletal-related events vs non-skeletal-related events
Function after resection of humeral metastases: analysis of 59 consecutive patients	Bickels, J.; Kollender, Y.; Wittig, J. C.; Meller, I.; Malawer, M. M.	2005	irrelevant comparison: endoprosthesis vs cemented nailing
Focal anatomic resurfacing implantation for bilateral humeral and femoral heads' avascular necrosis in a patient with Hodgkin's lymphoma and literature review	Bilge, O.; Doral, M. N.; Miniaci, A.	2015	Case Report
Incidence of venous thrombosis in a large cohort of 66,329 cancer patients: results of a record linkage study	Blom, J. W.; Vanderschoot, J. P.; Oostindier, M. J.; Osanto, S.; van der Meer, F. J.; Rosendaal, F. R.	2006	risk factors, not postop
Pathologic fracture and healthcare resource utilisation: A retrospective study in eight European countries	Body, J. J.; Acklin, Y. P.; Gunther, O.; Hechmati, G.; Pereira, J.; Maniadakis, N.; Terpos, E.; Finek, J.; von Moos, R.; Talbot, S.; Sleeboom, H.	2016	irrelevant outcomes
Young age and autologous stem cell transplantation are associated with improved survival in newly diagnosed multiple myeloma	Bove, V.; Garrido, D.; Riva, E.	2021	irrelevant comparison
Humeral stress shielding following cemented endoprosthetic reconstruction: An under-reported complication?	Braig, Z. V.; Tagliero, A. J.; Rose, P. S.; Elhassan, B. T.; Barlow, J. D.; Wagner, E. R.; Sanchez-Sotelo, J.; Houdek, M. T.	2021	irrelevant topic; stress shielding
Gender, anthropometric factors and risk of colorectal cancer with particular reference to tumour location and TNM stage: a cohort study	Brandstedt, J.; Wangefjord, S.; Nodin, B.; Gaber, A.; Manjer, J.; Jirstrom, K.	2012	irrelevant topic; colorectal cancer

Article Title	Authors	Year	Reason for Exclusion
Analysis of predictors of pain response in patients with bone metastasis undergoing palliative radiotherapy: Does age matter?	Cacicedo, J.; Gomez-Iturriaga, A.; Navarro, A.; Morillo, V.; Willisch, P.; Lopez-Guerra, J. L.; Illescas, A.; Casquero, F.; Del Hoyo, O.; Ciervide, R.; Martinez-Indart, L.; Bilbao, P.; Rades, D.	2018	irrelevant topic; palliative care
Reconstruction by allograft-prosthetic composite reverse shoulder arthroplasty after proximal humerus tumor resection: clinical and radiographic assessment at a minimum 2 years' follow-up	Callamand, G.; Barret, H.; Saint-Genez, F.; Bonnevialle, P.; Mansat, P.; Bonnevialle, N.	2021	No comparison group
Prosthetic joint replacement for long bone metastases: Analysis of 154 cases	Camnasio, F.; Scotti, C.; Peretti, G. M.; Fontana, F.; Fraschini, G.	2008	Irrelevant topic; patient population not all humerus
Prognostic factors for survival in patients with metastatic lung adenocarcinoma: An analysis of the SEER database	Campos-Balea, B.; de Castro Carpeno, J.; Massuti, B.; Vicente-Baz, D.; Perez Parente, D.; Ruiz-Gracia, P.; Crama, L.; Cobo Dols, M.	2020	irrelevant topic; SEER database used
New concepts in the surgical treatment of actual and impending pathological fractures in metastatic disease	Cappellari, A.; Trovarelli, G.; Crimi, A.; Pala, E.; Angelini, A.; Berizzi, A.; Ruggieri, P.	2020	irrelevant comparison; plate vs prosthesis
Humeral metastasis of renal cancer: Surgical options and review of literature	Casadei, R.; Drago, G.; Di Pressa, F.; Donati, D.	2018	no comparison group
Metastatic renal cell carcinoma: Patterns and predictors of metastases-A contemporary population-based series	Chandrasekar, T.; Klaassen, Z.; Goldberg, H.; Kulkarni, G. S.; Hamilton, R. J.; Fleshner, N. E.	2017	Irrelevant topic; predictors of metastatic disease
Comparison of the use of the humerus intramedullary nail and dynamic compression plate for the management of diaphyseal fractures of the humerus. A randomised controlled study	Changulani, M.; Jain, U. K.; Keswani, T.	2007	irrelevant topic; no tumors
Prognosis-Based Shoulder Hemiarthroplasty After Resection of Proximal Humeral Malignancy	Chen, C. M.; Wu, P. K.; Tsai, S. W.; Chen, C. F.; Chen, W. M.	2017	Irrelevant topic; patient population, some <18 years old
Ante-grade intramedullary nailing for the treatment of humeral shaft metastatic bone tumor	Chen, J. L.; Yeh, T. T.; Pan, R. Y.; Wu, C. C.	2014	case series

Article Title	Authors	Year	Reason for Exclusion
Prognostic factors and survival according to tumor subtype in newly diagnosed breast cancer with liver metastases: A competing risk analysis	Chen, Q. F.; Huang, T.; Shen, L.; Wu, P.; Huang, Z. L.; Li, W.	2019	irrelevant topic; SEER database used
Risk factors for bone metastasis from renal cell cancer	Chen, X. Y.; Lan, M.; Zhou, Y.; Chen, W. Z.; Hu, D.; Liu, J. M.; Huang, S. H.; Liu, Z. L.; Zhang, Z. H.	2017	irrelevant topic; bone metastasis vs no bone metastasis
Risk factors and prognostic predictors for Cervical Cancer patients with lung metastasis	Chen, X.; Chen, L.; Zhu, H.; Tao, J.	2020	irrelevant topic; SEER database used
Role of BMI and age in predicting pathologic vertebral fractures in newly diagnosed multiple myeloma patients: A retrospective cohort study	Chen, Y. L.; Liu, Y. C.; Wu, C. H.; Yeh, C. M.; Chiu, H. I.; Lee, G. Y.; Lee, Y. T.; Hsu, P.; Lin, T. W.; Gau, J. P.; Hsiao, L. T.; Chiou, T. J.; Liu, J. H.; Liu, C. J.	2018	irrelevant topic; spinal metastases
Reconstruction of the Shoulder and Humerus in Metastatic Bone Disease	Cheng, E. Y.; Ogilvie, C. M.	2019	review
Long bone fractures: treatment patterns and factors contributing to use of intramedullary nailing	Chitnis, A.; Ray, B.; Sparks, C.; Grebenyuk, Y.; Vanderkarr, M.; Holy, C. E.	2020	irrelevant comparison; metastatic cancer vs not
Intramedullary Nailing for Pathological Fractures of the Proximal Humerus	Choi, E. S.; Han, I.; Cho, H. S.; Park, I. W.; Park, J. W.; Kim, H. S.	2016	irrelevant comparison; only compares nailing to other study results
Skeletal Complications and Mortality in Thyroid Cancer: A Population-Based Study	Choksi, P.; Papaleontiou, M.; Guo, C.; Worden, F.; Banerjee, M.; Haymart, M.	2017	irrelevant topic; SEER database used
Gender differences in pain and patient reported outcomes: a secondary analysis of the NCIC CTG SC. 23 randomized trial	Chow, S.; Ding, K.; Wan, B. A.; Brundage, M.; Meyer, R. M.; Nabid, A.; Chabot, P.; Coulombe, G.; Ahmed, S.; Kuk, J.; Dar, A. R.; Mahmud, A.; Fairchild, A.; Wilson, C. F.; Wu, J. S. Y.; Dennis, K.; DeAngelis, C.; Wong, R. K. S.; Zhu, L.; Chow, E.	2017	irrelevant topic; vertebrae and hip/pelvis radiotherapy

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Patient Reported Outcomes After Radiation Therapy for Bone Metastases as a Function of Age: A Secondary Analysis of the NCIC CTG SC-Twenty-Three Randomized Trial	Chow, S.; Ding, K.; Wan, B. A.; Brundage, M.; Meyer, R. M.; Nabid, A.; Chabot, P.; Coulombe, G.; Ahmed, S.; Kuk, J.; Dar, A. R.; Mahmud, A.; Fairchild, A.; Wilson, C. F.; Wu, J. S. Y.; Dennis, K.; DeAngelis, C.; Wong, R. K. S.; Zhu, L.; Chow, E.	2018	Irrelevant topic; out-comes of radiotherapy as a function of age
Analysis of 90-Day Readmissions After Total Shoulder Arthroplasty	Chung, A. S.; Makovicka, J. L.; Hydrick, T.; Scott, K. L.; Arvind, V.; Hattrup, S. J.	2019	irrelevant topic; readmissions
Hospitalization of hospice patients with cancer	Cintron, A.; Hamel, M. B.; Davis, R. B.; Burns, R. B.; Phillips, R. S.; McCarthy, E. P.	2003	Irrelevant topic; patient population, primary lung or colorectal cancer
Surgical treatment in bone metastases in the appendicular skeleton	Clara-Altamirano, M. A.; Garcia-Ortega, D. Y.; Martinez-Said, H.; Caro-Sanchez, C. H. S.; Herrera-Gomez, A.; Cuellar-Hubbe, M.	2018	irrelevant comparison; 8 subjects with humerus tumor, no comparison treatment
Intramedullary Nail Fixation for the Treatment of Pathologic Humeral Shaft Fractures	Colello, M. J.; Hunter, M. D.; Tanner, S. L.; Porter, S. E.	2020	irrelevant topic; reamed vs unreamed nails
The invisible nail: a technique report of treatment of a pathological humerus fracture with a radiolucent intramedullary nail	Collis, P. N.; Clegg, T. E.; Seligson, D.	2011	review
Constrained or unconstrained shoulder replacement for musculoskeletal tumor resections?	Cundy, W. J.; McArthur, M. S.; Dickinson, I. C.; Rowell, P. D.; Sommerville, S. M. M.	2020	irrelevant topic; constrained vs unconstrained
Predictors of overall survival in non-small-cell lung cancer patients with metastatic spinal cord compression treated with short-course radiotherapy	da Silva, G. T.; da Costa, T. G. P.; De Bessa, C. M.; Zamboni, M. M.; Bergmann, A.; Thuler, L. C. S.	2021	irrelevant topic; radiotherapy
Risk of venous thromboembolism in bone and soft-tissue sarcoma patients undergoing surgical intervention: a report from prior to the initiation of SCIP measures	Damron, T. A.; Wardak, Z.; Glodny, B.; Grant, W.	2011	risk factors, not postop
The impact of insurance status on outcomes after surgery for spinal metastases	Dasenbrock, H. H.; Wolinsky, J. P.; Sciubba, D. M.; Witham, T. F.; Gokaslan, Z. L.; Bydon, A.	2012	irrelevant topic; spinal metastases

Article Title	Authors	Year	Reason for Exclusion
Risk of venous thromboembolism after shoulder arthroplasty in the Medicare population	Day, J. S.; Ramsey, M. L.; Lau, E.; Williams, G. R.	2015	irrelevant topic; 0.5% pts had metastatic tumors
Retrospective, multicenter, observational study of 112 surgically treated cases of humerus metastasis	de Geyer, A.; Bourgoin, A.; Rousseau, C.; Ropars, M.; Bonnevialle, N.; Bouthors, C.; Descamps, J.; Niglis, L.; Sailhan, F.; Bonnevialle, P.; SoFcot,	2020	no comparison group
Racial disparities in clinical presentation, type of intervention, and in-hospital outcomes of patients with metastatic spine disease: An analysis of 145,809 admissions in the United States	De la Garza Ramos, R.; Benton, J. A.; Gelfand, Y.; Echt, M.; Flores Rodriguez, J. V.; Yanamadala, V.; Yassari, R.	2020	irrelevant topic; spinal metastases
Racial Disparities in Perioperative Morbidity Following Oncological Spine Surgery	De la Garza Ramos, R.; Choi, J. H.; Naidu, I.; Benton, J. A.; Echt, M.; Yanamadala, V.; Passias, P. G.; Shin, J. H.; Altschul, D. J.; Goodwin, C. R.; Sciubba, D. M.; Yassari, R.	2021	irrelevant topic; spinal metastases
Timing of Prophylactic Anticoagulation and Its Effect on Thromboembolic Events After Surgery for Metastatic Tumors of the Spine	De la Garza Ramos, R.; Longo, M.; Gelfand, Y.; Echt, M.; Kinon, M. D.; Yassari, R.	2019	Irrelevant topic; case series
Operative treatment of humeral shaft fractures. Comparison of plating and intramedullary nailing	Denies, E.; Nijs, S.; Sermon, A.; Broos, P.	2010	irrelevant topic; no metastatic bone disease/tumor
Chondroblastoma: Is intralesional curettage with the use of adjuvants a sufficient way of therapy?	Deventer, N.; Deventer, N.; Gosheger, G.; de Vaal, M.; Budny, T.; Laufer, A.; Heitkoetter, B.; Luebben, T.	2021	review
Risk factors of regional lymph node (RLN) metastasis among patients with bone sarcoma and survival of patients with RLN-positive bone sarcoma	Dong, Y.; Wu, W.; Kang, H.; Xiong, W.; Ye, D.; Fang, Z.; Guan, H.; Liao, H.; Li, F.	2021	irrelevant topic; SEER database used
Prognostic factors for survival in patients with high-grade osteosarcoma using the Surveillance, Epidemiology, and End Results (SEER) Program database	Duchman, K. R.; Gao, Y.; Miller, B. J.	2015	irrelevant topic; SEER database used

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Functional and Oncological Outcome After Treatment of Chondroblastoma With Intralesional Curettage	Ebeid, W. A.; Hasan, B. Z.; Badr, I. T.; Mesregah, M. K.	2019	no comparison group
Present day controversies and consensus in curettage for giant cell tumor of bone	Errani, C.; Tsukamoto, S.; Ciani, G.; Donati, D. M.	2019	Irrelevant topic; Giant cell tumor of bone
Survival Analysis of 3 Different Age Groups and Prognostic Factors among 402 Patients with Skeletal High-Grade Osteosarcoma. Real World Data from a Single Tertiary Sarcoma Center	Evenhuis, R. E.; Acem, I.; Rueten-Budde, A. J.; Karis, D. S. A.; Fiocco, M.; Dorleijn, D. M. J.; Speetjens, F. M.; Anninga, J.; Gelderblom, H.; van de Sande, M. A. J.	2021	combined age group populations include <18
Risk factors and nomogram for newly diagnosis of bone metastasis in bladder cancer: A SEER-based study	Fan, Z.; Huang, Z.; Hu, C.; Tong, Y.; Zhao, C.	2020	irrelevant topic; SEER database used
Bone Metastasis in Renal Cell Carcinoma Patients: Risk and Prognostic Factors and Nomograms	Fan, Z.; Huang, Z.; Huang, X.	2021	irrelevant topic; SEER database used
Intramedullary nailing of humeral shaft fractures. A retrospective study of 126 cases	Flinkkila, T.; Hyvonen, P.; Lakovaara, M.; Linden, T.; Ristiniemi, J.; Hamalainen, M.	1999	no comparison treatment
Pathological fractures of the humeral shaft	Flinkkila, T.; Hyvonen, P.; Leppilahti, J.; Hamalainen, M.	1998	no comparison group
Pathologic fractures due to metastatic disease. A retrospective study of 160 surgically treated fractures	Fourneau, I.; Broos, P.	1998	Irrelevant topic; patient population not all humerus
An expandable nailing system for the management of pathological humerus fractures	Franck, W. M.; Olivieri, M.; Jannasch, O.; Hennig, F. F.	2002	irrelevant topic; no comparison group
Salvage of the upper extremity in cases of tumorous destruction of the proximal humerus	Fuhrmann, R. A.; Roth, A.; Venbrocks, R. A.	2000	No comparison group
Modular prosthetic reconstruction of major bone defects of the distal end of the humerus	Funovics, P. T.; Schuh, R.; Adams, S. B., Jr.; Sabeti-Aschraf, M.; Dominkus, M.; Kotz, R. I.	2011	irrelevant topic; tumor group vs reconstruction group
Thirty-day Outcomes After Surgery for Metastatic Bone Disease of the Extremities: An Analysis of the NSQIP Database	Gallaway, K. E.; Ahn, J.; Callan, A. K.	2020	no comparison group

Article Title	Authors	Year	Reason for Exclusion
Complications and functional outcomes of reconstruction with an osteoarticular allograft after intra-articular resection of the proximal aspect of the humerus	Getty, P. J.; Peabody, T. D.	1999	case series
Metastatic Esophageal Carcinoma: Prognostic Factors and Survival	Ghazy, H. F.; El-Hadaad, H. A.; Wahba, H. A.; Abbas, R.; Abbas, O. A.	2021	irrelevant topic; esophageal cancer
Impact of Asian ethnicity on outcome in metastatic EGFR-mutant non-small cell lung cancer	Gibson, A. J. W.; D'Silva, A.; Elegbede, A. A.; Tudor, R. A.; Dean, M. L.; Bebb, D. G.; Hao, D.	2019	irrelevant topic; 56% bone metastasis
Humeral Shaft Fracture Fixation: Incidence Rates and Complications as Reported by American Board of Orthopaedic Surgery Part II Candidates	Gottschalk, M. B.; Carpenter, W.; Hiza, E.; Reisman, W.; Roberson, J.	2016	irrelevant topic; no tumor/metastatic bone disease
The outcome of locking plate fixation for the treatment of periarticular metastases	Gregory, J. J.; Ockendon, M.; Cribb, G. L.; Cool, P. W.; Williams, D. H.	2011	case series
Body composition predictors of mortality in patients undergoing surgery for long bone metastases	Groot, O. Q.; Bongers, M. E. R.; Buckless, C. G.; Twining, P. K.; Kapoor, N. D.; Janssen, S. J.; Schwab, J. H.; Torriani, M.; Bredella, M. A.	2022	irrelevant topic; biomarkers
Clinical Outcome Differences in the Treatment of Impending Versus Completed Pathological Long-Bone Fractures	Groot, O. Q.; Lans, A.; Twining, P. K.; Bongers, M. E. R.; Kapoor, N. D.; Verlaan, J. J.; Newman, E. T.; Raskin, K. A.; Lozano-Calderon, S. A.; Janssen, S. J.; Schwab, J. H.	2021	irrelevant topic; no humerus
High Risk of Venous Thromboembolism After Surgery for Long Bone Metastases: A Retrospective Study of 682 Patients	Groot, O. Q.; Ogink, P. T.; Janssen, S. J.; Paulino Pereira, N. R.; Lozano-Calderon, S.; Raskin, K.; Hornicek, F.; Schwab, J. H.	2018	all outcomes are combined
High Risk of Symptomatic Venous Thromboembolism After Surgery for Spine Metastatic Bone Lesions: A Retrospective Study	Groot, O. Q.; Ogink, P. T.; Paulino Pereira, N. R.; Ferrone, M. L.; Harris, M. B.; Lozano-Calderon, S. A.; Schoenfeld, A. J.; Schwab, J. H.	2019	all post op data is combined

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Quality of life of patients with proximal humerus metastasis treated with cement spacer	Guo, W.; Gao, X.; Wang, D.; Wang, T.; Tang, L.; Wang, Y.; Liu, B.	2019	irrelevant comparison; surgical vs nonsurgical group
Prognostic Significance of Young Age and Non-Bone Metastasis at Diagnosis in Patients with Metastatic Prostate Cancer: a SEER Population-Based Data Analysis	Guo, Y.; Mao, S.; Zhang, A.; Wang, R.; Zhang, Z.; Zhang, J.; Wang, L.; Zhang, W.; Wu, Y.; Ye, L.; Yang, B.; Yao, X.	2019	irrelevant topic; SEER database used
Curettage with cement augmentation of large bone defects in giant cell tumors with pathological fractures in lower-extremity long bones	Gupta, S. P.; Garg, G.	2016	case series
Results of the treatment of bone metastases with modular prosthetic replacement--analysis of 67 patients	Guzik, G.	2016	<5 patients per group
Prevalence and risk factors of preoperative venous thromboembolism in patients with malignant musculoskeletal tumors: an analysis based on D-dimer screening and imaging	Hayashida, K.; Kawabata, Y.; Saito, K.; Fujita, S.; Choe, H.; Kato, I.; Takeyama, M.; Inaba, Y.	2022	irrelevant comparison
Clinical Characteristics and Survival Outcomes in Neuroblastoma With Bone Metastasis Based on SEER Database Analysis	He, B.; Mao, J.; Huang, L.	2021	irrelevant topic; SEER database used
Megaprosthetic replacement of the distal humerus: still a challenge in limb salvage	Henrichs, M. P.; Liem, D.; Gosheger, G.; Streitbuerger, A.; Nottrott, M.; Andreou, D.; Hardes, J.	2019	case series
Effect of socioeconomic status as measured by education level on survival in breast cancer clinical trials	Herndon, J. E., 2nd; Kornblith, A. B.; Holland, J. C.; Paskett, E. D.	2013	irrelevant topic; breast cancer
Prognostic factors following pathological fractures	Hill, T.; D'Alessandro, P.; Murray, K.; Yates, P.	2015	irrelevant topic; <50% humerus
Shoulder and elbow function following Marchetti-Vicenzi humeral nail fixation	Hossain, S.; Roy, N.; Ayeko, C.; Elsworth, C. F.; Jacobs, L. G.	2003	no comparison group
The Personalized Shoulder Reconstruction Assisted by 3D Printing Technology After Resection of the Proximal Humerus Tumours	Hu, H.; Liu, W.; Zeng, Q.; Wang, S.; Zhang, Z.; Liu, J.; Zhang, Y.; Shao, Z.; Wang, B.	2019	case series

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Risk factors, prognostic factors, and nomograms for bone metastasis in patients with newly diagnosed infiltrating duct carcinoma of the breast: a population-based study	Huang, Z.; Hu, C.; Liu, K.; Yuan, L.; Li, Y.; Zhao, C.; Hu, C.	2020	irrelevant topic; SEER database used
Surgical fixation of pathologic fractures: an evaluation of evolving treatment methods	Hunt, K. J.; Gollogly, S.; Randall, R. L.	2006	case series
Risk of skeletal related events among elderly prostate cancer patients by site of metastasis at diagnosis	Hussain, A.; Aly, A.; Daniel Mullins, C.; Qian, Y.; Arellano, J.; Onukwugha, E.	2016	irrelevant topic; SEER database used
Treatment of pathological fractures of the humerus with Ender nails	Hyder, N.; Wray, C. C.	1993	no comparison group
Immediate family support is important to discharge home for cancer patient with bone metastasis after rehabilitation: A retrospective study	Ikeguchi, R.; Nankaku, M.; Yamawaki, R.; Tanaka, H.; Hamada, R.; Kawano, T.; Murao, M.; Kitamura, G.; Sato, T.; Nishikawa, T.; Noguchi, T.; Kuriyama, S.; Sakamoto, A.; Matsuda, S.	2021	irrelevant topic; rehabilitation outcomes
Intramedullary interlocking nailing for humeral fractures: experiences with the Russell-Taylor humeral nail	Ikpeme, J. O.	1994	no comparison group
Locked intramedullary nailing of humeral shaft fractures. Implant design, surgical technique, and clinical results	Ingman, A. M.; Waters, D. A.	1994	population did not have metastatic bone disease
Resection of the proximal humerus for metastases and replacement with RPS prosthesis	Ippolito, V.; Saccalani, M.; Ianni, L.; Spaggiari, L.; Cavina, F.; Modonesi, F.; Bonetti, L.; Sartori, G.	2003	no comparison group
Management of metastatic humeral fractures: Variations according to orthopedic subspecialty, tumor characteristics	Janssen, S. J.; Bramer, J. A. M.; Guitton, T. G.; Hornicek, F. J.; Schwab, J. H.	2018	irrelevant outcomes; tumor characteristics and ortho surgeon specialties
Complications after surgery for metastatic humeral lesions	Janssen, S. J.; van Dijke, M.; Lozano-Calderon, S. A.; Ready, J. E.; Raskin, K. A.; Ferrone, M. L.; Hornicek, F. J.; Schwab, J. H.	2016	case series

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Factors associated with improved outcomes following decompressive surgery for prostate cancer metastatic to the spine	Ju, D. G.; Zadnik, P. L.; Groves, M. L.; Hwang, L.; Kaloostian, P. E.; Wolinksy, J. P.; Witham, T. F.; Bydon, A.; Gokaslan, Z. L.; Sciubba, D. M.	2013	Irrelevant topic; outcomes based on surgery
Reverse shoulder replacement after resection of the proximal humerus for bone tumours	Kaa, A. K.; Jorgensen, P. H.; Sojbjerg, J. O.; Johannsen, H. V.	2013	case series
Revision rate of reconstructions in surgically treated diaphyseal metastases of bone	Kask, G.; Nieminen, J.; Parry, M. C.; van Iterson, V.; Pakarinen, T. K.; Ratasvuori, M.; Laitinen, M. K.	2019	humerus data combined with other body parts
Statistical analysis of prognostic factors for survival in patients with spinal metastasis	Kataoka, M.; Kunisada, T.; Tanaka, M.; Takeda, K.; Itani, S.; Sugimoto, Y.; Misawa, H.; Senda, M.; Nakahara, S.; Ozaki, T.	2012	irrelevant topic; treatment options
Characteristics and Prognostic Factors of Bone Metastasis in Patients With Colorectal Cancer	Kawamura, H.; Yamaguchi, T.; Yano, Y.; Hozumi, T.; Takaki, Y.; Matsumoto, H.; Nakano, D.; Takahashi, K.	2018	Irrelevant outcomes
Does surgical technique influence the burden of lung metastases in patients with pathologic long bone fractures?	Kendal, J. K.; Heard, B. J.; Abbott, A. G.; Moorman, S. W.; Saini, R.; Puloski, S. K. T.; Monument, M. J.	2022	irrelevant topic; lung metastases
Assessment of whole body MRI and sestamibi technetium-99m bone marrow scan in prediction of multiple myeloma disease progression and outcome: a prospective comparative study	Khalafallah, A. A.; Snarski, A.; Heng, R.; Hughes, R.; Renu, S.; Arm, J.; Dutchke, R.; Robertson, I. K.; To, L. B.	2013	irrelevant topic; imaging
Minimally invasive surgery of humeral metastasis using flexible nails and cement in high-risk patients with advanced cancer	Kim, J. H.; Kang, H. G.; Kim, J. R.; Lin, P. P.; Kim, H. S.	2011	case series
Outcomes after extensive manual curettage and limited burring for atypical cartilaginous tumour of long bone	Kim, W.; Lee, J. S.; Chung, H. W.	2018	no comparison group
Closed intramedullary nailing with percutaneous cement augmentation for long bone metastases	Kim, Y. I.; Kang, H. G.; Kim, J. H.; Kim, S. K.; Lin, P. P.; Kim, H. S.	2016	irrelevant topic; femur and humerus data combined

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Results with the isoelastic shoulder prosthesis in primary and secondary tumors of the proximal humerus	Klestil, T.; Kerber, W.; Sterzinger, W.; Krismer, M.	1993	No comparison group
Outcomes of critically ill cancer patients in a university hospital setting	Kress, J. P.; Christenson, J.; Pohlman, A. S.; Linkin, D. R.; Hall, J. B.	1999	irrelevant topic; critically ill cancer patients
Early Experience in Pathologic Humerus Fracture Treated With the Photodynamic Bone Stabilization System Shows Limitations Related to Patient Selection	Krumme, J.; MacConnell, A.; Wallace, M.; Aboulafia, A.; Jelinek, J.; Adams, B.; Henshaw, R.	2021	no comparison group
Closed retrograde nailing of pathological humeral fractures	Kumta, S. M.; Quintos, A. D.; Griffith, J. F.; Chow, L. T.; Wong, K. C.	2002	no comparison group
Proximal humeral reconstruction using nail cement spacer in primary and metastatic tumours of proximal humerus	Kundu, Z. S.; Gogna, P.; Gupta, V.; Kamboj, P.; Singla, R.; Sangwan, S. S.	2013	case series
Clinical significance of trabecular bone score for prediction of pathologic fracture risk in patients with multiple myeloma	Lee, E. M.; Kim, B.	2018	irrelevant topic; fracture vs no fracture
Cement Intercalary Reconstruction After Bone Tumor Resection	Lesensky, J.; Mavrogenis, A. F.	2021	case series
Precise resection and biological reconstruction for patients with bone sarcomas in the proximal humerus	Li, J.; Wang, Z.; Guo, Z.; Wu, Y.; Chen, G.; Pei, G.	2012	case series
Prognostic factors and survival according to tumour subtype in women presenting with breast cancer bone metastases at initial diagnosis: a SEER-based study	Li, X.; Zhang, X.; Liu, J.; Shen, Y.	2020	irrelevant topic; SEER database used
Bone defect reconstruction with autologous bone inactivated with liquid nitrogen after resection of primary limb malignant tumors: An observational study	Li, Y.; Yang, Y.; Huang, Z.; Shan, H.; Xu, H.; Niu, X.	2020	case series
Systematic Pan-Cancer Population-Based Analysis Reveals the Incidence and Prognosis of Lung Metastases at Diagnosis	Liang, X.; Cheng, Y.; Zhou, W.; Ni, J.; Li, Y.; Feng, G.	2021	irrelevant topic; SEER database used
Treatment of humeral shaft fractures by retrograde locked nailing	Lin, J.; Hou, S. M.; Hang, Y. S.; Chao, E. Y.	1997	irrelevant topic; no metastatic bone disease

Article Title	Authors	Year	Reason for Exclusion
Osteosynthesis of pathologic fractures and prophylactic internal fixation of metastases in long bones	Linclau, L.; Dokter, G.	1992	no treatment or comparison group
Treatment and outcome of malignant bone tumors of the proximal humerus: biological versus endoprosthetic reconstruction	Liu, T.; Zhang, Q.; Guo, X.; Zhang, X.; Li, Z.; Li, X.	2014	case series
Comparison of percutaneous long bone cementoplasty with or without embedding a cement-filled catheter for painful long bone metastases with impending fracture	Liu, X. W.; Jin, P.; Liu, K.; Chen, H.; Li, L.; Li, M.; Tang, H.; Sun, G.	2017	irrelevant topic; cement filled catheter
Reverse shoulder endoprosthesis for pathologic lesions of the proximal humerus: a minimum 3-year follow-up	Maclean, S.; Malik, S. S.; Evans, S.; Gregory, J.; Jeys, L.	2017	case series
Pathologic fracture of the distal humerus due to a textiloma	Maier, M.; Bratschitsch, G.; Friesenbichler, J.; Bodo, K.; Leithner, A.; Holzer, L. A.	2016	case report
What Is the Value of Undergoing Surgery for Spinal Metastases at Dedicated Cancer Centers?	Malik, A. T.; Khan, S. N.; Voskuil, R. T.; Alexander, J. H.; Drain, J. P.; Scharschmidt, T. J.	2021	irrelevant topic; spinal metastases
Minimally invasive plate osteosynthesis with locking plate for metastatic humeral fractures	Matsumura, T.; Saito, T.; Akiyama, T.; Takeshita, K.	2021	case series
Custom endoprosthetic reconstruction for malignant bone disease in the humeral diaphysis	McGrath, A.; Sewell, M. D.; Hanna, S. A.; Pollock, R. C.; Skinner, J. A.; Cannon, S. R.; Briggs, T. W.	2011	case series
Impact of symptomatic skeletal events on health-care resource utilization and quality of life among patients with castration-resistant prostate cancer and bone metastases	McKay, R.; Haider, B.; Duh, M. S.; Valderrama, A.; Nakabayashi, M.; Fiorillo, M.; Ristovska, L.; Wen, L.; Kantoff, P.	2017	irrelevant topic; symptomatic skeletal events
Operative treatment of humeral shaft fractures. The Leuven experience	Meekers, F. S.; Broos, P. L.	2002	irrelevant topic; no tumor/metastatic bone disease
Aspirin for Prophylaxis Against Venous Thromboembolism After Orthopaedic Oncologic Surgery	Mendez, G. M.; Patel, Y. M.; Ricketti, D. A.; Gaughan, J. P.; Lackman, R. D.; Kim, T. W. B.	2017	no comparison group

Article Title	Authors	Year	Reason for Exclusion
Risk factors for metastatic disease at presentation with osteosarcoma: an analysis of the SEER database	Miller, B. J.; Cram, P.; Lynch, C. F.; Buckwalter, J. A.	2013	irrelevant topic; SEER database used
Socioeconomic measures influence survival in osteosarcoma: an analysis of the National Cancer Data Base	Miller, B. J.; Gao, Y.; Duchman, K. R.	2017	Irrelevant topic; patient population, half under 18yo
Does surgery or radiation provide the best overall survival in Ewing's sarcoma? A review of the National Cancer Data Base	Miller, B. J.; Gao, Y.; Duchman, K. R.	2017	Irrelevant topic; patient population
Deep vein thrombosis following the treatment of lower limb pathologic bone fractures - a comparative study	Mioc, M. L.; Prejbeanu, R.; Vermesan, D.; Haragus, H.; Niculescu, M.; Pop, D. L.; Balanescu, A. D.; Malita, D.; Deleanu, B.	2018	irrelevant topic; 64% metastatic
Is It Appropriate to Treat Sarcoma Metastases With Intramedullary Nailing?	Moon, B. S.; Dunbar, D. J.; Lin, P. P.; Satcher, R. L.; Bird, J. E.; Lewis, V. O.	2017	case series
Simultaneous nailing of skeletal metastases: is the mortality really that high?	Moon, B.; Lin, P.; Satcher, R.; Lewis, V.	2011	case series
Postoperative survival and ambulatory outcome in metastatic spinal tumors : prognostic factor analysis	Moon, K. Y.; Chung, C. K.; Jahng, T. A.; Kim, H. J.; Kim, C. H.	2011	irrelevant topic; post op survival
Treatment of Pathological Humerus-Shaft Tumoral Fractures with Rigid Static Interlocking Intramedullary Nail-22 Years of Experience	Moura, D. L.; Alves, F.; Fonseca, R.; Freitas, J.; Casanova, J.	2019	not in English
Evaluation of Intramedullary Methods with Polymethylmethacrylate for Fixation of Bone Lesions of the Extremities	Moura, M.; Sanches, D. P.; Pinto, A. F.; Milano, S. S.; Villela, M. M.	2021	not in English
Treatment of metastatic bone lesions in the upper extremity: indications for surgery	Muramatsu, K.; Ihara, K.; Iwanagaa, R.; Taguchi, T.	2010	case series

Article Title	Authors	Year	Reason for Exclusion
Risk factors for recurrence after operation in patients with pT1a renal cell carcinoma: sub-analysis of the multi-institutional national database of the Japanese Urological Association	Nakajima, N.; Miyajima, A.; Shinohara, N.; Obara, W.; Kondo, T.; Kimura, G.; Kume, H.; Fujimoto, H.; Sugiyama, T.; Nonomura, N.; Hongo, F.; Fukumori, T.; Takahashi, M.; Kanayama, H. O.; Eto, M.	2022	irrelevant topic; renal cancer
Early Improvement in Pain and Functional Outcome but Not Quality of Life After Surgery for Metastatic Long Bone Disease	Nooh, A.; Goulding, K.; Isler, M. H.; Mottard, S.; Arteau, A.; Dion, N.; Turcotte, R.	2018	irrelevant topic; humerus data combined, treatment comparison cannot be extracted
Functional Outcomes and Complications After Oncologic Reconstruction of the Proximal Humerus	Nota, S.; Teunis, T.; Kortlever, J.; Ferrone, M.; Ready, J.; Gebhardt, M.; Raskin, K.; Hornicek, F.; Schwab, J.; Lozano Calderon, S.	2018	no comparison group
Minimally invasive treatment of pathological fractures of the humeral shaft	Ofluoglu, O.; Erol, B.; Ozgen, Z.; Yildiz, M.	2009	no comparison group
Allograft reconstruction of the humerus: Complications and revision surgery	Ogink, P. T.; Teunissen, F. R.; Massier, J. R.; Raskin, K. A.; Schwab, J. H.; Lozano-Calderon, S. A.	2019	no comparison group
Impact of hospital volume on postoperative complications and in-hospital mortality after musculoskeletal tumor surgery: analysis of a national administrative database	Ogura, K.; Yasunaga, H.; Horiguchi, H.; Ohe, K.; Shinoda, Y.; Tanaka, S.; Kawano, H.	2013	irrelevant topic; hospital volume
Enchondromas and atypical cartilaginous tumors at the proximal humerus treated with intralesional resection and bone cement filling with or without osteosynthesis: retrospective analysis of 42 cases with 6 years mean follow-up	Omlor, G. W.; Lohnherr, V.; Lange, J.; Gantz, S.; Merle, C.; Fellenberg, J.; Raiss, P.; Lehner, B.	2018	irrelevant topic; no metastatic bone disease
Prediction of Long Bone Fractures in Multiple Myeloma Patients in an Advanced Imaging World	Or, O.; Saiyed, R.; Marty, E.; Boyer, A.; Jahnwar, Y. S.; Niesvizky, R.; Lane, J. M.	2021	irrelevant topic; PET/CT imaging

Article Title	Authors	Year	Reason for Exclusion
Surgical treatment of extra-articular distal-third diaphyseal fractures of the humerus using a modified posterior approach and an extra-articular plate	Paramo-Diaz, P.; Arroyo-Hernandez, M.; Rodriguez Vega, V.; Aroca-Peinado, M.; Leon-Baltasar, J. L.; Caba-Doussoux, P.	2017	no comparison group
Joint-preserving palliative surgery using self-locking screws of intramedullary nail and percutaneous cementoplasty for proximal humeral metastasis in the advanced cancer patients	Park, J. W.; Kim, Y. I.; Kang, H. G.; Kim, J. H.; Kim, H. S.	2018	case series
Preliminary results: use of multi-hole injection nails for intramedullary nailing with simultaneous bone cement injection in long-bone metastasis	Park, J. W.; Kim, Y. I.; Kang, H. G.; Kim, J. H.; Kim, H. S.	2019	case series
Aspirin and compression devices versus low-molecular-weight heparin and PCD for VTE prophylaxis in orthopedic oncology patients	Patel, A. R.; Crist, M. K.; Nemitz, J.; Mayerson, J. L.	2010	Irrelevant topic; patient population, not all metastatic and hip included
Effect of Pharmacologic Prophylaxis on Venous Thromboembolism After Radical Prostatectomy: The PREVENTER Randomized Clinical Trial	Patel, H. D.; Faisal, F. A.; Trock, B. J.; Joice, G. A.; Schwen, Z. R.; Pierorazio, P. M.; Johnson, M. H.; Bivalacqua, T. J.; Han, M.; Gorin, M. A.; Carter, H. B.; Partin, A. W.; Pavlovich, C. P.; Allaf, M. E.	2020	irrelevant comparison; <4% metastatic tumors
Drivers of Readmission and Reoperation After Surgery for Vertebral Column Metastases	Patel, J.; Pennington, Z.; Hersh, A. M.; Hung, B.; Schilling, A.; Antar, A.; Elsamadicy, A. A.; de la Garza Ramos, R.; Lubelski, D.; Larry Lo, S. F.; Sciubba, D. M.	2021	irrelevant topic; spinal metastases
Histologic Subtype, Tumor Grade, Tumor Size, and Race Can Accurately Predict the Probability of Synchronous Metastases in T2 Renal Cell Carcinoma	Pecoraro, A.; Palumbo, C.; Knipper, S.; Rosiello, G.; Luzzago, S.; Tian, Z.; Shariat, S. F.; Saad, F.; Lavallee, L.; Briganti, A.; Kapoor, A.; Fiori, C.; Porpiglia, F.; Karakiewicz, P. I.	2020	irrelevant topic; nephrectomy
Limb Sparing Resection for Tumors Involving the Distal Humerus and Reconstruction with a Modular Endoprosthesis	Peterson, J. R.; Villalobos, C. E.; Zamora, R.; Wittig, J. C.	2015	case series
Surgical treatment of pathologic fractures of humerus	Piccioli, A.; Maccauro, G.; Rossi, B.; Scaramuzzo, L.; Frenos, F.; Capanna, R.	2010	no comparison group

Article Title	Authors	Year	Reason for Exclusion
Carbon-fiber reinforced intramedullary nailing in musculoskeletal tumor surgery: a national multicentric experience of the Italian Orthopaedic Society (SIOT) Bone Metastasis Study Group	Piccioli, A.; Piana, R.; Lisanti, M.; Di Martino, A.; Rossi, B.; Camnasio, F.; Gatti, M.; Maniscalco, P.; Gherlinzoni, F.; Spinelli, M. S.; Donati, D. M.; Biagini, R.; Capanna, R.; Denaro, V.; Italian Orthopaedic Society Bone Metastasis Study, Group	2017	no comparison group
Distally Unlocked Intramedullary Nailing With Cement Fixation for Impending and Actual Pathologic Humerus Fractures: A Retrospective Case Series	Pizzo, R. A.; Hoskins, T.; Patel, J. N.; Miller, J. M.; Goyette, D.; Mazzei, C.; Wittig, J. C.	2020	no comparison group
Internal fixation of proximal humerus fractures using the locking proximal humerus plate	Plecko, M.; Kraus, A.	2005	irrelevant topic; fracture types
Treatment of pathological humeral shaft fractures with intramedullary nailing. A retrospective study	Pretell, J.; Rodriguez, J.; Blanco, D.; Zafra, A.; Resines, C.	2010	case series
Insurance status as a mediator of clinical presentation, type of intervention, and short-term outcomes for patients with metastatic spine disease	Price, M. J.; De la Garza Ramos, R.; Dalton, T.; McCray, E.; Pennington, Z.; Erickson, M.; Walsh, K. M.; Yassari, R.; Sciubba, D. M.; Goodwin, A. N.; Goodwin, C. R.	2022	irrelevant topic; medicare/medicaid
Gender disparities in clinical presentation, treatment, and outcomes in metastatic spine disease	Price, M.; Goodwin, J. C.; De la Garza Ramos, R.; Baeta, C.; Dalton, T.; McCray, E.; Yassari, R.; Karikari, I.; Abd-El-Barr, M.; Goodwin, A. N.; Rory Goodwin, C.	2021	irrelevant topic; spinal metastases
Rapid-prototype endoprosthesis for palliative reconstruction of an upper extremity after resection of bone metastasis	Pruksakorn, D.; Chantarapanich, N.; Arpornchayanon, O.; Leerapun, T.; Sitthiseripratip, K.; Vatanapatimakul, N.	2015	case series
En bloc resection and intercalary prosthesis implantation for the treatment of humeral diaphyseal bone metastases	Pu, F.; Zhang, Z.; Wang, B.; Liu, J.; Shao, Z.	2021	case series
A study of 853 high grade osteosarcomas from a single institution-Are outcomes in Indian patients different?	Puri, A.; Byregowda, S.; Gulia, A.; Crasto, S.; Chinaswamy, G.	2018	Irrelevant topic; Non-metastatic cancer

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Bone metastasis in esophageal adenocarcinoma and squamous cell carcinoma: a SEER-based study	Qin, Y.; Mao, J.; Liang, X.; Wang, N.; Yuan, M.; Zhu, J.; Wu, D.; Wang, Q.	2022	irrelevant topic; bone metastasis vs no bone metastasis
Do Disparities in Wait Times to Operative Fixation for Pathologic Fractures of the Long Bones and 30-day Complications Exist Between Black and White Patients? A Study Using the NSQIP Database	Raad, M.; Puvanesarajah, V.; Wang, K. Y.; McDaniel, C. M.; Srikumaran, U.; Levin, A. S.; Morris, C. D.	2022	irrelevant topic; 13% had humerus fractures
Bone-Specific Metastasis Pattern of Advanced-Stage Lung Adenocarcinoma According to the Localization of the Primary Tumor	Radeczky, P.; Moldvay, J.; Fillinger, J.; Szeitz, B.; Ferencz, B.; Boettiger, K.; Rezeli, M.; Bogos, K.; Renyi-Vamos, F.; Hoetzenecker, K.; Hegedus, B.; Megyesfalvi, Z.; Dome, B.	2021	irrelevant topic; lung cancer
Risk factors for detectable metastatic disease at presentation in Ewing sarcoma - An analysis of the SEER registry	Ramkumar, D. B.; Ramkumar, N.; Miller, B. J.; Henderson, E. R.	2018	Irrelevant topic; patient population
Healing of Pathologic Humeral Fractures in Patients with Metastatic Disease: Consideration for Operative Fixation in Patients	Rao, S. S.; El Abiad, J. M.; Puvanesarajah, V.; Raad, M.; Morris, C. D.; Forsberg, J. A.; Levin, A. S.	2020	no comparison group
Do locking plates have a role in orthopaedic oncological reconstruction	Rastogi, S.; Kumar, A.; Khan, S. A.	2010	no comparison group
Venous thromboembolism after surgical treatment of non-spinal skeletal metastases - An underdiagnosed complication	Ratasvuori, M.; Lassila, R.; Laitinen, M.	2016	no outcomes of interest
Predictors of prognosis of synchronous brain metastases in small-cell lung cancer patients	Reddy, S. P.; Dowell, J. E.; Pan, E.	2020	irrelevant topic; SEER database used
Interlocking intramedullary nailing of pathological fractures of the shaft of the humerus	Redmond, B. J.; Biermann, J. S.; Blasier, R. B.	1996	no comparison group
Intramedullary Nailing Versus Plate Osteosynthesis for Humeral Shaft Metastatic Lesions	Ricard, M. M.; Stavropoulos, N. A.; Nooh, A.; Ste-Marie, N.; Goulding, K.; Turcotte, R.	2021	case series
Seidel intramedullary nailing of humeral diaphyseal fractures: a preliminary report	Riemer, B. L.; Butterfield, S. L.; D'Ambrosia, R.; Kellam, J.	1991	no comparison group

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Two freezing cycles ensure interface sterilization by cryosurgery during bone tumor resection	Robinson, D.; Halperin, N.; Nevo, Z.	2001	no comparison group
Retrograde nailing of humeral shaft fractures	Rommens, P. M.; Blum, J.; Runkel, M.	1998	no comparison group
Racial differences in the distribution of bladder cancer metastases: a population-based analysis	Rosiello, G.; Palumbo, C.; Deuker, M.; Stolzenbach, L. F.; Martin, T.; Tian, Z.; Gallina, A.; Montorsi, F.; Black, P.; Kassouf, W.; Shariat, S. F.; Saad, F.; Briganti, A.; Karakiewicz, P. I.	2020	irrelevant topic; bladder cancer
Prognosis of renal cell carcinoma with bone metastases: Experience from a large cancer centre	Ruatta, F.; Derosa, L.; Escudier, B.; Colomba, E.; Guida, A.; Baciarello, G.; Loriot, Y.; Fizazi, K.; Albiges, L.	2019	irrelevant topic; spinal metastases
Closed humeral shaft fractures treated by elastic intramedullary retrograde nail	Sala, F.; Chiodini, F.; Bau, D.; Ceriani, A.; Borromeo, U. M.	2002	no comparison group
Effect of metastatic site on emergency department disposition in men with metastatic prostate cancer	Sammon, J. D.; Kaczmarek, B. F.; Ravi, P.; Sun, M.; Roghmann, F.; Sukumar, S.; Ghani, K.; Sharma, P.; Karakiewicz, P. I.; Peabody, J. O.; Elder, J. S.; Menon, M.; Trinh, Q. D.	2013	Irrelevant topic; ED admission rates in prostate cancer
Treatment results of pathological fractures of the long bones: a retrospective analysis of 88 patients	Sarahrudi, K.; Hora, K.; Heinz, T.; Millington, S.; Vecsei, V.	2006	irrelevant topic; humerus data combined, treatment comparison cannot be extracted
Silver-coated endoprosthetic replacement of the proximal humerus in case of tumour-is there an increased risk of periprosthetic infection by using a trevira tube?	Schmolders, J.; Koob, S.; Schepers, P.; Kehrer, M.; Frey, S. P.; Wirtz, D. C.; Pennekamp, P. H.; Strauss, A. C.	2017	irrelevant comparison: tube vs no tube
Predictors of 30- and 90-Day Survival Following Surgical Intervention for Spinal Metastases: A Prognostic Study Conducted at Four Academic Centers	Schoenfeld, A. J.; Leonard, D. A.; Saadat, E.; Bono, C. M.; Harris, M. B.; Ferrone, M. L.	2016	Irrelevant topic; Surgical intervention and survival rates
Racial disparities in the development of breast cancer metastases among older women: a multilevel study	Schootman, M.; Jeffe, D. B.; Gillanders, W. E.; Aft, R.	2009	Irrelevant topic; risk of developing metastases, incorrect patient population

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Metastatic lesions of the humerus treated with the isoelastic diaphysis prosthesis	Schurmann, M.; Gradl, G.; Andress, H. J.; Kauschke, T.; Hertlein, H.; Lob, G.	2000	no comparison group
Surgical management and outcome of skeletal metastatic disease of the humerus	Schwabe, P.; Ruppert, M.; Tsitsilonis, S.; Melcher, I.; Schaser, K. D.; Mardian, S.	2014	case series
Comparison of Latino and non-Latino patients with Ewing sarcoma	Sharib, J.; Horvai, A.; Gray Hazard, F. K.; Daldrup-Link, H.; Goldsby, R.; Marina, N.; DuBois, S. G.	2014	Irrelevant topic; patient population
Comparative analysis of the surgical treatment results for multiple myeloma bone disease of the spine and the long bone/soft tissue	Shen, J.; Du, X.; Zhao, L.; Luo, H.; Xu, Z.	2018	Irrelevant topic; MM surgical interventions, spine vs. long bones
Models for Predicting Early Death in Patients With Stage IV Esophageal Cancer: A Surveillance, Epidemiology, and End Results-Based Cohort Study	Shi, M.; Zhai, G. Q.	2022	irrelevant topic; esophageal cancer
Reconstructing humerus defects after tumor resection using an intramedullary cortical allograft strut	Shih, H. N.; Shih, L. Y.; Cheng, C. Y.; Hsu, K. Y.; Chang, C. H.	2002	no comparison group; describes surgical methods
Pathological fractures of the proximal humerus treated with a proximal humeral locking plate and bone cement	Siegel, H. J.; Lopez-Ben, R.; Mann, J. P.; Ponce, B. A.	2010	no comparison group
Ninety day mortality and its predictors after primary shoulder arthroplasty: an analysis of 4,019 patients from 1976-2008	Singh, J. A.; Sperling, J. W.; Cofield, R. H.	2011	no comparison group
The preoperative machine learning algorithm for extremity metastatic disease can predict 90-day and 1-year survival: An external validation study	Skalitzky, M. K.; Gulbrandsen, T. R.; Groot, O. Q.; Karhade, A. V.; Verlaan, J. J.; Schwab, J. H.; Miller, B. J.	2022	irrelevant topic; validation vs development
Epidemiology of musculoskeletal tumors in Shiraz, south of Iran	Solooki, S.; Vosoughi, A. R.; Masoomi, V.	2011	patient population; <18
Impact of the homogeneous and heterogeneous risk factors on the incidence and survival outcome of bone metastasis in NSCLC patients	Song, Q.; Shang, J.; Zhang, C.; Zhang, L.; Wu, X.	2019	irrelevant topic; SEER database used

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Extent of Surgery Does Not Influence 30-Day Mortality in Surgery for Metastatic Bone Disease: An Observational Study of a Historical Cohort	Sorensen, M. S.; Hindso, K.; Hovgaard, T. B.; Petersen, M. M.	2016	Irrelevant topic; surgery influence on mortality
Risk factors for infections in newly diagnosed Multiple Myeloma patients: A Danish retrospective nationwide cohort study	Sorrig, R.; Klausen, T. W.; Salomo, M.; Vangsted, A.; Gimsing, P.	2019	Irrelevant topic; risk factors for infection in newly diagnosed MM
No recurrences in selected patients after curettage with cryotherapy for grade I chondrosarcomas	Souna, B. S.; Belot, N.; Duval, H.; Langlais, F.; Thomazeau, H.	2010	no comparison group
Locked intramedullary nailing of symptomatic metastases in the humerus	Spencer, S. J.; Holt, G.; Clarke, J. V.; Mohammed, A.; Leach, W. J.; Roberts, J. L.	2010	no comparison group
Long-term survival of proximal humerus allografts for reconstruction following resection of malignant bone tumours	Squire, G.; Grundy, T. J.; Ferran, N. A.; Harper, W. M.; Ashford, R. U.	2013	case series
Prognostic factors for patients with skeletal metastases from carcinoma of the breast	Stevenson, J. D.; McNair, M.; Cribb, G. L.; Cool, W. P.	2016	Irrelevant outcomes
Improvement of the shoulder function after large segment resection of the proximal humerus with the use of an inverse tumour prosthesis	Streitbuerger, A.; Henrichs, M.; Gosheger, G.; Ahrens, H.; Nottrott, M.; Guder, W.; Dieckmann, R.; Hardes, J.	2015	case series
Risk factors for surgical site infection after posterior fixation surgery and intraoperative radiotherapy for spinal metastases	Sugita, S.; Hozumi, T.; Yamakawa, K.; Goto, T.; Kondo, T.	2016	Irrelevant topic; risk factors for surgical site infection
Frequency and Prognosis of Pulmonary Metastases in Newly Diagnosed Gastric Cancer	Sun, Z.; Liu, H.; Yu, J.; Huang, W.; Han, Z.; Lin, T.; Chen, H.; Zhao, M.; Hu, Y.; Jiang, Y.; Li, G.	2019	Irrelevant topic; patient population
Liver Metastases in Newly Diagnosed Gastric Cancer: A Population-Based Study from SEER	Sun, Z.; Zheng, H.; Yu, J.; Huang, W.; Li, T.; Chen, H.; Hu, Y.; Zhao, M.; Liu, H.; Jiang, Y.; Li, G.	2019	Irrelevant topic; patient population
Complications using the Seidel intramedullary humeral nail: outcome in 31 patients	Svend-Hansen, H.; Skettrup, M.; Rathcke, M. W.	1998	no comparison group

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Cancer's impact on employment and earnings--a population-based study from Norway	Syse, A.; Tretli, S.; Kravdal, O.	2008	Irrelevant topic; cancer survivors and working life
Bone Diaphysis Metastases, the Ways and Results of Surgical Treatment Saving the Joints	Szczerba, P.; Guzik, G.; Bohatyrewicz, A.; Kotrych, D.	2019	irrelevant topic; <50% humerus
Assessment of the risk factors for impending fractures following radiotherapy for long bone metastases using CT scan-based virtual simulation: a retrospective study	Tatar, Z.; Soubrier, M.; Dillies, A. F.; Verrelle, P.; Boisgard, S.; Lapeyre, M.	2014	irrelevant topic; <50% humerus
The treatment of primary and metastatic renal cell carcinoma (RCC) with image-guided stereotactic body radiation therapy (SBRT)	Teh, B.; Bloch, C.; Galli-Guevara, M.; Doh, L.; Richardson, S.; Chiang, S.; Yeh, P.; Gonzalez, M.; Lunn, W.; Marco, R.; Jac, J.; Paulino, A.; Lu, H.; Butler, E.; Amato, R.	2007	irrelevant topic; radiation therapy
Segmental limb reconstruction after tumor resection	Temple, H. T.; Kuklo, T. R.; Lehman, R. A., Jr.; Heekin, R. D.; Berrey, B. H.	2000	no comparison group
Prognostic variables for survival and skeletal complications in patients with multiple myeloma osteolytic bone disease	Terpos, E.; Berenson, J.; Cook, R. J.; Lipton, A.; Coleman, R. E.	2010	Irrelevant topic; patients on zoledronic acid with pamidronate
Outcome of surgical management of bony metastases to the humerus and shoulder girdle: a retrospective analysis of 93 patients	Thai, D. M.; Kitagawa, Y.; Choong, P. F.	2006	no comparison group
Interlocking nailing of humeral shaft fractures	Thomsen, N. O.; Mikkelsen, J. B.; Svendsen, R. N.; Skovgaard, N.; Jensen, C. H.; Jorgensen, U.	1998	case report
Treatment of pathologic fractures of the humerus with Seidel nailing	Tome, J.; Carsi, B.; Garcia-Fernandez, C.; Marco, F.; Lopez-Duran Stern, L.	1998	no comparison group
Novel nomogram to predict risk of bone metastasis in newly diagnosed thyroid carcinoma: a population-based study	Tong, Y.; Hu, C.; Huang, Z.; Fan, Z.; Zhu, L.; Song, Y.	2020	Irrelevant topic; nomogram development/validation
Treatment of pathologic fracture of the humerus	Vail, T. P.; Harrelson, J. M.	1991	no comparison group

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Proximal humerus reconstruction after tumour resection: biological versus endoprosthetic reconstruction	van de Sande, M. A.; Dijkstra, P. D.; Taminiau, A. H.	2011	no comparison group
The Seidel locking humeral nail: the Nottingham experience	Varley, G. W.	1995	no comparison group
Management of Metastatic Disease of the Upper Extremity	Voskuil, R. T.; Mayerson, J. L.; Scharschmidt, T. J.	2021	review
The homogeneous and heterogeneous risk factors for occurrence and prognosis in lung cancer patients with bone metastasis	Wang, B.; Chen, L.; Huang, C.; Lin, J.; Pan, X.; Shao, Z.; Hu, S.; Zhang, X.; Wang, X.	2019	Irrelevant topic; patient population, not all metastatic
Survival and prognostic factors in Chinese patients with osteosarcoma: 13-year experience in 365 patients treated at a single institution	Wang, W.; Yang, J.; Wang, Y.; Wang, D.; Han, G.; Jia, J.; Xu, M.; Bi, W.	2017	Irrelevant topic; not all metastatic
Prognostic Factors Associated With Bone Lymphoma Primarily Presenting in the Spine	Wang, Y.; Li, J.; Wei, R.; Liu, C.; Nataraj, A.; Yan, J.	2019	irrelevant topic; no metastatic bone disease
Functional outcomes and complications of reconstruction of the proximal humerus after intra-articular tumor resection	Wang, Z.; Guo, Z.; Li, J.; Li, X. D.; Sang, H. X.	2010	irrelevant comparison: prosthesis and resection
Complications and survival after surgical treatment of 214 metastatic lesions of the humerus	Wedin, R.; Hansen, B. H.; Laitinen, M.; Trovik, C.; Zaikova, O.; Bergh, P.; Kalen, A.; Schwarz-Lausten, G.; Vult von Steyern, F.; Walloe, A.; Keller, J.; Weiss, R. J.	2012	case series
Fixation of pathological humeral fractures by the cemented plate technique	Weiss, K. R.; Bhumbra, R.; Biau, D. J.; Griffin, A. M.; Deheshi, B.; Wunder, J. S.; Ferguson, P. C.	2011	no comparison group
Race does not predict the development of metastases in men with nonmetastatic castration-resistant prostate cancer	Whitney, C. A.; Howard, L. E.; Amling, C. L.; Aronson, W. J.; Cooperberg, M. R.; Kane, C. J.; Terris, M. K.; Freedland, S. J.	2016	Irrelevant topic; impact of race on development of metastases in non-met cancer
Survival analysis after intramedullary stabilization for metastatic disease of the femur: prognostic value of common laboratory parameters	Willoughby, J. E.; Baker, J. F.	2021	Irrelevant topic; patient population

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Stabilisation of pathological humerus fractures using cement augmented plating: A case series	Wilson, W. T.; Pickup, A. R.; Findlay, H.; Gupta, S.; Mahendra, A.	2021	no comparison group
Ethnic and racial differences in patients with Ewing sarcoma	Worch, J.; Matthay, K. K.; Neuhaus, J.; Goldsby, R.; DuBois, S. G.	2010	Irrelevant topic; patient population
Venous thromboembolism in patients with acute leukemia, lymphoma, and multiple myeloma	Wun, T.; White, R. H.	2010	review
Racial disparities in bone metastasis patterns and targeted screening and treatment strategies in newly diagnosed lung cancer patients	Xu, G.; Cui, P.; Zhang, C.; Lin, F.; Xu, Y.; Guo, X.; Cai, J.; Baklaushev, V. P.; Peltzer, K.; Chekhonin, V. P.; Wang, X.; Wang, G.	2020	irrelevant topic; SEER database used
Analysis of definitive chemo-radiotherapy for esophageal cancer with supra-clavicular node metastasis based on CT in a single institutional retrospective study: a propensity score matching analysis	Xu, H. Y.; Wu, S. X.; Luo, H. S.; Chen, C. Y.; Lin, L. X.; Huang, H. C.	2018	Irrelevant topic; patient population
Predictors for survival in patients with bone metastasis of small cell lung cancer: A population-based study	Xue, M.; Chen, G.; Chen, X.; Hu, J.	2021	irrelevant topic; SEER database used
Deep-vein thrombosis after resection of musculoskeletal tumours of the lower limb	Yamaguchi, T.; Matsumine, A.; Niimi, R.; Nakamura, T.; Matsubara, T.; Asanuma, K.; Hasegawa, M.; Sudo, A.	2013	irrelevant topic; <4% metastatic tumors
Survival Outcomes of Newly Diagnosed Multiple Myeloma at a Tertiary Care Center in North India (IMAGe: 001A Study)	Yanamandra, U.; Sharma, R.; Shankar, S.; Yadav, S.; Kapoor, R.; Pramanik, S.; Ahuja, A.; Kumar, R.; Sharma, S.; Das, S.; Chatterjee, T.; Somasundaram, V.; Verma, T.; Mishra, K.; Singh, J.; Sharma, A.; Nair, V.	2021	irrelevant outcomes
Analysis of prognostic factors relating to postoperative survival in spinal metastases	Yang, S. B.; Cho, W.; Chang, U. K.	2012	irrelevant topic; spinal metastases
Risk factors and survival outcomes of laryngeal squamous cell carcinoma patients with lung metastasis: A population-based study	Yang, W.; Mei, X.; Zhou, Y.; Su, R.; Lei, W.; Zheng, S.; Zhu, R.; Guo, L.; Tao, Y.; Su, Y.; Li, J.; Ding, C.; Zou, S.; Li, X.; Hu, H.	2021	irrelevant topic; SEER database used

Article Title	Authors	Year	Reason for Exclusion
Mid- to long-term effects of two different biological reconstruction techniques for the treatment of humerus osteosarcoma involving caput humeri	Yao, W.; Cai, Q.; Wang, J.; Hou, J.	2020	case series
Incidence, prognosis and nomograms of breast cancer with bone metastases at initial diagnosis: a large population-based study	Yao, Y. B.; Zheng, X. E.; Luo, X. B.; Wu, A. M.	2021	irrelevant topic; SEER database used
Metastatic bone disease. A study of the surgical treatment of 166 pathologic humeral and femoral fractures	Yazawa, Y.; Frassica, F. J.; Chao, E. Y.; Pritchard, D. J.; Sim, F. H.; Shives, T. C.	1990	irrelevant topic; no humerus
Risk and prognostic nomograms for hepatocellular carcinoma with newly-diagnosed pulmonary metastasis using SEER data	Ye, G.; Wang, L.; Hu, Z.; Liang, J.; Bian, Y.; Zhan, C.; Lin, Z.	2019	irrelevant topic; SEER database used
Management of humeral impending or pathological fractures with intramedullary nailing: reaming versus non reaming technique-a retrospective comparative study	Younis, M.; Barnhill, S. W.; Maguire, J.; Pretell-Mazzini, J.	2020	irrelevant topic; reamed vs unreamed nails
Incidence and risk factors for preoperative deep venous thrombosis in 314 consecutive patients undergoing surgery for spinal metastasis	Zacharia, B. E.; Kahn, S.; Bander, E. D.; Cederquist, G. Y.; Cope, W. P.; McLaughlin, L.; Hijazi, A.; Reiner, A. S.; Laufer, I.; Bilsky, M.	2017	risk factors, not postop
Correlation and Survival Analysis of Distant Metastasis Site and Prognosis in Patients With Hepatocellular Carcinoma	Zhan, H.; Zhao, X.; Lu, Z.; Yao, Y.; Zhang, X.	2021	irrelevant topic; SEER database used
Bone Metastases Pattern in Newly Diagnosed Metastatic Bladder Cancer: A Population-Based Study	Zhang, C.; Liu, L.; Tao, F.; Guo, X.; Feng, G.; Chen, F.; Xu, Y.; Li, L.; Han, X.; Baklaushev, V. P.; Bryukhovetskiy, A. S.; Wang, X.; Wang, G.	2018	Irrelevant outcomes
Evaluation of bone grafting for treatment of low-grade chondrosarcoma of long bones	Zhang, G.; Cheon, S.; Park, I.	2021	irrelevant topic; chondrosarcoma
Analysis of Homogeneous and Heterogeneous Factors for Bone Metastasis in Esophageal Cancer	Zhang, J.; Ma, W.; Wu, H.; Wang, J.; Lin, Y.; Wang, X.; Zhang, C.	2019	irrelevant topic; SEER database used

Article Title	Authors	Year	Reason for Exclusion
Population-based evaluation of the risk factors and prognosis among renal cell carcinoma patients with initially diagnosed lung metastases	Zhang, Z.; Liang, C.; Hou, B.; Zhou, L.	2021	irrelevant topic; SEER database used
Intercalary prosthetic reconstruction for pathologic diaphyseal humeral fractures due to metastatic tumors: outcomes and improvements	Zhao, J.; Yu, X. C.; Xu, M.; Zheng, K.; Hu, Y. C.; Wang, F.; Lun, D. X.	2018	<5 patients per group
Intercalary prosthetic replacement is a reliable solution for metastatic humeral shaft fractures: retrospective, observational study of a single center series	Zhao, Z.; Ye, Z.; Yan, T.; Tang, X.; Guo, W.; Yang, R.	2021	case series
Incidence, prognostic factors, and a nomogram of lung cancer with bone metastasis at initial diagnosis: a population-based study	Zheng, X. Q.; Huang, J. F.; Lin, J. L.; Chen, L.; Zhou, T. T.; Chen, D.; Lin, D. D.; Shen, J. F.; Wu, A. M.	2019	Irrelevant outcomes
The IlluminOss R photodynamic bone stabilization system for pathological osteolyses and fractures of the humerus: indications, advantages and limits in a series of 12 patients at 24 months of minimum follow-up	Zoccali, C.; Attala, D.; Pugliese, M.; di Uccio, A. S.; Baldi, J.	2021	case series

Appendix VI: MSTS GEBM EtDF Scoring Rubric

Criteria	Detailed considerations	Judgements (points)	Score
What is the baseline quality/strength of the evidence? See above.	Baseline strength of recommendation is listed above	No evidence (0) Low (3) Moderate (4) High (5)	
What is the value and importance of the outcomes to clinical practice?	Are the outcomes assessed by the studies impactful (e.g., pain reduction, functional improvement, etc.)?	None (0) Low (2) Moderate (3) High (5)	
What is the magnitude of the desired effect?		None (0) Low (2) Moderate (3) High (5)	
What is the magnitude of undesirable effects/complications?		High (0) Moderate (1) Low (2) None (3)	
Do the benefits outweigh the risks?	Do the benefits clearly outweigh the risks or is there a balance of benefits and harms?	No (0) Probably No (1) Uncertain (2) Probably Yes (3) Yes (5)	
What amount of resources are required to produce the desired effect?	What is the estimated equipment need, space, time, and ability of any institution to provide these needs?	Prohibitive (0) High (1) Moderate (2) Minimal (3) None (5)	
What is the cost to produce the desired effect?	What is the estimated monetary cost?	Prohibitive (0) High (1) Moderate (2) Minimal (3) None (4)	
Is the intervention/outcomes acceptable to key stakeholders?	-Are there any stakeholders who wouldn't accept risk to benefit ratio, the costs, the importance of outcomes? -Would anyone morally object to intervention (in regard to ethical principles such as no maleficence, beneficence, or justice)? -Would intervention effect people's autonomy?	No (0) Probably No (1) Uncertain (2) Probably Yes (4) Yes (5)	
Is the intervention feasible to implement?	-Is intervention sustainable? -Any barriers limiting the feasibility of implementing recommendation?	No (0) Probably No (1) Uncertain (2) Probably Yes (4) Yes (5)	
Total Score			

Appendix VII: PICO Action Statement Final Voting

PICO	Agreement %	Average Rating	Panelist 1	Panelist 2	Panelist 3	Panelist 4	Panelist 5	Panelist 6	Panelist 7	Panelist 8	Panelist 9	Panelist 10	Panelist 11	Panelist 12	Panelist 13
1	70.0%	3.8		4	1	5	4	5	1	5		5	3	5	
2	100.0%	4.9	5	5	5	5		5		4	5	5		5	5
3	90.0%	4.7	5	4	3	5		5		5	5		5	5	5
4	100.0%	4.8	5		4	5	5	5	5	5	5	4		5	
5	100.0%	4.6	5			5	5	5	4		5	4	4	4	5
6	80.0%	4.5		5		5	5	5	5	5	3	5	2		5
7	88.9%	4.7	5	5	3	5	4	5	5				5		5

Supermajority = 67% agreement

Key:
1 = Strongly Disagree
2 = Disagree
3 = Neither Agree nor Disagree
4 = Agree
5 = Strongly Agree

Appendix VIII: Evidence Tables for PICO Questions

PICO 1: Plating vs. Intramedullary Nailing vs Photodynamic Polymer for Midshaft Pathologic Humerus Fractures

Reference Title	Quality	Outcome Details	Duration	Treatment 1	Treatment 2	Effect Measure	Result (95% CI)	Favored Treatment
Hoellwarth, 2020	Low	Reoperations	1 yrs	Photodynamic Bone Stabilization	Intramedullary Nail	Mean Difference	0.04 (-0.10, 0.19)	NS
Hoellwarth, 2020	Low	Reoperations	2 yrs	Photodynamic Bone Stabilization	Intramedullary Nail	Mean Difference	0.09 (-0.07, 0.27)	NS
Hoellwarth, 2020	Low	Reoperations	614 days	Photodynamic Bone Stabilization	Intramedullary Nail	Mean Difference	0.08 (-0.09, 0.25)	NS
Hoellwarth, 2020	Low	Broken Implants	1 yrs	Photodynamic Bone Stabilization	Intramedullary Nail	Mean Difference	0.10 (-0.03, 0.24)	Intramedullary Nail
Hoellwarth, 2020	Low	Broken Implants	2 yrs	Photodynamic Bone Stabilization	Intramedullary Nail	Mean Difference	0.15 (-0.006, 0.32)	Intramedullary Nail
Hoellwarth, 2020	Low	Broken Implants	614 days	Photodynamic Bone Stabilization	Intramedullary Nail	Mean Difference	0.15 (-0.00, 0.32)	Intramedullary Nail
Hoellwarth, 2020	Low	Survival	1 yrs	Photodynamic Bone Stabilization	Intramedullary Nail	Mean Difference	0.02 (-0.18, 0.23)	NS
Hoellwarth, 2020	Low	Survival	2 yrs	Photodynamic Bone Stabilization	Intramedullary Nail	Mean Difference	0.24 (-0.009, 0.49)	NS
Hoellwarth, 2020	Low	Survival	614 days	Photodynamic Bone Stabilization	Intramedullary Nail	Mean Difference	0.15 (-0.08, 0.40)	NS
Hoellwarth, 2020	Low	Reoperations	1 yrs	Photodynamic Bone Stabilization	Cemented Plate Fixation	Mean Difference	0.05 (-0.10, 0.22)	NS
Hoellwarth, 2020	Low	Reoperations	2 yrs	Photodynamic Bone Stabilization	Cemented Plate Fixation	Mean Difference	0.06 (-0.14, 0.26)	NS
Hoellwarth, 2020	Low	Reoperations	614 days	Photodynamic Bone Stabilization	Cemented Plate Fixation	Mean Difference	0.01 (-0.20, 0.23)	NS
Hoellwarth, 2020	Low	Broken Implants	1 yrs	Photodynamic Bone Stabilization	Cemented Plate Fixation	Mean Difference	0.05 (-0.10, 0.22)	NS
Hoellwarth, 2020	Low	Broken Implants	2 yrs	Photodynamic Bone Stabilization	Cemented Plate Fixation	Mean Difference	0.06 (-0.14, 0.26)	NS
Hoellwarth, 2020	Low	Broken Implants	614 days	Photodynamic Bone Stabilization	Cemented Plate Fixation	Mean Difference	0.01 (-0.20, 0.23)	NS
Hoellwarth, 2020	Low	Survival	1 yrs	Photodynamic Bone Stabilization	Cemented Plate Fixation	Mean Difference	0.02 (-0.23, 0.28)	NS
Hoellwarth, 2020	Low	Survival	2 yrs	Photodynamic Bone Stabilization	Cemented Plate Fixation	Mean Difference	0.05 (-0.25, 0.36)	NS
Hoellwarth, 2020	Low	Survival	614 days	Photodynamic Bone Stabilization	Cemented Plate Fixation	Mean Difference	0.04 (-0.26, 0.34)	NS
Hoellwarth, 2020	Low	Reoperations	1 yrs	Intramedullary Nail	Cemented Plate Fixation	Mean Difference	-0.01 (-0.12, 0.09)	NS
Hoellwarth, 2020	Low	Reoperations	2 yrs	Intramedullary Nail	Cemented Plate Fixation	Mean Difference	0.03 (-0.10, 0.17)	NS
Hoellwarth, 2020	Low	Reoperations	614 days	Intramedullary Nail	Cemented Plate Fixation	Mean Difference	0.06 (-0.09, 0.22)	NS
Hoellwarth, 2020	Low	Broken Implants	1 yrs	Intramedullary Nail	Cemented Plate Fixation	Mean Difference	0.04 (-0.04, 0.13)	NS
Hoellwarth, 2020	Low	Broken Implants	2 yrs	Intramedullary Nail	Cemented Plate Fixation	Mean Difference	0.09 (-0.03, 0.22)	NS
Hoellwarth, 2020	Low	Broken Implants	614 days	Intramedullary Nail	Cemented Plate Fixation	Mean Difference	0.14 (-0.006, 0.29)	Intramedullary Nail
Hoellwarth, 2020	Low	Survival	1 yrs	Intramedullary Nail	Cemented Plate Fixation	Mean Difference	-0.007 (-0.21, 0.20)	NS
Hoellwarth, 2020	Low	Survival	2 yrs	Intramedullary Nail	Cemented Plate Fixation	Mean Difference	0.18 (-0.05, 0.42)	NS
Hoellwarth, 2020	Low	Survival	614 days	Intramedullary Nail	Cemented Plate Fixation	Mean Difference	0.11 (-0.11, 0.35)	NS

Sarahrudi, 2009	Low	Radial Nerve Palsy	2.1 mos	Open Reduction and Internal Plate Fixation	Intramedullary Fixation	Mean Difference	0.19 (-0.02, 0.35)	Intramedullary Nail
Sarahrudi, 2009	Low	Refracture	2.1 mos	Open Reduction and Internal Plate Fixation	Intramedullary Fixation	Mean Difference	0.04 (-0.04, 0.13)	NS
Sarahrudi, 2009	Low	Implant Loosening	2.1 mos	Open Reduction and Internal Plate Fixation	Intramedullary Fixation	Mean Difference	0.04 (-0.04, 0.13)	NS
Sarahrudi, 2009	Low	Instability	2.1 mos	Open Reduction and Internal Plate Fixation	Intramedullary Fixation	Mean Difference	-0.1 (-0.23, 0.03)	NS
Sarahrudi, 2009	Low	Local Tumor Progression	2.1 mos	Open Reduction and Internal Plate Fixation	Intramedullary Fixation	Mean Difference	-0.05 (-0.14, 0.04)	NS
Dijkstra, 1996	Low	Subjective Relief of Pain - Excellent	4 wks	Intramedullary Nail	ORIF Plate	Mean Difference	0.19 (-0.10, 0.49)	NS
Dijkstra, 1996	Low	Subjective Relief of Pain - Good	4 wks	Intramedullary Nail	ORIF Plate	Mean Difference	-0.2 (-0.56, 0.04)	NS
Dijkstra, 1996	Low	Subjective Relief of Pain - Fair	4 wks	Intramedullary Nail	ORIF Plate	Mean Difference	0.005 (-0.13, 0.14)	NS
Dijkstra, 1996	Low	Subjective Relief of Pain - Poor	4 wks	Intramedullary Nail	ORIF Plate	Mean Difference	0.05 (-0.05, 0.16)	NS
Dijkstra, 1996	Low	Objective Relief of Pain - Excellent	4 wks	Intramedullary Nail	ORIF Plate	Mean Difference	-0.3 (-0.61, -0.05)	NS
Dijkstra, 1996	Low	Objective Relief of Pain - Good	4 wks	Intramedullary Nail	ORIF Plate	Mean Difference	0.31 (-0.009, 0.61)	NS
Dijkstra, 1996	Low	Objective Relief of Pain - Fair	4 wks	Intramedullary Nail	ORIF Plate	Mean Difference	-0.08 (-0.31, 0.13)	NS
Dijkstra, 1996	Low	Objective Relief of Pain - Poor	4 wks	Intramedullary Nail	ORIF Plate	Mean Difference	0.11 (-0.03, 0.25)	NS
Dijkstra, 1996	Low	Function - Excellent	4 wks	Intramedullary Nail	ORIF Plate	Mean Difference	-0.0 (-0.36, 0.26)	NS
Dijkstra, 1996	Low	Function - Good	4 wks	Intramedullary Nail	ORIF Plate	Mean Difference	0.04 (-0.26, 0.35)	NS
Dijkstra, 1996	Low	Function - Fair	4 wks	Intramedullary Nail	ORIF Plate	Mean Difference	0.005 (-0.13, 0.14)	NS
Dijkstra, 1996	Low	Function - Poor	4 wks	Intramedullary Nail	ORIF Plate	Mean Difference	0 (0, 0)	NS
Dijkstra, 1996	Low	Wound Dehiscence	4 wks	Intramedullary Nail	ORIF Plate	Mean Difference	-0.05 (-0.14, 0.04)	NS
Dijkstra, 1996	Low	Wound Haematoma	4 wks	Intramedullary Nail	ORIF Plate	Mean Difference	0.005 (-0.13, 0.14)	NS
Dijkstra, 1996	Low	Radial Nerve Paresis	4 wks	Intramedullary Nail	ORIF Plate	Mean Difference	-0.05 (-0.14, 0.04)	NS
Dijkstra, 1996	Low	Rebleeding	4 wks	Intramedullary Nail	ORIF Plate	Mean Difference	-0.05 (-0.14, 0.04)	NS
Dijkstra, 1996	Low	Primary Tumor	4 wks	Intramedullary Nail	ORIF Plate	Mean Difference	-0.03 (-0.25, 0.17)	NS
Dijkstra, 1996	Low	Sepsis	4 wks	Intramedullary Nail	ORIF Plate	Mean Difference	0.005 (-0.14, 0.04)	NS
Dijkstra, 1996	Low	Cardiac	4 wks	Intramedullary Nail	ORIF Plate	Mean Difference	0.05 (-0.05, 0.16)	NS
Dijkstra, 1996	Low	Angulation	4 wks	Intramedullary Nail	ORIF Plate	Mean Difference	0.005 (-0.13, 0.14)	NS

Dijkstra, 1996	Low	Rotation	4 wks	Intramedullary Nail	ORIF Plate	Mean Difference	0.05 (-0.05, 0.16)	NS
Dijkstra, 1996	Low	Refracture at the end of fixation device	4 wks	Intramedullary Nail	ORIF Plate	Mean Difference	0.05 (-0.05, 0.16)	NS

PICO 4: Role of Cement vs. No Cement

Reference Title	Quality	Outcome Details	Duration	Treatment 1	Treatment 2	Effect Measure	Result (95% CI)	Favored Treatment
Laitinen, 2011	Low	Pain Relief at Operated Site	1 wks	Cemented Nails	Non-Cemented Nails	Mean Difference	-0.6 (-3.3, 2.1)	NS
Laitinen, 2011	Low	Pain Relief at Operated Site	6 mos	Cemented Nails	Non-Cemented Nails	Mean Difference	-0.93 (-2.4, 0.54)	NS
Laitinen, 2011	Low	Pain Relief at Operated Site	6 mos	Cemented Nails	Non-Cemented Nails	Mean Difference	-0.62 (-2.01, 0.77)	NS
Laitinen, 2011	Low	Use of Analgesics	1 wks	Cemented Nails	Non-Cemented Nails	Mean Difference	0 (-3.8, 3.8)	NS
Laitinen, 2011	Low	Use of Analgesics	6 mos	Cemented Nails	Non-Cemented Nails	Mean Difference	-0.7 (-3.22, 1.8)	NS
Laitinen, 2011	Low	Use of Analgesics	6 mos	Cemented Nails	Non-Cemented Nails	Mean Difference	-0.4 (-2.9, 2.1)	NS

PICO 5: Shoulder Arthroplasty Reconstruction Options

Reference Title	Quality	Outcome Details	Duration	Treatment 1	Treatment 2	Effect Measure	Result (95% CI)	Favored Treatment
Houdek, 2021	Low	Subluxation (>25%)	2 yrs	Hemiarthroplasty	Reverse Arthroplasty	Mean Difference	-0.3 (-0.54, -0.1)	Reverse Arthroplasty
Houdek, 2021	Low	Allograft Resorption	3 yrs	Hemiarthroplasty	Reverse Arthroplasty	Mean Difference	-0.002 (-0.20, 0.19)	NS
Houdek, 2021	Low	Periprosthetic or Allograft Fracture	4 yrs	Hemiarthroplasty	Reverse Arthroplasty	Mean Difference	-0.015 (-0.18, 0.14)	NS
Houdek, 2021	Low	Infection	5 yrs	Hemiarthroplasty	Reverse Arthroplasty	Mean Difference	0.004 (-0.07, 0.08)	NS
Houdek, 2021	Low	Reoperations	6 yrs	Hemiarthroplasty	Reverse Arthroplasty	Mean Difference	-0.03 (-0.19, 0.12)	NS
Houdek, 2021	Low	Revision Procedure	7 yrs	Hemiarthroplasty	Reverse Arthroplasty	Mean Difference	-0.01 (-0.08, 0.05)	NS
Grosel, 2019	Low	Revision Procedure	8 yrs	Hemiarthroplasty	Reverse Arthroplasty	Mean Difference	0.02 (-0.02, 0.07)	NS
Grosel, 2019	Low	Death	9 yrs	Hemiarthroplasty	Reverse Arthroplasty	Mean Difference	0.71 (-0.56, 0.85)	Reverse Arthroplasty
Grosel, 2019	Low	Local Recurrence	10 yrs	Hemiarthroplasty	Reverse Arthroplasty	Mean Difference	0.07 (-0.006, 0.16)	NS
Grosel, 2019	Low	Infection	11 yrs	Hemiarthroplasty	Reverse Arthroplasty	Mean Difference	0.07 (-0.006, 0.16)	NS
Grosel, 2019	Low	Dislocation and Subluxation Events	12 yrs	Hemiarthroplasty	Reverse Arthroplasty	Mean Difference	0.27 (-0.08, 0.45)	NS
Grosel, 2019	Low	ROM; Forward Flexion	13 yrs	Hemiarthroplasty	Reverse Arthroplasty	Mean Difference	-57 (-146.4, 32.4)	Reverse Arthroplasty
Grosel, 2019	Low	American Shoulder and Elbow Surgeons Score	14 yrs	Hemiarthroplasty	Reverse Arthroplasty	Mean Difference	4 (-82.3, 90.3)	NS
Grosel, 2019	Low	Simple Shoulder Test Score	15 yrs	Hemiarthroplasty	Reverse Arthroplasty	Mean Difference	1.4 (-3.09, 5.89)	NS
Grosel, 2019	Low	VAS	NA	Hemiarthroplasty	Reverse Arthroplasty	Mean Difference	-0.1 (-3.5, 3.3)	NS

PICO 6: Equity/Disparities Present in the Treatment of Metastatic Bone Disease Patients

Reference Title	Quality	Outcome Details	Duration	Treatment 1	Treatment 2	Effect Measure	Result (95% CI)	Favored Treatment

Hung, 2021	Low	KPS Score <70	White	Black	Mean Difference	-0.2 (-0.31, -0.0)	Black
Hung, 2021	Low	Frankel Grade A-C	White	Black	Mean Difference	-0.05 (-0.13, 0.01)	NS
Hung, 2021	Low	ASA Class >2	White	Black	Mean Difference	0.01 (-0.07, 0.10)	NS
Hung, 2021	Low	Complications	White	Black	Mean Difference	-0.02 (-0.13, 0.08)	NS
tHung, 2021	Low	Deceased	White	Black	Mean Difference	0.00 (-0.02, 0.03)	NS
Hung, 2021	Low	Length of Stay	White	Black	Mean Difference	-0.06 (-0.13, -0.002)	White
Hung, 2021	Low	Prolonged Length of Stay	White	Black	Mean Difference	-0.06 (-0.16, 0.03)	NS
Herget, 2021	Low	Age	<60	>60	Mean Difference	-0.04 (-0.10, 0.007)	NS
Herget, 2021	Low	Sex	Female	Male	Mean Difference	0.05 (-0.004, 0.10)	NS
Huang, 2019	Low	Sex	Female	Male	Mean Difference	0.60 (-0.49, 0.71)	Males
Rades, 2020 A	Low	Age	<65	>66	Mean Difference	0.005 (-0.10, 0.11)	NS
Rades, 2020 A	Low	Sex	Female	Male	Mean Difference	-0.1 (-0.24, -0.02)	Males
Rades, 2020 B	Low	Age	<70	>71	Mean Difference	0.03 (-0.22, 0.29)	NS
Rades, 2020 B	Low	Sex	Female	Male	Mean Difference	-0.4 (-0.67, -0.2)	Males
Rades, 2019	Low	Age	<60	61-70	Mean Difference	0.002 (-0.05, 0.06)	NS
Rades, 2019	Low	Age	<60	>70	Mean Difference	-0.1 (-0.17, -0.05)	>70
Rades, 2019	Low	Age	61-70	>70	Mean Difference	-0.1 (-0.17, -0.05)	>70
Rades, 2019	Low	Sex	Female	Male	Mean Difference	0.01 (-0.04, 0.08)	NS
Scott, 2018	Low	Sex	Female	Male	Mean Difference	0.21 (-0.06, 0.35)	Females
Vos, 2019	Low	Sex	Female	Male	Mean Difference	-0.06 (-0.10, -0.02)	Males
Vos, 2019	Low	Socioeconomic Status	High	Medium	Mean Difference	-0.1 (-0.13, -0.06)	Medium
Vos, 2019	Low	Socioeconomic Status	High	Low	Mean Difference	-0.03 (-0.06, -0.001)	Low
Vos, 2019	Low	Socioeconomic Status	Medium	Low	Mean Difference	0.06 (-0.03, 0.10)	Medium
Wisanuyotin, 2018	Low	Sex	Female	Male	Mean Difference	0.05 (-0.07, 0.19)	NS
Wisanuyotin, 2018	Low	Age	<60	>60	Mean Difference	-0.01 (-0.15, 0.11)	NS
Wong, 2013	Low	Age	<60	>60	Mean Difference	0.23 (-0.16, 0.30)	<60
Wong, 2013	Low	Sex	Female	Male	Mean Difference	0.52 (-0.46, 0.57)	Females
Raschka, 2022	Low	Age	<65	>65	Mean Difference	-0.1 (-0.30, -0.07)	NS
Raschka, 2022	Low	Sex	Female	Male	Mean Difference	-0.04 (-0.16, 0.07)	NS

Appendix IX: Guideline Development Group Disclosures

Felasfa Wodajo, MD – Onkos Surgical: Paid consultant

Nate Mesko, MD – Bone Support: Paid consultant

Musculoskeletal Tumor Society: Board or committee member

ONKOS Surgical: Paid consultant; Paid presenter or speaker

Stryker: Paid consultant; Paid presenter or speaker

Nicholas Tedesco, DO – Doctorpedia: Stock or stock Options

Journal of the American Osteopathic Academy of Orthopedics: Editorial board

Medscape: Publishing royalties, financial or material support

Musculoskeletal Tumor Society: Board or committee member

RomTech, Inc.: Stock or stock Options

Cecilia Belzarena, MD – Nothing to disclose.

Alexander Christ, MD – AAOS: Board or committee member

DJ Orthopaedics: Other financial or material support

Intellijoint Surgical: Paid consultant

Musculoskeletal Tumor Society: Board or committee member

Orthopaedic Research Society: Board or committee member

Smith & Nephew: Paid consultant

Matthew Colman, MD –Alphatec Spine: IP royalties; Paid consultant

AO Spine North America: Board or committee member; Research support

Cervical Spine Research Society: Board or committee member

CSRS: Research support

DePuy, A Johnson & Johnson Company: Paid presenter or speaker

K2M: Paid presenter or speaker

K2M/Stryker Spine: Paid consultant

LSRS: Board or committee member

Musculoskeletal Tumor Society: Board or committee member

North American Spine Society: Board or committee member

Orthofix: Paid consultant

Orthofix, Inc.: Paid presenter or speaker

Spinal Elements: IP royalties; Paid consultant

Xenix Medical: Paid consultant

Yee-Cheen Doung, MD – Musculoskeletal Tumor Society: Board or committee member

Michelle Ghert, MD – Journal of Orthopaedic Research: Editorial or governing board

Clinical Orthopaedics and Related Research: Editorial or governing board

Musculoskeletal Tumor Society: Board or committee member

Stryker: Paid consultant; Paid presenter or speaker

Trey Gurich, MD – Nothing to disclose.

Matthew Houdek, MD – Link Orthopaedics: Paid consultant

Mid-America Orthopaedic Association: Board or committee member

Musculoskeletal Tumor Society: Board or committee member

Dipak Ramkumar, MD – Nothing to disclose.

Geoffrey Siegel, MD – Annals of Medical Case Reports- Oncology: Editorial or governing board

Steve Thorpe, MD – AAOS: Board or committee member

Musculoskeletal Tumor Society: Board or committee member

Matthew Wallace, MD – Nothing to disclose.