**CAT Final Name: Sierra Teegarden**

**Search Question:** Clearly state the question (including outcomes or criteria to be tracked)

A 36-year-old female presents to CitiMed for follow-up evaluation and management of injuries sustained from being struck by a motor vehicle while in the crosswalk. She sustained a fracture to her left femur, tibia, and fibula upon impact. She is concerned about how her injuries will heal and states that wants a “quick and speedy recovery back to her baseline” because she is eager to gain functionality in her left work so she can get back to her normal routine. She states the PA at her orthopedics office mentioned that PTH hormone may be an effective adjunctive treatment for her fracture healing process but she would like more information and to know if this is a treatment modality I would recommend for her.

Does synthetic parathyroid hormone (Teriparatide) injections improve long bone fracture healing?

**Question Type:** What kind of question is this? (boxes are now checkable in Word)

[ ] Prevalence [ ] Screening [ ] Diagnosis

[ ] Prognosis [ ] Treatment [ ] Harms

I will only be considering randomized-controlled trials and systematic reviews/meta-analysis based on RCTs to answer this PICO question. The risk of bias and confounding factors such as differences in functional therapies and surgical corrections is too high to consider observational studies/retrospective cohort studies to answer this question. Additionally, I will look for RCTs that use placebo since determining fracture healing may contain subjective components such as self-reported sensations, pain scales, and functional scoring.

**PICO search terms:**

|  |  |  |  |
| --- | --- | --- | --- |
| **P** | **I** | **C** | **O** |
| fracture | PTH | Standard treatment | Fracture healing |
| Long bone fracture | Parathyroid hormone | placebo | Fracture union |
| Femoral fracture | teriparatide |  | Bone healing |
| Tibial fracture | Synthetic PTH |  |  |
| Fibular fracture |  |  |  |
| Broken bone |  |  |  |

**Search tools and strategy used:**

Please indicate what data bases/tools you used, provide a list of the terms you searched together in each tool, and how many articles were returned using those terms and filters.
Explain how you narrow your choices to the few selected articles.

**Search tools and strategy used:**

**Filters/limits applied:**

1. Full text
2. Publication date: Within 10 years
3. Language: English
4. Article Type: Meta-Analysis, Systematic review, Randomized Control Trial, Randomized Control Study, Retrospective Cohort Study, Prospective Cohort Study
5. Age: None selected

**Databases used:**

1. PubMed
2. Google Scholar
3. Science Direct
4. Wiley Online Library

**Results found:**

**Number of articles returned once relevant limits are added**

|  |  |  |  |
| --- | --- | --- | --- |
| **Database** | **Filter** | **Terms Searched** | **Articles Returned** |
| **PubMed** | Full text/English/Meta-analysis/Systematic Review/Randomized control trial/Randomized control study/Sort by relevance | Parathyroid hormone fracture healing | 17 |
| Teriparatide fracture | 155 |
| **Google Scholar** | 2012-2022/Include citations/All in title | Teriparatide fracture healing | 63 |
| **ScienceDirect** | English/2012-2022/Research Articles/Sort by relevance | Teriparatide fracture healing | 278 |
| **Wiley Online Library** | English/Anywhere/Journals/Open access content/Sorted by Relevance/ | Teriparatide fracture healing | 34 |

My initial search included the phrase “parathyroid hormone fracture healing”, however it only yielded 17 results which prompted me to broaden my search terms. Since “Teriparatide” is the name of the synthetic PTH hormone that is given, I tried that term instead which ended up yielding more results. I also omitted the term “healing” in hopes that it may yield more articles related to fracture healing that may have been titled with other synonymous terms. However, this expanded my search too broadly so I then added the term “healing” back into the rest of my searches. Enough related articles were returned on all of the databases I used and many of the results from the different databases were duplicates of each other. When examing further, I found that a large portion of the related articles were study protocols rather than completed studies with results which further limited my selection. I then ranked each article based on level of evidence, publication date, region, patient population, and other relevant characteristics (such as adult population) which lead me to the four articles chosen for this PICO.

**Results found:**

**Article 1**

|  |
| --- |
| **Citation**: Hong H, Song T, Liu Y, Li J, Jiang Q, Song Q, Deng Z. The effectiveness and safety of parathyroid hormone in fracture healing: A meta-analysis. Clinics (Sao Paulo). 2019;74:e800. doi: 10.6061/clinics/2019/e800. Epub 2019 Apr 25. PMID: 31038646; PMCID: PMC6467172. |
| **Type of Study: Meta-analysis of randomized controlled trials** |
| **Abstract:**The very large economic and social burdens of fracture-related complications make rapid fracture healing a major public health goal. The role of parathyroid hormone (PTH) in treating osteoporosis is generally accepted, but the effect of PTH on fracture healing is controversial. This meta-analysis was designed to investigate the efficacy and safety of PTH in fracture healing. The EMBASE, PubMed, and Cochrane Library databases were systematically searched from the inception dates to April 26, 2018. The primary randomized clinical trials comparing PTH treatment for fracture healing with placebo or no treatment were identified. We did not gain additional information by contacting the authors of the primary studies. Two reviewers independently extracted the data and evaluated study quality. This meta-analysis was executed to determine the odds ratio, mean difference, standardized mean difference, and 95% confidence intervals with random-effects models. In total, 8 randomized trials including 524 patients met the inclusion criteria. There were significant differences in fracture healing time, pain relief and function improvement. There were no significant differences in the fracture healing rate or adverse events, including light-headedness, hypercalcemia, nausea, sweating and headache, except for slight bruising at the injection site. We determined that the effectiveness and safety of PTH in fracture healing is reasonably well established and credible. |
| **Reason for Selection:** I chose this meta-analysis because it directly answers my PICO question by demonstrating whether PTH can promote fracture healing by comparing PTH treatment to placebo treatment or no treatment in patients with one or more fractures.  |
| **Key Points:*** PTH treatment in patients with fracture was better than placebo or no treatment based on healing time, pain scores, and functional outcomes
* Previous studies were inconsistent with the effect of PTH on fracture healing
* 524 patients aged 21-94 years old with fractures from 8 RCTs involving recently published primary studies were included
* The placebo group had longer fracture healing time, higher fracture pain degree, and worse functional outcomes
* Methods included teriparatide injected subcutaneously at 20 micrograms per day or PTH administered at 100 micrograms per day
* This study was published in 2019
* **Dose & Duration:** 20 μg Teriparatide or 100 μg PTH administered subcutaneously (Anabolic effects of synthetic teriparatide vs PTH are equal to each other at this ratio). Treatment ranged from 4-24 months
* While equal early callus formation was observed in all duration groups, better functional outcomes were observed in groups exceeding 4 weeks of therapy.
 |

**Article 2:**

|  |
| --- |
| **Citation**: Bhandari M, Jin L, See K, Burge R, Gilchrist N, Witvrouw R, Krohn KD, Warner MR, Ahmad QI, Mitlak B. Does Teriparatide Improve Femoral Neck Fracture Healing: Results From A Randomized Placebo-controlled Trial. Clin Orthop Relat Res. 2016 May;474(5):1234-44. doi: 10.1007/s11999-015-4669-z. Epub 2016 Mar 1. PMID: 26932738; PMCID: PMC4814417. |
| **Type of Study: Randomized (Placebo) Controlled Trial** |
| **Abstract:****Background**There is a medical need for therapies that improve hip fracture healing. Teriparatide (Forteo®/ Forsteo®, recombinant human parathyroid hormone) is a bone anabolic drug that is approved for treatment of osteoporosis and glucocorticoid-induced osteoporosis in men and postmenopausal women at high fracture risk. Preclinical and preliminary clinical data also suggest that teriparatide may enhance bone healing.**Questions/purposes**We wished to test the hypotheses that treatment with teriparatide versus placebo would improve femoral neck fracture healing after internal fixation as measured by (1) frequency of revision surgery, (2) radiographic fracture healing, and (3) other outcomes including pain control, gait speed, and safety.**Methods**We initiated two separate, but identically designed, clinical trials to meet FDA requirements to provide substantial evidence to support approval of a new indication. The two prospective, randomized double-blind, placebo-controlled Phase III studies were designed to evaluate the effect of subcutaneous teriparatide (20 μg/day) for 6 months versus placebo on fracture healing at 24 months. The trials were conducted concurrently with a planned enrollment of 1220 patients per trial. However, enrollment was stopped owing to very slow patient accrual, and an a priori decision was made to pool the results of those studies for statistical analyses before study completion; pooling was specified in both protocols. Randomization was stratified by fixation (sliding hip screw or multiple cancellous screws) and fracture type (displaced or nondisplaced). An independent Central Adjudication Committee reviewed revision surgical procedures and radiographs. A total of 159 patients were randomized in the two trials (81 placebo, 78 teriparatide). The combined program had very low power to detect the originally expected treatment effect but had approximately 80% power to detect a larger difference of 12% between treatment groups for risk of revision surgery.**Results**The proportion of patients undergoing revision surgery at 12 months was 14% (11 of 81) in the placebo group versus 17% (13 of 78) in the teriparatide group. Central Adjudication Committee review excluded two of these patients treated with placebo from the primary analysis. After exclusions, the proportion of patients who did not undergo revision surgery at 12 months (primary endpoint) was not different between the study and placebo groups, at 88% in the placebo group (90% CI, 0.79–0.93) versus 84% in the teriparatide group (90% CI, 0.75–0.90; p = 0.743). There also were no differences between groups in the proportion of patients achieving radiographic fracture healing at 12 months (75% [61 of 81] placebo versus 73% [57 of 78] teriparatide; odds ratio, 0.89; 90% CI, 0.46–1.72; p = 0.692) or in measures of pain control (such as pain during ambulation, 92% [55 of 62] placebo versus 91% [52 of 57] teriparatide; odds ratio, 0.91; 90% CI, 0.25–3.37; p = 0.681). The frequency of patients reporting adverse events was 49% [40 of 81] in the placebo group versus 45% [35 of 78] in the teriparatide group (p = 0.634) during the 6-month treatment period.**Conclusions**The small sample size limited this study’s power to detect potential differences, and the results are exploratory. With the patients available, teriparatide did not decrease the risk of revision surgery, improve radiographic signs of fracture healing, or decrease pain compared with the placebo. The adverse event data observed were consistent with the teriparatide safety profile. Functional and health outcome data from the studies may help improve our understanding of patients recovering from femoral neck fractures. Further large controlled studies are required to determine the effect of teriparatide on fracture healing. |
| **Reason for Selection:**I chose this RCT because it used a placebo and tested the hypotheses that treatment with teriparatide (synthetic PTH) would improve femoral neck fracture healing after internal fixation. Not only does it examine the efficacy of PTH treatment on healing a long bone, but it is examining the femur which is one of the bones fractured in my patient in which this question was derived from. |
| **Key Points:*** The proportion of patients undergoing revision surgery at 12 months was 14% in the placebo group versus 17% in the teriparatide group. However, two patients were subsequently excluded two patients from the placebo group and the new findings showed no difference between the two groups.
* There was no difference between groups in the proportion of patients achieving radiographic fracture healing at 12 months
* There was no difference between the two groups in pain control
* This study concluded that teriparatide did not decrease the risk of revision surgery, improve radiographic signs of fracture healing, or decrease pain compared with placebo.
* The adverse events were consistent with the teriparatide safety profile.
* The level of evidence was level II, prospective study
* There were 159 participants split between the teriparatide and placebo group
* This study was published in 2016
* **Dose & Duration:** 20 μg or 40 μg/day administered subcutaneously at either 6 months duration or 24 months duration vs placebo.
* No difference was observed in 20 vs 40 μg/day dosing for accelerated radiographic healing of wrist fractures
 |

**Article 3:**

|  |
| --- |
| **Citation**: Yoon BH, Kim KC. Does Teriparatide Improve Fracture Union?: A Systematic Review. J Bone Metab. 2020 Aug;27(3):167-174. doi: 10.11005/jbm.2020.27.3.167. Epub 2020 Aug 31. PMID: 32911581; PMCID: PMC7571240. |
| **Type of Study: Systematic Review** |
| **Abstract:** We conducted an updated review of the evidence of teriparatide (TPTD) for fracture healing for the following questions. (1) Does it decrease fracture healing time?; (2) Can it be an alternative treatment for nonunion?; (3) Does it aid the union of atypical femoral fracture (AFF)? We searched PubMed, EMBASE, and Cochrane Library including “Fracture” AND “nonunion” AND “Teriparatide”. In total, 57 publications met our inclusion criteria were summarized. This systemic review of the available literature revealed that TPTD works positively with regard to enhancing fracture healing time and union of AFF. There are also many case studies on the use of TPTD could be a potential new safe treatment for nonunion with no side effects. However, level 1 studies on the evidence of TPTD are still lacking so far. Over the last decade, a growing body of evidence has accumulated suggesting that TPTD can be an adjunct to enhance fracture healing or a therapeutic option to treat nonunion, but greater evidences from large volume prospective trials are needed. |
| **Reason for Selection:**I chose to include this systematic review because it evaluated if teriparatide decreased fracture healing time, aided in the union of atypical femoral fractures, and if it could be used as an alternative treatment for nonunion. One the aims specifically looked at the femur, which again, is one of the bones in question for my original patient. |
| **Key Points:*** Although teriparatide might reduce the risk of nonunion, it appears that the main clinical advantage is the acceleration of time to fracture healing and enhanced bone formation
* Based on this evidence, it can be hypothesized that teriparatide could be a preventative treatment and supportive treatment in fractures at high risk of nonunion and complexed fractures in osteoporotic bone
* This study was published in 2020
* Included studies were those that had patients treated with daily 20 or 40 micrograms of recombinant human PTH hormone or weekly 56.5 micrograms to induce fracture healing or nonunion
* Patients with illnesses that affect bone or calcium metabolism were excluded from this study
* 57 publications were selected for systematic review
* **Dosing & Duration:** 20 μg/day Teriparatide or 100 μg/day PTH administered subcutaneously for 3 to 9 months.
* Successful union was observed in all reports between 3 to 9 months.
* Article concludes it is still unknown whether a standard dose or duration of TPTD is optimal due to a paucity of randomized studies
 |

**Article 4:**

|  |
| --- |
| **Citation**: Shi Z, Zhou H, Pan B, Lu L, Liu J, Kang Y, Yao X, Feng S. Effectiveness of Teriparatide on Fracture Healing: A Systematic Review and Meta-Analysis. PLoS One. 2016 Dec 20;11(12):e0168691. doi: 10.1371/journal.pone.0168691. PMID: 27997614; PMCID: PMC5173248. |
| **Type of Study: Systematic Review & Meta-analysis** |
| **Abstract:****Purpose**Nowadays, the efficacy of teriparatide in treating osteoporosis was widely accepted, but the discussion about using teriparatide to enhance fracture healing hasn’t come to an agreement. This meta-analysis was conducted to evaluate the effectiveness of teriparatide for fracture healing.**Methods**We searched PubMed, the Cochrane Library, and Embase in August 2016 for randomized controlled trials (RCTs) which concerned the treatment of teriparatide for fracture healing.**Results**Finally, a total of 380 patients were randomly assigned in the 5 trials included in this meta-analysis. There was a significant effectiveness with regards to function improvement in patients following fracture, however, there was no significant effectiveness with regards to time of radiographic fracture healing, fracture healing rate and reduction in pain.**Conclusions**This analysis showed that administration of teriparatide following fracture lacked the effectiveness for fracture healing. Moreover, teriparatide administration had no apparent adverse effects. These results should be interpreted with caution because of some clear limitations. If we want to confirm whether teriparatide improves fracture healing, more high-quality randomized controlled trials are needed. |
| **Reason for Selection:** I chose this meta-analysis because if its’ high level of evidence and purpose which evaluated the efficacy of teriparatide in enhancing fracture healing. Additionally, it was recently published in 2016 and derived from randomized controlled trials. |
| **Key Points:*** 380 total participants were randomly assigned in the 5 trials included in the meta-analysis
* There was a significant effectiveness in regard to functional improvement in patients following fracture, however, there was no significant effectiveness in regards to time of radiographic fracture healing, fracture healing rate and reduction in pain
* The study concluded that administration of teriparatide following fracture lacked the effectiveness for fracture healing.
* Teriparatide administration had no apparent adverse effects
* This study was published in 2016
* **Dose & Duration:** 20 μg or 40 μg/day teriparatide or 100 μg/day PTH for a duration of 4 to 24 months.
* No direct analysis on optimal dose/duration, results unclear based on individual studies being inconsistent with each other in uniform dosages for duration.
 |

**Article 5:**

|  |
| --- |
| **Citation**: Greenspan SL, Vujevich K, Britton C, Herradura A, Gruen G, Tarkin I, Siska P, Hamlin B, Perera S. Teriparatide for treatment of patients with bisphosphonate-associated atypical fracture of the femur. Osteoporos Int. 2018 Feb;29(2):501-506. doi: 10.1007/s00198-017-4286-7. Epub 2017 Oct 30. PMID: 29085957; PMCID: PMC6468986. |
| **Type of Study: Randomized clinical trial** |
| **Abstract:****Summary**The Fracture Improvement with Teriparatide (Fix-IT) study randomized 13 women with an atypical femur fracture to immediate vs delayed teriparatide therapy; all were followed for 12 months. Results suggested a trend for superior healing and lesser bone mineral density declines in the immediate vs delayed group with no differences in adverse events.**Purpose**Little clinical data are available on the use of teriparatide for the treatment of bisphosphonate-associated atypical femur fractures (AFF). The goal of the Fix-IT study was to determine if immediate therapy with teriparatide was superior for fracture healing after an AFF compared to a 6-month delay in teriparatide therapy.**Methods**This randomized pilot clinical trial included 13 women with an AFF who were randomized to immediate teriparatide vs a delay of 6 months. All were followed for 12 months on teriparatide. The primary outcomes included individual and composite measures of radiologic bone healing (scored 1 point [no healing] to 4 points [complete healing]) at 6 and 12 months. Secondary outcomes included bone mineral density of the unfractured contralateral hip, spine, 1/3 distal radius, and adverse events.**Results**We found there was a trend for superior healing with the composite score (12.6 vs 11.2 at 6 months and 15.4 vs 13.2 at 12 months), and lesser bone mineral density declines at the 1/3 distal radius (12-month change − 1.9 vs − 6.1%) in the immediate vs the delayed group. There were no differences in adverse events. There was one implant failure in the delayed group.**Conclusions**There is a preliminary signal for greater improvements with immediate teriparatide therapy vs delayed therapy. However, because an AFF is a rare event, and only a small number of patients were included, the results must be interpreted with caution. |
| **Reason for Selection:** I chose this study because my first four articles focus on Teriparatide use for healing traditional fractures and this article expands the potential benefits of this drug by examining its’ use in bisphosphonate-associated atypical fractures. It specifically examines immediate vs delayed treatment with teriparatide for skeletal healing of atypical femoral fractures. |
| **Key Points:*** Patients with acute atypical femur fracture who previously had taken bisphosphonate, had greater improvement in fracture healing if teriparatide was started immediately after the fracture vs delayed use at 6 months.
* The changes in bone mineral density were not significantly different at the spine or hip between the immediate and delayed group of teriparatide except for less loss at the distal 1/3 of the radius
* Limitations of the study included the coordinator and patients not being blind to study allocation and number of participants were small.
* Additionally, because atypical femur fracture secondary to teriparatide use is a rare event, the number of participants were small so results must be interpreted with caution
* Treatment with teriparatide was well tolerated and appears to be safe
* **Dose & Duration:** Teriparatide 20 μg/day subcutaneously for either 12 months or delayed treatment starting at 6 months and ending at 12 months. All groups were supplemented with Vitamin D and Calcium
 |

**Article 6:**

|  |
| --- |
| **Citation**: Lou S, Lv H, Wang G, Zhang L, Li M, Li Z, Zhang L, Tang P. The Effect of Teriparatide on Fracture Healing of Osteoporotic Patients: A Meta-Analysis of Randomized Controlled Trials. Biomed Res Int. 2016;2016:6040379. doi: 10.1155/2016/6040379. Epub 2016 Jun 26. PMID: 27429980; PMCID: PMC4939202. |
| **Type of Study: Meta-analysis of RCTs** |
| **Abstract:**Purpose. This meta-analysis is to assess the effectiveness of teriparatide in fracture healing and clinical function improvement of the osteoporotic patients. Methods. We searched PubMed, Embase, Web of Science, and the Cochrane databases for randomized and quasi-randomized controlled trials comparing teriparatide to placebo, no treatment, or comparator interventions in the osteoporotic patients. Results. Five studies with 251 patients were included. Patients treated with teriparatide therapy had a significant shorter radiological fracture healing time compared with those in the control group (mean difference [MD] −4.54 days, 95% confidence interval [CI] −8.80 to −0.28). Stratified analysis showed that lower limb group had significant shorter healing time (MD −6.24 days, 95% CI −7.20 to −5.29), but upper limb group did not (MD −1 days, 95% CI −2.02 to 0.2). Patients treated with teriparatide therapy showed better functional outcome than those in the control group (standardized mean difference [SMD] −1.02, 95% CI −1.81 to −0.22). Patients with therapy duration over 4 weeks would have better functional outcome (SMD −1.68, 95% CI −2.07 to −1.29). Conclusions. Teriparatide is effective in accelerating fracture healing and improving functional outcome of osteoporotic women. However, more clinical studies are warranted in order to determine whether the results are applicable to males and the clinical indications for teriparatide after osteoporotic fractures. |
| **Reason for Selection:** I selected this article because like article 5, it expands upon the populations with fractures that may benefit from Teriparatide use. This meta-analysis assesses the effectiveness of the drug in patients with osteoporotic fractures as well as clinical functional improvements. |
| **Key Points:*** Teriparatide promoted osteoporotic fracture healing
* Teriparatide use was associated with improved functional outcomes
* Evidence of both outcomes was confirmed by the GRADE system
* Limitations included small participant pools in each of the five studies included.
* Because more than 75% of osteoporotic fractures occurred in women, and only six patients were males, the primary results are more applicable to osteoporotic women than men.
* **Dose & Duration:** Teriparatide 20 μg/day or PTH 100 μg/day administered subcutaneously. Two studies used Teriparatide 40 μg/day. Duration of treatment varied from 4-24 months.
* Better functional outcomes observed in patients that had therapy with a duration longer than four weeks.
 |

**Links:**

Article 1 – https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6467172/

Article 2 – https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4814417/

Article 3 – https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7571240/

Article 4 – https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5173248/

Article 5 – https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6468986/

Article 6 – https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4939202/

**Summary of the Evidence**:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Author (Date) | Level of Evidence | Sample/Setting(# of subjects/ studies, cohort definition etc. ) | Outcome(s) studied | Key Findings | Limitations and Biases |
| Hong H, Song T, Liu Y, Li J, Jiang Q, Song Q, Deng Z. 2019 | Meta-analysis of RCTs | Sample: 8 RCTs with 524 participants. 79.6% women and 20.4% men. Mean age 73 years old. Upper limb fractures, pelvis, and lower limb fractures.Search strategy: The EMBASE, PubMed, and Cochrane Library databases from inception dates – April 26, 2018.Identified: Articles comparing PTH treatment for fracture healing with placebo or no treatment | Whether PTH can promote fracture healing by comparing PTH treatment to a placebo treatment or no treatment in patients with fracture.Analytics included: Odds ratio, mean difference, standardized mean difference, and 95% confidence intervals with random-effects models | **Results:**-There was statistically significant difference in fracture healing time (MD -3.05, 95% CI -5.96 to -0.14, p=0.04; I^2 of heterogeneity 97%, p-value heterogeneity <0.00001).-There was no statistically significant difference in the fracture healing rate (OR 7.84, 95% CI 0.47 to 130.27, p=0.15; I2 of heterogeneity 85%, p-value of heterogeneity =0.0002)-There was a statistically significant difference in fracture pain degree (SMD -1.42, 95% CI -2.55 to -0.29, p=0.01; I2 of heterogeneity 94%, P value of heterogeneity <0.00001)-The patients with PTH treatment were significantly superior to those with a placebo or no treatment in functional outcome (SMD -1.28, 95% CI -2.33 to -0.24, p=0.02; I2 of heterogeneity 88%, p-value of heterogeneity <0.00001)**Adverse events:** Peichl et al. declared that no deaths or adverse events were recorded. Huang et al. and Kanakaris et al. did not mention the relevant statistics about adverse events. Five trials reported adverse events with inconsistent methods. In comparing the PTH treatment group with a control group, there was no significant difference in light-headedness, hypercalcemia, nausea, sweating, and headache, except for slight bruising at the injection site. | There was no evidence showing obvious publication bias by examining the symmetry of the funnel plots, but a funnel shape reference line could not be provided by the software due to the small number of studies. There were no blind methods in the trials by Huang et al. and Johansson et al., no random processing in the trial by Huang et al., and inconsistent results in the trial by Bhandari et al.;The most common reasons for the decreased level of evidence were the possible risk of bias and inconsistency. |
| Bhandari M, Jin L, See K, Burge R, Gilchrist N, Witvrouw R, Krohn KD, Warner MR, Ahmad QI, Mitlak B. 2016 | Randomized Controlled TrialLevel II Evidence, prospective study | Trials were conducted concurrently and pool the results of the studies for statistical analyses.A total of 159 patients were randomized in the two trials (81 placebo, 78 teriparatide).Randomization was stratified by fixation (sliding hip screw or multiple cancellous screws) and fracture type (displaced or nondisplaced). The combined program had very low power to detect the originally expected treatment effect but had approximately 80% power to detect a larger difference of 12% between treatment groups for risk of revision surgery. | The two prospective, randomized double-blind, placebo-controlled Phase III studies designed to evaluate the effect of subcutaneous teriparatide (20 μg/day) for 6 months versus placebo on fracture healing at 24 months.  | -The proportion of patients who did not undergo revision surgery at 12 months (primary endpoint) was not different between the study and placebo groups, at 88% in the placebo group (90% CI, 0.79–0.93) versus 84% in the teriparatide group (90% CI, 0.75–0.90; p = 0.743). -There were no differences between groups in the proportion of patients achieving radiographic fracture healing at 12 months (75% [61 of 81] placebo versus 73% [57 of 78] teriparatide; odds ratio, 0.89; 90% CI, 0.46–1.72; p = 0.692) or in measures of pain control (such as pain during ambulation, 92% [55 of 62] placebo versus 91% [52 of 57] teriparatide; odds ratio, 0.91; 90% CI, 0.25–3.37; p = 0.681). -The frequency of patients reporting adverse events was 49% [40 of 81] in the placebo group versus 45% [35 of 78] in the teriparatide group (p = 0.634) during the 6-month treatment period.**Adverse events:**Two deaths occurred in the teriparatide group during the treatment period (pneumonia, subdural hematoma), and one death occurred in the placebo group during the observation period (myocardial infarction). Per Central Adjudication Committee assessment, these three deaths were not related to the study drug or the original hip fracture. | -The majority of patients were recruited from Asia or Europe; very few were from the United States.-During the first 12 months of recruitment, only 161 patients had been randomized in both trials, which were approximately 7% of the planned study cohort, and few of these patients were from the study sites in the United States. Therefore, the goal of the studies could not be achieved in a clinically relevant time-Because the cohort size was smaller than planned, the studies were substantially underpowered to detect the treatment effect included in the original study protocols. Since the treatment effect size was not known with certainty, the study was continued to explore whether a larger treatment effect could have been present. Therefore, the results presented here are exploratory and should be interpreted with caution. |
| Yoon BH, Kim KC. 2020 | Systematic review | -Search of PubMed, EMBASE, and Cochrane Library including “Fracture” AND “nonunion” AND “Teriparatide”-Inclusion criteria: patients treated with daily 20 - 40 μg of recombinant human parathyroid hormone (PTH; 1-34) or weekly 56.5 μg to induce fracture healing or nonunion. Exclusion criteria: patients with illnesses that affect bone or calcium metabolism or underwent surgical treatment for pathologic fracture. -113 citations relevant articles were reviewed, and 57 publications were selected | -Does teriparatide decrease fracture healing time?-Can teriparatide be an alternative treatment for nonunion?-Does teriparatide aid the union of atypical femoral fracture? | -Two studies showed that short-term daily TPTD use improved radiographic fracture healing of a hip fracture and reduced complication rates. -There was a significantly shorter time-to-union with TPTD use (mean, 12.3 vs. 10.6 weeks, respectively [P=0.002]) and improved pain function score were found in the TPTD-treated groups -TPTD significantly decreased mean time to fracture healing (12.1 vs. 14.8 weeks; P=0.002) and VAS pain scores (P=0.008) and increased function score (P=0.02).-The frequency of patients reporting postoperative surgery-related complications was also markedly lower in the TPTD-treated groups  | -It is unknown whether a standard dose or duration of TPTD is optimal-results were limited by the paucity of the randomized studies-Results regarding fracture healing time of atypical femur fracture are from studies not sufficiently powered because they were all case reports and case series with a lack of level 1 studies on the evidence of TPTD in promoting bone healing in AFF. |
| Shi Z, Zhou H, Pan B, Lu L, Liu J, Kang Y, Yao X, Feng S. 2016 | Systematic Review & Meta-analysis | -Search of PubMed, the Cochrane Library, and Embase in August 2016 for randomized controlled trials (RCTs) which concerned the treatment of teriparatide for fracture healing.Inclusion criteria:(1) the type of study design was a RCT; (2) participants were adults with acute fractures and were treated with teriparatide following fracture; (3) the teriparatide intervention was compared with placebo treatment at the same time, no therapy or comparator interventions.Exclusion criteria:(1) participants previously used teriparatide or parathyroid hormone, unless patients had undergone a wash-out period; (2) contraindication to any of the study drugs, formerly or currently on any of them; (3) serum calcium above the reference level and liver enzymes more than double of the upper limit; (4) non-RCTs or studies published as the following article type: abstracts, review articles and letters.-5 articles were included in the analysis with a total of 380 patients. 88.9% female, 11.1% male. Fracture types including distal radius fracture, femoral neck fracture, proximal humeral fracture, lower-extremity stress fracture and pelvic fracture. Median age 57.9 years. | -Effect of teriparatide on the time of fracture healing, fracture healing rate, pain, and functional recovery. | -Patients treated with early teriparatide therapy had no statistically significant difference in radiological fracture healing times compared with patients in control group (MD -3.60, 95% CI -8.70 to 1.49; I2 of heterogeneity 98%, P<0.00001; random effects model)-patients treated with teriparatide therapy had no statistically significant difference in fracture healing rate compared with the patients in the control group (OR 9.05, 95% CI 0.22 to 380.5; I2 of heterogeneity 90%, P<0.00001; random effects model)patients who were treated with teriparatide had no statistically significant difference in pain score compared with the patients in the control group (SMD -1.47, 95% CI -3.12 to 0.18; I2 of heterogeneity 95%, P<0.00001; random effects model)- Patients who were treated with teriparatide showed significantly better functional outcome than those in the control group (SMD -1.36, 95% CI -2.03 to 0.69; I2 of heterogeneity 75%, P = 0.02; random effects model)-Significant differences were identified between the experimental group and the control group with regard to slight bruising at the injection site, and there was no statistically significant difference between the experimental group and the control group regarding nausea, sweating, hypercalcemia, and headache | -Results showed significant heterogeneity and after performing sensitivity analysis found that the trials significantly affected the heterogeneity.-Sample sizes of most of the included studies and study number included in the analysis were small-There was significant diversity of the control groups and included trial groupsConsistency of interventions was difficult to guarantee-The majority of patients were females, resulting in the analysis being more applicable to females than males. |
| Greenspan SL, Vujevich K, Britton C, Herradura A, Gruen G, Tarkin I, Siska P, Hamlin B, Perera S. 2017 | Randomized Clinical trial | -included were 13 women with atypical femur fracture who were randomized to immediate teriparatide vs delayed teriparatide treatment at 6 months.-Ages of 74.2 +/- 2.5 years. 11 Caucasian, 1 African-American, 1 Asian-American. Six had past history of estrogen use and all had been on a bisphosphonate in the past.-Setting: University of Pittsburgh medical center presbyterian hospital between 2013-2015-participants followed over 12 months | -Primary outcomes include individual and composite measures of radiologic bone healing scored 1-4 points at 6 and 12 months.-Secondary outcomes included bone mineral density of unfractured contralateral hip, spine, 1/3 distal radius, and adverse events | -There were no material differences in the healing indices at 6 months between the immediate and delayed group. However, composite score (cortical continuity, persistence of alignment, decreased conspicuity of fracture, and increased callus formation) was 12.6 vs 11.2 in the two groups (immediate and delayed, respectively; p = 0.3820). There was one implant failure/breakage at 12 months in the delayed group.- There were no significant differences in the bone mineral density of the spine, total hip, femoral neck, or 1/3 distal radius at 6 or 12 months. There was a suggestion of less bone loss at the 1/3 distal radius at 12 months in the immediate group compared to delayed (− 1.9 ± 1.7% vs − 6.1 ± 2.1; p = 0.1605).- There were no significant differences in the quality of life questionnaire, pain assessment, hospitalizations, falls, or adverse events between the two groups at 6 and 12 months. | -coordinator and patients were not blind to study allocation.-The numbers of participants were small with only six to seven in each group-The differences in healing may have been due to the surgeon and surgical procedure-the sample sizes are very small to verify the assumptions underlying traditional significance testing, and thus, the p values should be viewed with caution. |
| Lou S, Lv H, Wang G, Zhang L, Li M, Li Z, Zhang L, Tang P. 2016 | Meta-analysis of RCTs |  Searched PubMed, the Cochrane Library, and Embase from 1966-2015 using the terms: “teriparatide” or “Parathyroid Hormone” or “forteo” or “PTH (1–34)” or “PTH (1–84)” or “parathormone” or “parathyrin” and “fractures healing” or “healing” and “fractures, bone” or “broken bone” or “bone fracture” or “fractures.” Inclusion Criteria:-study design was a RCT-participants had osteoporosis with fractures-the intervention was teriparatide initiation compared with placebo, no treatment control group, or comparator interventionsExclusion criteria: -participants younger than 50 years of age-contraindication to any of the study drugs, formerly or currently on any of them-serum calcium above the reference level and liver enzymes more than double of the upper reference level-history of any disease affecting bone metabolism -articles which were not available or had repeated data. |  -Time of fracture healing, as determined by radiography, which was defined as the time of cortical bridging in three of four cortices-Functional outcome defined as an improvement in mobility at week 12 and assessed with the Timed “Up and Go” test or the self-administered “Patient-rated wrist evaluation” or “disabilities of the arm, shoulder, and hand” score or the ”Johanson hip rating questionnaire” | -patients treated with teriparatide had statistically significant difference in radiological fracture healing time compared with the control group (MD −4.54, 95% CI −8.80 to −0.28; I 2 of heterogeneity 96%, P < 0.00001; random effects model) (Figure 3). As I 2 = 96% indicated significant heterogeneity, a sensitivity analysis was performed and found that one trial significantly affected the pooled MD. Therefore, a subgroup analysis, consisting of upper limb group (MD −1, 95% CI −2.02 to 0.2; P = 0.05; random effects model) and lower limb group (MD −6.24, 95% CI −7.20 to −5.29; I 2 of heterogeneity 0%, P = 0.70; random effects model), was performed. A visible difference was found between the upper limb and the lower limb.- Patients who were treated with teriparatide showed significantly better functional outcome than those in the control group (SMD −1.02, 95% CI −1.81 to −0.22; I 2 of heterogeneity 85%, P = 0.00002; random effects model) (Figure 4). Since I 2 = 85% symbolized significant heterogeneity, a subgroup analysis was performed, in which one group represented that treatment time exceeded 4 weeks (SMD −1.68, 95% CI −2.07 to −1.29; I 2 of heterogeneity 0%, P = 0.55; random effects model) and the other represented that treatment time was equal to 4 weeks (SMD −0.31, 95% CI −0.81 to 0.18; I 2 of heterogeneity 0%, P = 0.34; random effects model). The duration of treatment was the key factor for the function outcome. |  The most common reasons for the decreased level of evidence were the heterogeneity and suspected publication bias. |

**Conclusion(s):**

Hong H, Song T, Liu Y, Li J, Jiang Q, Song Q, Deng Z. (2019 Apr 25): **Article one found that PTH treatment in patients with fracture was better than placebo or no treatment based on healing time, pain scores, and functional outcomes.** The placebo group had longer fracture healing time, higher fracture pain degree, and worse functional outcomes.

Yoon BH, Kim KC. (2020 Aug 31): **Article three found that the main clinical advantage of teriparatide is the acceleration of time to fracture healing and enhanced bone formation.** Based on the evidence, teriparatide could be both preventative and supportive treatment in fractures at high risk of nonunion and complex fractures of osteoporotic bone.

Shi Z, Zhou H, Pan B, Lu L, Liu J, Kang Y, Yao X, Feng S. (2016 Dec 20): **Article four found that teriparatide was effective for functional improvement in patients following fracture, but there was no significant effectiveness in regards to radiographic fracture healing, healing rate, and reduction in pain.** **Another important finding of article four was that Teriparatide had no apparent adverse effects.**

Lou S, Lv H, Wang G, Zhang L, Li M, Li Z, Zhang L, Tang P. (2016 Jun 26):. **Article six found that teriparatide promoted osteoporotic fracture healing and improved functional outcomes, but because most study participants were women, the primary results must be interpreted with caution for males.**

Bhandari M, Jin L, See K, Burge R, Gilchrist N, Witvrouw R, Krohn KD, Warner MR, Ahmad QI, Mitlak B. (2016 Mar 1.): **Article two found that teriparatide accelerates the time of fracture healing, enhances bone formation, and may reduce the risk of nonunion.** **However, it did not decrease the risk of revision surgery, improve radiographic signs of fracture healing, or decrease pain compared with placebo.**

Greenspan SL, Vujevich K, Britton C, Herradura A, Gruen G, Tarkin I, Siska P, Hamlin B, Perera S. (2017 Oct 30): **Article five found that patients with an acute atypical femur fracture associated with bisphosphonate use that greater improvement in fracture healing when teriparatide was started immediately vs delayed use at 6 months. The changes in bone mineral density were not significantly different between the two groups.** The largest limitation of this study was that because atypical femur fractures from bisphosphonates are a relatively rare occurrence, the participant pool was small so results must be interpreted with caution.

**Dosage & Duration Conclusion:** All six of the included studies used synthetic teriparatide with PTH interchangeably. The anabolic effects of 20 μg of Teriparatide and 100 μg of PTH are equal. Additionally, all articles examined the aforementioned dosages while three of them also included a dosage of 40 μg/day of Teriparatide but no analysis was able to be drawn due to differences in treatment duration between the two dosages except for article two which noted that there was no difference in accelerated radiographic healing of wrist fracture between the groups that received 20 μg and 40 μg per day but there was benefit in not delaying the initiation of treatment. When looking at the individual studies, there was not an obvious superiority nor adverse effects reported in the higher dosage form. For the duration, the articles ranged from 4 – 24 months. There were no consistent findings on which duration showed maximum benefit but both article one and article six observed better functional outcomes in studies that exceeded four weeks of therapy duration.

**Clinical Bottom Line:**

PICO Question: Does synthetic parathyroid hormone (Teriparatide) injections improve long bone fracture healing

Clinical Bottom Line: Parathyroid Hormone injections should be recommended as an adjunctive treatment for long bone fracture healing in adults, especially for women > 50 years of age. Short-term dosages of Teriparatide at 20 - 40 micrograms per day subcutaneously or human PTH at 100 micrograms per day should be give acutely at fracture onset and continued until the fracture is both clinically and radiologically resolved but should not exceed a duration of two years since these were the dosages and intervals most used in the methods of the studies evaluated.

Weight of the Evidence: When weighing the evidence of the four articles selected for this PICO question, I rank the articles in the following order from highest level of evidence to lowest level of evidence: Article 1 > Article 3 > Article 4 > Article 6 > Article 2 > Article 5.

1. Hong H, Song T, Liu Y, Li J, Jiang Q, Song Q, Deng Z. (2019 Apr 25): I give article one the most weight because it is the most recently published meta-analysis. Being a meta-analysis, it can be completely objective in evaluating the research findings which is an advantage over the systematic reviews. It also had a large participant pool of 524 adult individuals across eight different randomized controlled trials.
2. Yoon BH, Kim KC. (2020 Aug 31): Article 3 was given the next highest weight of evidence because it is the most recent publication (2020) and an extensive systematic review that selected 57 different publications.
3. Shi Z, Zhou H, Pan B, Lu L, Liu J, Kang Y, Yao X, Feng S. (2016 Dec 20): Article four was ranked the third highest level of evidence because although it is both a systematic review and meta-analysis, it was published in 2016 making it the oldest publication along with article two that was also published in 2016. It also included less participants than articles one and three with 380 total individuals.
4. Lou S, Lv H, Wang G, Zhang L, Li M, Li Z, Zhang L, Tang P. (2016 Jun 26): Article six is ranked the next highest level of evidence. Although it is a meta-analysis of randomized controlled trials, the individual studies were of smaller caliber than the ones included in the aforementioned articles. Additionally, article six examined fracture healing specifically in osteoporotic fractures. While this article is useful to expand upon what fracture types PTH hormone shows benefit in, it does not address fracture healing in the original fracture mechanism of this article which was trauma related.
5. Bhandari M, Jin L, See K, Burge R, Gilchrist N, Witvrouw R, Krohn KD, Warner MR, Ahmad QI, Mitlak B. (2016 Mar 1.): Article two was ranked the next body of evidence because it was also from 2016 and was only one randomized controlled trial with level two evidence. It also had the smallest participant size of 159 individuals, although it was one of the larger individual randomized controlled trials when looking at the individual studies with the systematic reviews and meta-analysis presented.
6. Greenspan SL, Vujevich K, Britton C, Herradura A, Gruen G, Tarkin I, Siska P, Hamlin B, Perera S. (2017 Oct 30): Article five was ranked the weakest body of evidence because it is an individual randomized clinical trial that was not double blinded and only examines PTH hormone use an atypical fracture type. This article examines the outcome of teriparatide use in bisphosphonate-associated atypical fractures, specifically looking at immediate vs delayed treatment at 6 months. The study also did not compare teriparatide against placebo but was chosen because it determined the benefit of teriparatide use at different time intervals after a fracture occurred.

Magnitude of Effects:

1. Hong H, Song T, Liu Y, Li J, Jiang Q, Song Q, Deng Z. (2019 Apr 25): **There was statistically significant difference in fracture healing time** (MD -3.05, 95% CI -5.96 to -0.14, p=0.04; I^2 of heterogeneity 97%, p-value heterogeneity <0.00001). **There was no statistically significant difference in the fracture healing rate** (OR 7.84, 95% CI 0.47 to 130.27, p=0.15; I2 of heterogeneity 85%, p-value of heterogeneity =0.0002). **There was a statistically significant difference in fracture pain degree** (SMD -1.42, 95% CI -2.55 to -0.29, p=0.01; I2 of heterogeneity 94%, P value of heterogeneity <0.00001). **The patients with PTH treatment were significantly superior to those with a placebo or no treatment in functional outcome** (SMD -1.28, 95% CI -2.33 to -0.24, p=0.02; I2 of heterogeneity 88%, p-value of heterogeneity <0.00001)
2. Yoon BH, Kim KC. (2020 Aug 31): **Two studies showed that short-term daily TPTD use improved radiographic fracture healing of a hip fracture and reduced complication rates. There was a significantly shorter time-to-union with TPTD use** (mean, 12.3 vs. 10.6 weeks, respectively [P=0.002]) **and improved pain function score were found in the TPTD-treated groups. TPTD significantly decreased mean time to fracture healing** (12.1 vs. 14.8 weeks; P=0.002) and VAS pain scores (P=0.008) and increased function score (P=0.02). **The frequency of patients reporting postoperative surgery-related complications was also markedly lower in the TPTD-treated groups.**
3. Shi Z, Zhou H, Pan B, Lu L, Liu J, Kang Y, Yao X, Feng S. (2016 Dec 20): **Patients treated with early teriparatide therapy had no statistically significant difference in radiological fracture healing times compared with patients in control group** (MD -3.60, 95% CI -8.70 to 1.49; I2 of heterogeneity 98%, P<0.00001; random effects model). **Patients treated with teriparatide therapy had no statistically significant difference in fracture healing rate compared with the patients in the control group** (OR 9.05, 95% CI 0.22 to 380.5; I2 of heterogeneity 90%, P<0.00001; random effects model). **Patients who were treated with teriparatide had no statistically significant difference in pain score compared with the patients in the control group** (SMD -1.47, 95% CI -3.12 to 0.18; I2 of heterogeneity 95%, P<0.00001; random effects model). **Patients who were treated with teriparatide showed significantly better functional outcome than those in the control group** (SMD -1.36, 95% CI -2.03 to 0.69; I2 of heterogeneity 75%, P = 0.02; random effects model**). Significant differences were identified between the experimental group and the control group with regard to slight bruising at the injection site, and there was no statistically significant difference between the experimental group and the control group regarding nausea, sweating, hypercalcemia, and headache.**
4. Lou S, Lv H, Wang G, Zhang L, Li M, Li Z, Zhang L, Tang P. (2016 Jun 26): **Patients treated with teriparatide had statistically significant difference in radiological fracture healing time compared with the control group** (MD −4.54, 95% CI −8.80 to −0.28; I 2 of heterogeneity 96%, P < 0.00001; random effects model) (Figure 3). As I 2 = 96% indicated significant heterogeneity, a sensitivity analysis was performed and found that one trial significantly affected the pooled MD. Therefore, a subgroup analysis, consisting of upper limb group (MD −1, 95% CI −2.02 to 0.2; P = 0.05; random effects model) and lower limb group (MD −6.24, 95% CI −7.20 to −5.29; I 2 of heterogeneity 0%, P = 0.70; random effects model), was performed**. A visible difference was found between the upper limb and the lower limb. Patients who were treated with teriparatide showed significantly better functional outcome than those in the control group** (SMD −1.02, 95% CI −1.81 to −0.22; I 2 of heterogeneity 85%, P = 0.00002; random effects model) (Figure 4). Since I 2 = 85% symbolized significant heterogeneity, a subgroup analysis was performed, in which one group represented that treatment time exceeded 4 weeks (SMD −1.68, 95% CI −2.07 to −1.29; I 2 of heterogeneity 0%, P = 0.55; random effects model) and the other represented that treatment time was equal to 4 weeks (SMD −0.31, 95% CI −0.81 to 0.18; I 2 of heterogeneity 0%, P = 0.34; random effects model). **The duration of treatment was the key factor for the function outcome.**
5. Bhandari M, Jin L, See K, Burge R, Gilchrist N, Witvrouw R, Krohn KD, Warner MR, Ahmad QI, Mitlak B. (2016 Mar 1.): **The proportion of patients who did not undergo revision surgery at 12 months (primary endpoint) was not different between the study and placebo groups**, at 88% in the placebo group (90% CI, 0.79–0.93) versus 84% in the teriparatide group (90% CI, 0.75–0.90; p = 0.743). **There were no differences between groups in the proportion of patients achieving radiographic fracture healing at 12 months** (75% [61 of 81] placebo versus 73% [57 of 78] teriparatide; odds ratio, 0.89; 90% CI, 0.46–1.72; p = 0.692) or in measures of pain control (such as pain during ambulation, 92% [55 of 62] placebo versus 91% [52 of 57] teriparatide; odds ratio, 0.91; 90% CI, 0.25–3.37; p = 0.681). The frequency of patients reporting adverse events was 49% [40 of 81] in the placebo group versus 45% [35 of 78] in the teriparatide group (p = 0.634) during the 6-month treatment period.
6. Greenspan SL, Vujevich K, Britton C, Herradura A, Gruen G, Tarkin I, Siska P, Hamlin B, Perera S. (2017 Oct 30): **There were no material differences in the healing indices at 6 months between the immediate and delayed group. However, composite score (cortical continuity, persistence of alignment, decreased conspicuity of fracture, and increased callus formation) was 12.6 vs 11.2 in the two groups** (immediate and delayed, respectively; p = 0.3820). **There was one implant failure/breakage at 12 months in the delayed group. There were no significant differences in the bone mineral density of the spine, total hip, femoral neck, or 1/3 distal radius at 6 or 12 months. There was a suggestion of less bone loss at the 1/3 distal radius at 12 months in the immediate group compared to delayed** (− 1.9 ± 1.7% vs − 6.1 ± 2.1; p = 0.1605). **There were no significant differences in the quality of life questionnaire, pain assessment, hospitalizations, falls, or adverse events between the two groups at 6 and 12 months.**

Clinical Significance:

Parathyroid Hormone injections should be recommended as an adjunctive treatment for long bone fracture healing in adults, especially for women > 50 years of age. Short-term dosages of Teriparatide at 20 μg/day or PTH at 100 μg/day administered subcutaneously should be given acutely at fracture onset and continued for at least four weeks or until the fracture is both clinically and radiologically resolved but should not exceed a duration of two years since these were the dosages and intervals most used and showing best efficacy in the methods of the studies evaluated. There is no direct analysis to show the use of 40 μg/day of teriparatide is superior at this point, and therefore, the smaller dosage should be recommended until new emerging evidence shows otherwise. The top three highest level of evidence articles all found at least one benefit to using PTH for bone healing and the top two highest level of evidence articles found more than one benefit. Additionally, no major adverse reactions were reported in any of the publications which increases my confidence in the safety of this treatment plan. To summarize, the addition of PTH/Teriparatide to long bone fracture healing may enhance the rate of healing and functional outcomes and decrease pain

Other Considerations:

PTH cannot be safely utilized in all individuals, specifically in individuals who have diseases/illnesses affecting bone metabolism. For example, Teriparatide should not be recommended for patients who are at increased risk for osteosarcoma including those with Paget’s disease, unexplained elevations of alkaline phosphatase, open epiphyses (i.e. pediatric patients), or prior external beam or implant radiation therapy involving the skeleton based on FDA data.