APPENDIX A. SEARCH STRATEGIES

MEDLINE search strategy

exp Transplantation, Autologous/ or exp Autografts/ or exp Bone Transplantation/
exp Bone Marrow Transplantation/ or exp Bone Substitutes/
exp Platelet-Derived Growth Factor/ or exp Platelet-Rich Plasma/
(orthobiologic* or (autologous and graft*) or (autogenous and graft*) or (autogenic and graft*) or autograft* or (iliac and graft*) or (tibia* and graft*) or (calcan* and graft*) or (fibul* and graft*) or "bone graft*").ti,ab.
("bone marrow aspirate*" or (bone adj2 transplantation) or "plasma product*" or "platelet-derived" or "platelet derived" or "platelet-rich" or "platelet rich" or "mesenchymal stem cell*" or "bone morphogen* protein*" or PRP or PDGF or MSC or rhPDGF-BB or BMP-2 or rhBMP-2 or BMP-7 or "tricalcium phosphate").ti,ab.
1 or 2 or 3 or 4 or 5
exp Foot Joints/
exp Foot Bones/
exp Ankle Joint/
(foot or ankle or naviculocuneiform or Lisfranc or Chopart or midfoot or mid-foot or hindfoot or hind-foot or calcaneous or calcaneal or talus or talar or subtalar or tarsal or tibiotalar or tibiotalocalcaneal or calcaneocuboid or talonavicular or mid-tarsal or midtarsal or tarsometatarsal or metatarsophalangeal).ti,ab.
exp Arthrodesis/ or (arthrodes* or fusion* or union* or fixation*).mp.
7 or 8 or 9 or 10
11 and 12
6 and 13
limit 14 to "all child (0 to 18 years)"
limit 15 to "all adult (19 plus years)"
14 not 15
16 or 17
limit 18 to (english language and humans and yr="1995 -Current")

APPENDIX B. CRITERIA USED IN QUALITY ASSESSMENT

We completed a critical appraisal included studies (retrospective chart reviews or prospective case series) based on a modification of the Joanna Briggs Institute 1) Critical Appraisal Checklist for Quasi-Experimental Studies[18] and 2) Critical Appraisal Checklist for Case Series.[19] Each item below was rated Yes/No/Unclear/Not Applicable.

Item	Rating
1. Is there evidence of ethical approval for the study?	
2. Were there clear criteria for inclusion?	
3. Was there complete inclusion of participants?	
4. Was there clear reporting of the demographics of the study participants?	
5. Were the study groups formed in a way that minimizes bias?	
6. Did the participants included in any comparison receive similar treatment/care other than the intervention of interest?	
7. Was follow-up complete with no differential follow-up between groups?	
8. Was outcome assessment blinded?	
9. Were outcomes measured in valid and reliable ways?	

APPENDIX C. PEER REVIEWER COMMENTS AND AUTHOR RESPONSES

Question Text	Comment	Author Response
Are the objectives, scope, and methods for this review clearly described?	Yes	Thank you
	Yes	
	Yes	
	Yes	
Is there any indication of bias in our synthesis of the evidence?	No	Thank you
	No	
	No	
	No	
Are there any published or unpublished studies that we may have overlooked?	No	Thank you
	No	
	No	
	No	
Additional suggestions or comments can be provided below. If applicable, please indicate the page and line numbers from the draft report.	Page 26--lines 22-28. Please note that cost data for biologics can be very difficult for surgeons to obtain from the vendors so it cannot be used in consideration of biologic use. Page 8--lines 29/30. Is the major complication of joint stiffness related to its use in long bone fracture treatment adjacent to joints, causing the stiffness? Page 8--line 41--typo? "than", not then Page 27--line 57 might read better as--"initial post surgical pain at the foot or ankle" for each example. I had to reread to understand this well. General questions/comments: 1. Was Vitamin D a consideration in the reviewed manuscripts? It is often a consideration for revision surgery, but not always looked at prior to the first arthrodesis attempt. 2. I appreciate the commentary on "selection bias". This is impossible to avoid in all the case series reports that are available for this review. 3. I also appreciate the commentary regarding off-label use for certain products. Off label use is a necessary issue with many of these products. 4. The recommendation for pre-authorization for the biologics appears to	Page 26: We agree that cost data can be difficult for surgeons to obtain and may vary between facilities and over time. Furthermore, the cost of the product is only one component of the overall cost of care, which includes the possibility for a second surgery or more complex surgical procedure versus improved health outcomes which may both lower future costs as well as improve health outcomes. However, given the limited evidence on effectiveness and the fact that these products are not specifically approved for this indication, clinicians and health systems should be aware that use of these products increases surgical cost and complexity. Health care systems, including the VA, should be more transparent regarding the cost of these products, negotiate lower cost options, and

	be appropriate. The cost of biologics must be more transparent to aid in decision making by the surgeon.	encourage clinician awareness and patient communication of these issues. Page 8: We modified this statement. Joint stiffness and pain was related to heterotopic bone formation. Page 8, Line 41: Thank you – changed to "than" Page 27: Thank you for the suggestion – we revised this sentence. 1. None of the included studies reported on Vitamin D. 2,3,4: Thank you. We have added some additional information regarding the importance of cost assessment, negotiation, and awareness for patients, clinicians, and health care systems.
	The use of orthobiologics in foot and ankle surgery is replete of data and controversial. I commend the authors for addressing the lack of knowledge around this topic by performing this exhaustive analysis of controlled studies on the use of orthobiologics. The results of this study are not surprising. Trying to make sense of the ever-expanding orthobiologics world is difficult. The results also indicate the heterogeneous nature of patients presenting for foot and ankle fusions and the hap-hazard nature of implementation of orthobiologics by clinicians. The report also highlights the low incidence of reported (and possibly the actual) harms when using orthobiologics. Finally, the report emphasizes the need for more rigorous studies evaluating the use of orthobiologics.	Thank you.
	p. 1 line 45 beginning with "Our focus....." some studies used allografts (bone) which would not be included in this sentence. Should be.	As requested in the topic nomination, our scope was limited to autogenous orthobiologics.

APPENDIX D. EVIDENCE TABLES

Table 1. Study Characteristics

Author, year Country Funding Study Design	Inclusion/Exclusion Criteria Arthrodesis Site	Orthobiologic(s) (n) Non-Orthobiologic(s) (n) Follow-up	Demographics	A Priori Comparison?
Abd-Ella, 2017[20] Country unclear Funding: No funding Prospective case series	Inclusion: Nonunion of talar neck or body fracture associated with extensive avascular necrosis of the talar dome Exclusion: Infection; septic AVN Indications for arthrodesis: NR	Orthobiologic(s): Mix of bulk strut graft and cancellous graft harvested from posterior iliac crest (n=9) Non-Orthobiologic(s): "No need for graft" (n=3) Number of sites: NR Number of surgeons: NR Follow-up: 23 months (range 12-60)	N=12 patients Age (years, mean): 27.7 Gender (% male): 67% Race/ethnicity: NR Smoking status: 33% smokers Obesity (%): NR BMI: NR Diabetes (%): 0% Bone mineral density: NR Medications related to healing: NR	A priori plan to compare orthobiologics to no orthobiologics: No
Anderson, 2013[21] USA Funding: Not Reported Retrospective chart review	Inclusion: Primary first MPJ arthrodesis Exclusion: Revision first MPJ fusion secondary to malunion or previous non-union, previously infected joint, history of Charcot neuroarthropathy, or history of first MPJ dislocation with sesamoidal fracture Indications for arthrodesis: End-stage deformity correction	Orthobiologic(s): Autograft (local; reduce to cancellous bone chips); cases with soft bone, bone voids, or bone cysts at fusion site (n=62 patients) Non-Orthobiologic(s): End-to-end arthrodesis; no graft interposition used or necessary (n=52 patients) NOTE: additional 51 patients received allograft (not included in outcomes) Number of surgical facilities: NR Number of surgeons:1 Follow-up: weekly (for first 2 weeks) then biweekly until clinical union	N=165 patients (including 51 receiving allograft) Age (years, mean): 62 Gender (% male): 44% Race/ethnicity: NR Smoking status:19% Obesity (%): 3% BMI: NR Diabetes (%): 7% Bone mineral density: NR Medications related to healing: NR	A priori plan to compare orthobiologics to no orthobiologics: Yes NOTE: Use of any graft was surgeon's judgment. Patients in the end-to-end arthrodesis groups all had sufficient bone quality. The 2 graft groups had different and less than desirable bone quality.
Bibbo, 2009[22] USA	Inclusion: High-risk, elective ankle and hindfoot fusions treated with rhBMP-2 augmentation	Orthobiologic(s): rhBMP-2 (INFUSE®) and autogenous iliac crest bone graft (n=17 fusions)	N=69 patients (112 fusion sites) (includes allograft group) Age (years, mean): 52	A priori plan to compare orthobiologics to no orthobiologics: No

Author, year Country Funding Study Design	Inclusion/Exclusion Criteria Arthrodesis Site	Orthobiologic(s) (n) Non-Orthobiologic(s) (n) Follow-up	Demographics	A Priori Comparison?
Funding: None Retrospective chart review	"High-risk" inclusion criteria: Smoking, diabetes, high energy injury, multiple surgeries, history of delayed/ non-union, alcohol abuse, immunosuppression, chronic infections, suboptimal inflow, collagen disorders, multiple medical comorbidities Exclusion: Active infection, peripheral vascular disease that might preclude healing, or any inability to participate in usual follow-up Indications for arthrodesis: NR	Non-Orthobiologic(s): rhBMP-2 only (n=85 fusions) Additional 10 fusions **received** rhBMP-2 and allograft (excluded from analysis) Number of surgical facilities: NR Number of surgeons: NR Follow-up: every 2-4 weeks	Gender (% male): 53% Race/ethnicity: NR Smoking status: 64% Obesity (%): NR BMI: NR Diabetes (%): 19% Bone mineral density: NR Medications related to healing: NR	Bone grafting performed only to fill osseous defects and correct malalignment.
Buda, 2018[23] USA Funding: None Retrospective chart review	Inclusion: Adults, single or multilevel TMT arthrodesis (CPT codes 28730 and 28735) Exclusion: Age <18, post-op follow-up <12 months, prior midfoot surgery, arthrodesis in context of acute foot trauma, concomitant foot procedure other than bone graft harvest Indications for arthrodesis: End-stage TMT arthritis	Intervention: TMT arthrodesis with autologous bone graft harvested from iliac crest or calcaneus (n=70 feet, 53% graft only, 47% graft + DBM) Control: TMT arthrodesis without autologous bone graft (n=18) Number of sites: 3 Number of surgeons: 9 Follow-up: mean of 77.5 months (range 12-179)	N=88 feet (189 joints) Age (years, mean): 57 Gender (% male): 20% Race/ethnicity: 91% white race Smoking status: Current 12.5% Obesity (%): 56% BMI: NR Diabetes (%): 9% Bone mineral density: NR (Osteoporosis: 12.5%) Medications related to healing: NR	A priori plan to compare orthobiologics to no orthobiologics: Yes
Cao, 2017[24] China Funding: Foundation Retrospective chart review	Inclusion: Isolated TN arthrodesis (n=16 patients) for stage III and IV Müller-Weiss disease Exclusion: Multiple site arthritis or infection, obvious deformity in hindfoot	Orthobiologic(s): Autoallergic iliac bone graft (n=5 patients with stage IV Müller-Weiss disease) Non-Orthobiologic(s): No bone graft (n=11 patients with stage III Müller-Weiss disease) Number of surgical facilities: 1	N=16 patients Age (years, mean): 50.3 Gender (% male): 12.5% Race/ethnicity: NR Smoking status: NR Obesity (%): NR BMI: NR Diabetes (%): NR Bone mineral density: NR	A priori plan to compare orthobiologics to no orthobiologics: No Only stage IV Müller-Weiss cases received graft. No-graft group was stage III Müller-Weiss cases only.

Author, year Country Funding Study Design	Inclusion/Exclusion Criteria Arthrodesis Site	Orthobiologic(s) (n) Non-Orthobiologic(s) (n) Follow-up	Demographics	A Priori Comparison?
	Indications for arthrodesis: Müller-Weiss disease (stages III and IV) NOTE: Additional 14 patients underwent TNC arthrodesis with tricortical autogenous graft (not reported here).	Number of surgeons: 2 Follow-up: 39.8 months (11-66) (TN group)	Medications related to healing: NR	
Chahal, 2006[25] Canada Funding: None Retrospective chart review	Inclusion: Isolated subtalar fusion (ISSA, n=67 patients or SBBDA, n=21 patients); hindfoot pain attributable to subtalar joint, preoperative diagnosis of primary or secondary osteoarthritis of subtalar joint Exclusion: Rheumatoid arthritis or previous triple fusion Indications for arthrodesis: Primary osteoarthritis: 19.3% Secondary osteoarthritis: 80.7% NOTE: SBBDA patients not included in outcomes analyses.	Orthobiologic(s): ISSA group only - local or iliac crest bone graft (n=46 with data, n=1 missing data) Non-Orthobiologic(s): ISSA group only - no graft (n=20) Number of surgical facilities: 2 Number of surgeons: 2 Follow-up: Radiographic outcome: 2 and 6 weeks; 3, 6, 12, and 24 months; every year after as required Functional outcome: Mean=35.5 months (10-83 months)	N=88 patients (includes 21 SBBDA patients) Age (years, mean): 46 Gender (% male): 61.4% Race/ethnicity: NR Smoking status: 43.7% smoked at least 1 week before and after surgery Obesity (%): NR BMI: NR Diabetes (%): 10.2% Bone mineral density: NR Medications related to healing: NR	A priori plan to compare orthobiologics to no orthobiologics: Yes Bone graft group: Local graft used if a lateral wall ostectomy was performed. Iliac crest bone graft used at surgeon's discretion.
Chen, 1996[26] Taiwan Funding: Not Reported Retrospective Chart Review	Inclusion: Internal compression tibiotalar arthrodesis Exclusion: NR Indications for arthrodesis: posttraumatic arthritis (45%), rheumatoid arthrosis (18%), paralytic ankle (10%), post-septic arthrosis (10%), nonunion after previous tibiotalar arthrodesis (10%), osteonecrosis of the talus (8%)	Orthobiologic(s): Tibial condyle graft (n=8 ankles) or sliding graft (n=7 ankles) (cases with severe bone loss or poor bone quality) Non-Orthobiologic(s): No graft (patients with good apposition and rigid fixation) (n=25 ankles) Number of surgical facilities: NR Number of surgeons: 1 Follow-up: Mean=4 years (3-7 years)	N=38 patients (40 ankles) Age (years, mean): 49 Gender (% male): 63% Race/ethnicity: NR Smoking status: NR Obesity (%): NR BMI: NR Diabetes (%): NR Bone mineral density: NR Medications related to healing: NR	A priori plan to compare orthobiologics to no orthobiologics: No

Author, year Country Funding Study Design	Inclusion/Exclusion Criteria Arthrodesis Site	Orthobiologic(s) (n) Non-Orthobiologic(s) (n) Follow-up	Demographics	A Priori Comparison?
Easley, 2000[27] USA No Funding Retrospective chart review	Inclusion: Failed nonoperative treatment; isolated subtalar arthrodesis (ISSA, n=150 feet or bone-block distraction arthrodesis, n=34 feet) Exclusion: NR Indications for arthrodesis: posttraumatic arthritis (73%), failure of previous subtalar arthrodesis (15%), primary subtalar arthritis (7%), residual congenital deformity (4%) NOTE: Bone-block distraction arthrodeses not included in outcome analyses.	Orthobiologic(s): Cancellous autograft (n=94 feet) Non-Orthobiologic(s): No bone graft (n=39 feet) NOTE: 17 feet underwent ISSA with cancellous allograft (excluded from analysis) Number of surgical facilities: NR Number of surgeons: NR Follow-up: Mean=51 months (24-130 months)	N=174 patients (184 feet) (includes 17 receiving cancellous allograft) Age (years, mean): 43 Gender (% male): 66% Race/ethnicity: NR Smoking status: 46% (smoked at time of arthrodesis) Obesity (%): NR BMI: NR Diabetes (%): NR Bone mineral density: NR Medications related to healing: NR	A priori plan to compare orthobiologics to no orthobiologics: Yes *Purpose was to identify factors influencing union rate Radiographic and clinical outcomes for N=139 patients (148 feet)
Fourman, 2014[28] USA Funding: None Retrospective chart review	Inclusion: Ankle arthrodesis with the Ilizarov technique Exclusion: Not deemed complex, had internal fixation for the ankle arthrodesis, inadequate follow-up (failure to appear for 3- and 6-month follow-up visits) Indications for arthrodesis: Complex patients (comorbidities precluding a successful arthrodesis using traditional internal fixation including systemic or local compromise, infection about or in ankle, simultaneous limb lengthening if <70 years with limb length discrepancy >2.5 cm, deformity of the ankle contraindicating internal fixation, osteopenia or poor skin quality)	Orthobiologic(s): rhBMP-2 (n=42 patients) Non-Orthobiologic(s): No rhBMP-2 (n=40 patients) Number of surgical facilities: 1 Number of surgeons: 1 Follow-up: Mean of 43 months from date of frame removal (range 16-84 months)	N=82 patients Age (years, mean): 57 Gender (% male): NR Race/ethnicity: NR Smoking status: 7% Obesity (%): 16% (BMI>30) BMI: 29.6 Diabetes (%): 11.5% Bone mineral density: NR Medications related to healing: NR	A priori plan to compare orthobiologics to no orthobiologics: Yes

Author, year Country Funding Study Design	Inclusion/Exclusion Criteria Arthrodesis Site	Orthobiologic(s) (n) Non-Orthobiologic(s) (n) Follow-up	Demographics	A Priori Comparison?
Grunander, 2012[29] USA Funding: None Retrospective chart review	Inclusion: Calcaneocuboid distraction arthrodesis with femoral head allograft Exclusion: Patient who received autogenous bone graft Indications for arthrodesis: Adult acquired flatfoot deformity	Orthobiologic(s): Femoral head allograft with platelet rich plasma (n=7 feet) Non-Orthobiologic(s): Femoral head allograft alone (n=9 feet) Number of surgical facilities: NR Number of surgeons: 1 Follow-up: Mean=23 months (8-39 months)	N=14 patients (16 feet) Age (years, mean): 43 Gender (% male): 71% Smoking status: 0% Obesity (%): NR BMI: NR Diabetes (%): 0% Bone mineral density: NR Medications related to healing: NR	A priori plan to compare orthobiologics to no orthobiologics: No PRP was used when it became available at study hospital (later cases in series)
Holm, 2015[30] USA Funding: NR Retrospective chart review	Inclusion: Comminuted intra-articular calcaneal fractures classified as Sanders type IV; treated with primary STJ arthrodesis 1998-2012; follow-up for ≥1 year Exclusion: Open fractures, concomitant fractures in other lower extremity or spinal locations, unavailability of complete radiographic file Indications for arthrodesis: Fracture related to MVA 44%; fall from height 56%	Orthobiologic(s): Autogenous bone from tibia (n=3) Non-Orthobiologic(s): No bone graft (n=6) NOTE: Additional 8 patients received cancellous allograft chips (not reported) Number of sites: 2 Number of surgeons: 2 Follow-up: mean 30 months (range 12-61 months)	N=9 patients Age (years, mean): 53.8 Gender (% male): 33% Race/ethnicity: NR Smoking status: NR Obesity (%): NR BMI: NR Diabetes (%): NR Bone mineral density: NR Medications related to healing: NR	A priori plan to compare orthobiologics to no orthobiologics: No
Lechler, 2012[31] Germany Funding: Not reported Prospective case series	Inclusion: Destruction of talonavicular joint; treated by talonavicular arthrodesis Exclusion: NR Indications for arthrodesis: Primary osteoarthritis: 53% Post-traumatic destruction: 13% Rheumatoid arthritis: 13% Psoriatic arthritis: 7%	Orthobiologic(s): Autologous spongious bone graft (iliac crest) (n=6) Non-Orthobiologic(s): No reported use of any orthobiologic (n=24) Number of sites: 1 Number of surgeons: NR Follow-up: 15.8 months (range 6-24 months)	N=30 patients (30 feet) Age (years, mean): 58.8 Gender (% male): 40% Race/ethnicity: NR Smoking status: NR Obesity (%): NR BMI: NR Diabetes (%): NR Bone mineral density: NR	A priori plan to compare orthobiologics to no orthobiologics: No

Author, year Country Funding Study Design	Inclusion/Exclusion Criteria Arthrodesis Site	Orthobiologic(s) (n) Non-Orthobiologic(s) (n) Follow-up	Demographics	A Priori Comparison?
	Peripheral neurological impairment: 10% Revision: 3%		Medications related to healing: NR	
Patil, 2011[32] United Kingdom Funding: Not reported Retrospective chart review	Inclusion: Primary subtalar fusion or triple arthrodesis using either local bone graft or autologous cancellous bone graft from iliac crest Exclusion: Revision subtalar fusion for malunion or nonunion Indications for arthrodesis: Primary osteoarthritis: 59% Post-traumatic arthritis: 35% Rheumatoid arthritis: 6% NOTE: Additional group of patients (n=9) received bovine cancellous bone (not reported)	Orthobiologic(s): Autologous iliac crest bone graft (n=4) Non-Orthobiologic(s): Local bone from excised surfaces (n=13) Number of sites: NR Number of surgeons: 1 Follow-up: 12 months	N=17 patients Age (years, mean): 56 Gender (% male): 59% Race/ethnicity: NR Smoking status: 6% (1 smoker) Obesity (%): NR BMI: NR Diabetes (%): NR Bone mineral density: NR Medications related to healing: NR	A priori plan to compare orthobiologics to no orthobiologics: No (purpose was to compare bovine cancellous bone grafting to no bovine grafting)
Plaass, 2009[33] Switzerland Funding: Not reported Prospective case series	Inclusion: Isolated tibiotalar arthrodesis with anterior double plating (2006-2007) Exclusion: NR Indications for arthrodesis: Main diagnoses were primary arthritis, post-traumatic osteoarthritis, and failed ankle replacement; 4 had non-united arthrodesis of the ankle and 9 had failed total ankle replacement	Orthobiologic(s): Demineralized bone matrix (DBX®) and/or Platelet concentrate (Symphony II®) DBX® (n=7) Symphony II® (n=1) Both (n=3) Non-Orthobiologic(s): No orthobiologic (n=5) Additional 13 received allograft with or without other orthobiologic (not reported here) Number of sites: NR Number of surgeons: NR Follow-up: 12 months	N=16 patients Age (years, mean): 54 DBX®: 56 Symphony II®: 39 Both: 40 No Orthobiologic: 64 Gender (% male): 62.5% DBX®: 57% Symphony II®: 100% Both: 67% No Orthobiologic: 60% Race/ethnicity: NR Smoking status: 38% tobacco use Obesity (%): NR BMI: NR Diabetes (%): 38%	A priori plan to compare orthobiologics to no orthobiologics: No

Author, year Country Funding Study Design	Inclusion/Exclusion Criteria Arthrodesis Site	Orthobiologic(s) (n) Non-Orthobiologic(s) (n) Follow-up	Demographics	A Priori Comparison?
			Bone mineral density: NR (radiographic signs of reduced bone quality noted in 38%) Medications related to healing: NR	
Rearick, 2014[34] USA Funding: None Retrospective chart review	Inclusion: Received rhBMP-2 during treatment for foot or ankle fracture, fusion, or osteotomy (2010-2012); minimum 12 months follow-up (Fusions included 10 midfoot, 10 tibiotalar, 8 tibiotalo-calcaneal, 7 subtalar, 4 triple, 1 each calcaneocuboid, talonavicular, & pantalar) Exclusion: Skeletally immature, pregnant, active infection, active malignancy (2 patients subsequently excluded from analysis due to loss to follow-up or ineligible procedure) Indications for arthrodesis: NR	Orthobiologic(s): rhBMP-2 plus autograft (n=14 sites; 11 local graft, 2 iliac crest graft, 1 calcaneus graft); used if larger bony defects were present Non-Orthobiologic(s): rhBMP-2 with no supplemental graft (n=60 sites) Number of sites: NR Number of surgeons: 3 Follow-up: Until bony union (mean=111 days in those with successful union)	N=48 patients (83 sites)* Age (years, mean): 52 Gender (% male): 63% Race/ethnicity: NR Smoking status: 25% tobacco use Obesity (%): NR BMI: NR Diabetes (%): 17% Bone mineral density: NR Medications related to healing: NR *Includes patients receiving allograft (9 sites)	A priori plan to compare orthobiologics to no orthobiologics: No
Rungprai, 2016[35] USA Funding: None Retrospective chart review	Inclusion: Open subtalar arthrodesis (2001-2003) Exclusion: Other arthrodesis sites or triple arthrodesis, revision subtalar arthrodesis, required structural bone grafts Indications for arthrodesis: Primary arthritis: 25% Posttraumatic arthritis: 49% Other: 26%	Orthobiologic(s): Cancellous autograft (n=12 feet); DBM with cancellous allograft (n=12 feet); BMP with cancellous allograft (n=12 feet); platelet concentrator with cancellous allograft (n=7 feet) Non-Orthobiologic(s): no bone graft (n=6 feet) Other patients received structural autograft (n=2 feet), structural allograft (n=4 feet), or cancellous allograft (n=5 feet)	N=57 patients (60 feet) Age (years, mean): 47 Gender (% male): 70% Race/ethnicity: NR Smoking status: 12% Obesity (%): NR BMI: 33.9 (range 18.4-56.8) Diabetes (%): 7% Bone mineral density: NR Medications related to healing: NR	A priori plan to compare orthobiologics to no orthobiologics: No

Author, year Country Funding Study Design	Inclusion/Exclusion Criteria Arthrodesis Site	Orthobiologic(s) (n) Non-Orthobiologic(s) (n) Follow-up	Demographics	A Priori Comparison?
	NOTE: Review also identified cases with arthroscopic subtalar arthrodesis – not reported here.	Number of sites: 1 Number of surgeons: 4 Follow-up: 25.8 months (range 6-126 months)		
Sun, 2019[36] China Funding: None Prospective case series	Inclusion: Traumatic subtalar arthritis; underwent minimally invasive subtalar arthrodesis (2011-2014); type I, II, or III calcaneal fracture (Zwipp classification); no severe deformity after early surgical treatment; STJ pain affecting normal daily life; normal or mildly deformed calcaneal morphology, uneven STJ surface, subchondral sclerosis of articular surface, and hypertrophy of joint edge (radiograph or CT) Exclusion: Type V calcaneal malunion; >1 joint fusion; treatment with drugs that might impact fracture healing and functional scores; peripheral bone fusion and joint trauma that affects functional score Indications for arthrodesis: Traumatic subtalar arthritis (100%)	Orthobiologic(s): Bone from iliac crest to supplement local graft (n=4) Non-Orthobiologic(s): Local graft only (n=11) Number of sites: 1 Number of surgeons: 1 Follow-up: 21 months (range 12-34)	N=15 patients Age (years, mean): 49 (range 36-56) Gender (% male): 53% Race/ethnicity: NR Smoking status: NR Obesity (%): NR BMI: NR Diabetes (%): NR Bone mineral density: NR Medications related to healing: excluded patients treated with drugs that might impact healing	A priori plan to compare orthobiologics to no orthobiologics: No
Weinraub, 2010[37] USA Funding: Not reported Retrospective chart review	Inclusion: Combined STJ and TNJ arthrodesis (2006-2009) using single medial incision approach Exclusion: None reported Indications for arthrodesis: Posterior tibial tendon dysfunction: 58% Tarsal coalition: 13%	Orthobiologic(s): PRP (n=7 patients); DBM (n=5); PRP/DBM (n=6); BMP (n=1); PGC (n=1); PRP/SC (n=1); DBM/SC (n=1) Non-Orthobiologic(s): No orthobiologic (n=18 patients) Additional 5 patients received bioactive glass (not reported here)	N=40 patients Age (years, mean): PRP: 45.6 DBM: 63.4 PRP/DBM: 56.8 Other: 60 No orthobiologic: 51.2 Gender (% male): NR Race/ethnicity: NR Smoking status: NR	A priori plan to compare orthobiologics to no orthobiologics: No Orthobiologics used at surgeon's discretion to fill any defects in the fusion site or as an adjunct in patients with biologic healing deficits.

Author, year Country Funding Study Design	Inclusion/Exclusion Criteria Arthrodesis Site	Orthobiologic(s) (n) Non-Orthobiologic(s) (n) Follow-up	Demographics	A Priori Comparison?
	Degenerative joint disease: 15% Rheumatoid arthritis: 5% Other: 10%	Number of sites: 5 practices Number of surgeons: 5 Follow-up: NR	Obesity (%): NR BMI: NR Diabetes (%): NR Bone mineral density: NR Medications related to healing: NR	
Wheeler, 2009[38] USA Funding: None Retrospective chart review	Inclusion: Treated by CPT code 27870 (Arthrodesis Procedures on Leg and Ankle Joint) Exclusion: Missing radiographs at 6 or 12 weeks Indications for arthrodesis: post-traumatic arthritis (50%), prior failed ankle fusions (13%), limb misalignment (22%), degenerative arthritis (13%), septic arthritis (4%)	Orthobiologic(s): Bone slurry (burr to scuff subchondral bone and correct misalignment of surfaces when uneven; small particles left in the joint and mixed with blood from bleeding bone surfaces) (n=32 patients). NOTE: includes 2 patients who received structural graft Non-Orthobiologic(s): No burr to produce bone slurry (n=22 patients) NOTE: includes 2 patients who received structural graft Number of surgical facilities: NR Number of surgeons: 3 Follow-up: 6 and 12 weeks	N=54 patients Age (years, mean): 52.4 Gender (% male): 64.8% Race/ethnicity: NR Smoking status: NR Obesity (%): NR BMI: NR Diabetes (%): NR Bone mineral density: NR Medications related to healing: NR	A priori plan to compare orthobiologics to no orthobiologics: Yes
Yavuz, 2014[39] Turkey Funding: Not Reported Retrospective chart review	Inclusion: Symptomatic subtalar arthrosis after conservative treatment for intra-articular calcaneal fracture Exclusion: NR Indications for arthrodesis: Talocalcaneal arthrosis	Orthobiologic(s): Iliac crest-derived cancellous autograft (n=8 patients) or cancellous allografts (n=3 patients) Non-Orthobiologic(s): No bone graft (n=9 patients) Number of surgical facilities: NR Number of surgeons: NR Follow-up: Mean=43 months (range 21-83 months)	N=20 patients (21 feet) Age (years, mean): 44 Gender (% male): 80% Race/ethnicity: NR Smoking status: NR Obesity (%): NR BMI: NR Diabetes (%): NR Bone mineral density: NR Medications related to healing: NR	A priori plan to compare orthobiologics to no orthobiologics: No Bone graft used in absence of appropriate surface contact; Allograft was used in the cases where patients refused to sign the informed consent form for autograft application.

Author, year Country Funding Study Design	Inclusion/Exclusion Criteria Arthrodesis Site	Orthobiologic(s) (n) Non-Orthobiologic(s) (n) Follow-up	Demographics	A Priori Comparison?
Yildirim, 2015[40] Turkey Funding: None Retrospective chart review	Inclusion: Isolated subtalar arthrodesis Exclusion: Degenerative changes of the ankle or other intertarsal joints, previous arthrodesis (any foot joint), osteotomy to correct coronal plane hindfoot deformity during same surgery Indications for arthrodesis: Degenerative subtalar arthritis secondary to calcaneal fracture (55%), nontraumatic arthritis due to hindfoot valgus deformity (18%), talocalcaneal coalition (15%), subtalar instability as a sequela of neurovascular conditions (6%), and flatfoot secondary to tibialis posterior tendon dysfunction (6%)	Orthobiologic(s): Grafting of joint space following removal of chondral surfaces with iliac crest autograft (n=16 feet) or cancellous allograft (n=3 feet) Non-Orthobiologic(s): No grafting (n=14 feet) Number of surgical facilities: NR Number of surgeons: NR Follow-up: Mean=36.8 months (range 24-74 months	N=31 patients (33 feet) Age (years, mean): 44 Gender (% male): 61% Race/ethnicity: NR Smoking status: NR Obesity (%): NR BMI: NR Diabetes (%): NR Bone mineral density: NR Medications related to healing: NR	A priori plan to compare orthobiologics to no orthobiologics: Yes

AVN=avascular necrosis; BMI=body mass index; BMP=bone morphogenic protein; CPT=Current Procedural Terminology; CT=computed tomography; DMB=demineralized bone matrix; ISSA=In situ subtalar arthrodesis; MPJ=metatarsophalangeal joint; MVA=motor vehicle accident; NR=not reported; PGC=platelet gel concentrate; PRP=platelet-rich plasma; rhBMP-2=recombinant human BMP-2; SBBDA=subtalar bone block distraction arthrodesis; SC=stem cell; STJ=subtalar joint; TMT=tarsometatarsal; TNJ=talonavicular joint; TNC=talonavicular-cuneiform

Table 2. Quality Criteria

	Is there evidence of ethical approval for the study?	Were there clear criteria for inclusion?	Was there complete inclusion of participants?	Was there clear reporting of the demographics of the study participants?	Were the study groups formed in a way that minimizes bias?	Did the participants included in any comparison receive similar treatment/care other than the intervention of interest?	Was follow-up complete with no differential follow-up between groups?	Was outcome assessment blinded?	Were outcomes measured in valid and reliable ways?
Abd=Ella 2017[20]	NR	No	Unclear	Yes	No – used to fill gap	Yes	Yes	Unclear	Yes – CT to confirm
Anderson, 2013[21]	No	Yes	Yes – consecutive	Yes	No—surgeon discretion and graft for less desirable bone quality	Yes	Unclear—not reported	Unclear—radiographs assessed in "time blinded fashion" by 3 independent podiatric surgeons	No—study-created office visit survey; CT not used
Bibbo, 2009[22]	Yes	Yes	Unclear	Yes	No—graft used to fill defects and correct misalignment	Yes	Yes	Unclear	Yes—CT used to confirm radiographs
Buda 2018[23]	Yes	Yes	Yes	Yes	Unclear – no reported rationale for use of graft	Unclear – no information about treatment/follow-up protocol	Yes – required to have 12 month follow-up for inclusion	No	No – not all non-unions confirmed with CT scans

	Is there evidence of ethical approval for the study?	Were there clear criteria for inclusion?	Was there complete inclusion of participants?	Was there clear reporting of the demographics of the study participants?	Were the study groups formed in a way that minimizes bias?	Did the participants included in any comparison receive similar treatment/care other than the intervention of interest?	Was follow-up complete with no differential follow-up between groups?	Was outcome assessment blinded?	Were outcomes measured in valid and reliable ways?
Cao, 2017[24]	Yes	No	No	No	No—more severe cases got graft	Yes	Yes	Unclear	No—radio-graphs only
Chahal, 2006[25]	Yes	Yes	Yes	Yes	No—surgeon discretion	No—ostectomy performed in local graft cases	No—graft group has missing data for 1 case	Yes—radiologic outcome independently assessed by radiologists	No—not all non-unions confirmed with CT scans
Chen, 1996[26]	No	No	Unclear	No	No—graft used in severe bone loss or poor bone quality	No – weight bearing delayed for graft patients	No—2 patients lost to follow up	Unclear	Unclear—radiographic methods not reported
Easley, 2000[27]	Yes	No	Yes - consecutive	Yes	Unclear – reason for use of autograft not reported	No—surgical procedure not standardized; different post-op if iliac crest graft harvested	No—18% patients lost to follow up and 80% completed both clinical and radiographic outcomes	Yes—3 investigators not involved in procedures conducted review	No—AOFAS preop scores assigned retrospectively for some patients; study created questionnaire

	Is there evidence of ethical approval for the study?	Were there clear criteria for inclusion?	Was there complete inclusion of participants?	Was there clear reporting of the demographics of the study participants?	Were the study groups formed in a way that minimizes bias?	Did the participants included in any comparison receive similar treatment/care other than the intervention of interest?	Was follow-up complete with no differential follow-up between groups?	Was outcome assessment blinded?	Were outcomes measured in valid and reliable ways?
Fourman, 2014[28]	Yes	Yes	Yes-"all"	Yes	No—use of rhBMP-2 came as change in practice	No-- some patients with larger defects got allograft	No—47% ("large proportion") did not receive CT	Unclear—surgeon at time of study not blinded; retrospective validation by blinded radiologist	Yes, CT exams used to assess bone bridging
Grunander, 2012[29]	Yes	Yes	Unclear	Yes	No—PRP used only in later cases (*ie*, when it became available)	Yes	Yes	Unclear	Yes—CT used to evaluate cases of questionable union
Holm, 2015[30]	Yes	Yes	Yes ("the" 17 cases)	Yes	No – used to fill void	Yes	Yes	No – surgeons reviewed their own cases	No – no CT confirmation
Lechler, 2012[31]	Yes	Yes	Yes - consecutive	No	No – surgeon discretion	Yes	Yes	Unclear – not reported	No – CT not used

	Is there evidence of ethical approval for the study?	Were there clear criteria for inclusion?	Was there complete inclusion of participants?	Was there clear reporting of the demographics of the study participants?	Were the study groups formed in a way that minimizes bias?	Did the participants included in any comparison receive similar treatment/care other than the intervention of interest?	Was follow-up complete with no differential follow-up between groups?	Was outcome assessment blinded?	Were outcomes measured in valid and reliable ways?
Patil, 2011[32]	NR	Yes	Unclear	Yes	Unclear – not reported	Yes	Yes – but 2/17 did not return questionnaire	Unclear	No – no CT confirmation
Plaass, 2009[33]	Yes	Yes	Yes - consecutive	Yes	No – DBM or platelets in high risk cases	No – weight bearing delayed for orthobiologic patients	Yes	Yes - radiographs	Yes – CT to confirm union if unclear on x-ray
Rearick, 2014[34]	Yes	Yes	Unclear	Yes	No – surgeon discretion and graft for larger bony defects	No – some use of bone stimulators	Yes	No – treating surgeon determined union	No – CT not routinely used
Rungprai, 2016[35]	Yes	Yes	Yes	Yes	No – graft used to fill defects as needed	Unclear	Yes for union data	No – blinded to 2nd rater but not to procedure	Unclear – some CT; nonunion on basis of clinical judgement

	Is there evidence of ethical approval for the study?	Were there clear criteria for inclusion?	Was there complete inclusion of participants?	Was there clear reporting of the demographics of the study participants?	Were the study groups formed in a way that minimizes bias?	Did the participants included in any comparison receive similar treatment/care other than the intervention of interest?	Was follow-up complete with no differential follow-up between groups?	Was outcome assessment blinded?	Were outcomes measured in valid and reliable ways?
Sun, 2019[36]	Yes	Yes	Unclear	No	No – iliac crest bone graft used if quantity of local bone was inadequate	Yes	Yes	Unclear	Unclear how many were confirmed with CT
Weinraub, 2010[37]	No	Yes	Yes	No	No –surgeon discretion to fill defects or if healing deficits	Yes	Yes	No – surgeon determined union	No – clinical judgement, no valid quality of life measure
Wheeler, 2009[38]	Yes	Yes	Unclear	No	Unclear – no reported rationale for additional procedure	Yes	Yes – required to have 6 or 12 week radiographs for inclusion	Yes – reviewers of radiographs were blinded	No – no CT confirmation or standard positioning for lateral radiographs
Yavuz, 2014[39]	No	No	Unclear	No	No-allograft used in cases when patients did not consent to autograft. Grafting performed in cases with absence of appropriate contact	Yes	Yes	Unclear	Unclear—radiographs used to confirm union (no CT)

	Is there evidence of ethical approval for the study?	Were there clear criteria for inclusion?	Was there complete inclusion of participants?	Was there clear reporting of the demographics of the study participants?	Were the study groups formed in a way that minimizes bias?	Did the participants included in any comparison receive similar treatment/care other than the intervention of interest?	Was follow-up complete with no differential follow-up between groups?	Was outcome assessment blinded?	Were outcomes measured in valid and reliable ways?
Yildirim, 2015[40]	No	Yes	Unclear	No	Unclear	Yes	Yes	Unclear	Unclear—X-rays used to confirm union. No CTs

AOFAS=American Orthopaedic Foot and Ankle Society; CT=computed tomography; rhBMP-2=recombinant human BMP-2

Table 3. Patient-centered Outcomes, Part 1

Author Year Study Design Follow-up	Wound Healing (describe measure)		Need for Reoperation/Reintervention % (n/N)		Pain (describe measure)	
	Orthobiologic(s)	Non-Orthobiologic(s)	Orthobiologic(s)	Non-Orthobiologic(s)	Orthobiologic(s)	Non-Orthobiologic(s)
Abd-Ella, 2017[20] Prospective case series Follow-up: 23 months (range 12-60)	No wound healing problems were encountered		0% (0/0)	100% (3/3)	NR	NR
Holm, 2015[30] Retrospective chart review Follow-up: mean 30 months (range 12-61)	NR	NR	0% (0/3)	0% (0/6)	VAS 0-9 (pain at most recent visit) Mean (SD) 2.0 (1.0) (n=3)	VAS 0-9 (pain at most recent visit) Mean (SD) 1.7 (1.4) (n=6)
Lechler, 2012[31] Prospective case series Follow-up: 15.8 months (range 6-24)	NR	NR	NR	NR	VAS score (subjective pain) not significantly influenced by autologous bone grafting (P=.52)	
Patil, 2011[32] Retrospective chart review Follow-up: 12 months	NR	NR	NR	NR	None reported pain on weightbearing	
Plaass, 2009[33] Prospective case series Follow-up: 12 months	Delayed wound healing DBM: 14% (1/7) Platelet 0% (0/1) Both 0% (0/2)	Delayed wound healing 0% (0/5)	NR	NR	AOFAS pain (range 0-40) DBM Only (n=7) Pre: 12.9 (12.5) Post: 27.1 (7.6) Platelet Only (n=1) Pre: 0.0 Post: 20.0 DBM+Platelet (n=3) Pre: 20.0 (0.0) Post: 26.7 (5.8)	AOFAS pain (range 0-40) No Orthobiologic (n=5) Pre: 8.0 (11.0) Post: 34.0 (5.5)

Author Year Study Design Follow-up	Wound Healing (describe measure)		Need for Reoperation/Reintervention % (n/N)		Pain (describe measure)	
	Orthobiologic(s)	Non-Orthobiologic(s)	Orthobiologic(s)	Non-Orthobiologic(s)	Orthobiologic(s)	Non-Orthobiologic(s)
Sun, 2019[36] Prospective case series Follow-up: 21 months	All posterolateral incisions healed smoothly in an average of 10-12 days		NR	NR	NR	NR
Weinraub, 2010[37] Retrospective Chart Review Follow-up: NR	NR	NR	NR	NR	CCJ pain (y/n) PRP/DBM 17% (1/6)	CCJ pain (y/n) 6% (1/18)
Wheeler, 2009[38] Retrospective chart review Follow-up: 6 and 12 weeks	NR	NR	0% (0/32) At 6 months	4.5% (1/22) At 6 months	NR	NR

AOFAS=American Orthopaedic Foot and Ankle Society (Ankle-Hindfoot Score for Pain: 40 point scale where 40=no pain); CCJ=calcaneocuboid joint; DBM=demineralized bone matrix; NR=not reported; PRP=platelet-rich plasma; SD=standard deviation; VAS=visual analog scale

Table 4. Patient-centered Outcomes, Part 2

Author Year Study Design Follow-up	Functional Outcome Clinically Meaningful Differences (describe measure)		Quality of Life Clinically Meaningful Differences (describe measure)		Function or Quality of Life Scale Scores (mean, SD) (describe measure)	
	Orthobiologic(s)	Non-Orthobiologic(s)	Orthobiologic(s)	Non-Orthobiologic(s)	Orthobiologic(s)	Non-Orthobiologic(s)
Abd-Ella, 2017[20] Prospective case series Follow-up: 23 months (range 12-60)	NR	NR	NR	NR	Subjective patient satisfaction graded good or excellent in all cases (4 options: excellent, good, fair, poor)	
Anderson, 2013[21] Retrospective chart review Follow-up: weekly (for first 2 weeks) then biweekly until clinical union	NR	NR	NR	NR	Patient satisfaction (willing to have procedure again) 98% (60/62) P=NS	Patient satisfaction (willing to have procedure again) 96% (50/52)

Author Year Study Design Follow-up	Functional Outcome Clinically Meaningful Differences (describe measure)		Quality of Life Clinically Meaningful Differences (describe measure)		Function or Quality of Life Scale Scores (mean, SD) (describe measure)	
	Orthobiologic(s)	Non-Orthobiologic(s)	Orthobiologic(s)	Non-Orthobiologic(s)	Orthobiologic(s)	Non-Orthobiologic(s)
Cao, 2017[24] Retrospective chart review Follow-up: 39.8 months	NR	NR	NR	NR	AOFAS Score Preop: 36.8 (3.0) Postop: 89.0 (2.1), P=.51 (calculated) Reported that all patients were satisfied with clinical results and able to walk “long distances” 6 months after surgery	AOFAS Score Preop: 38.6 (7.7) Postop: 87.6 (4.2)
Chen, 1996[26] Retrospective Chart Review Follow-up: 4 years (mean)	NR	NR	NR	NR	Morgan et al (1985)[a] clinical outcomes ratings: Excellent: 7% (1/15 feet) Good: 73% (11/15 feet) Fair: 13% (2/15 feet) Poor: 7% (1/15 feet)	Morgan et al (1985)[a] clinical outcomes ratings: Excellent: 44% (11/25 feet) Good: 52% (13/25 feet) Fair: 0% (0/25 feet) Poor: 4% (1/25 feet)
Easley, 2000[27] Retrospective chart review Follow-up: 51 months (mean)	NR	NR	NR	NR	Modified AOFAS Score (n=94 feet): Preop: NR Postop: 73 (25-94) P=NS Scale: Maximum=94	Modified AOFAS Score (n=39 feet): Preop: NR Postop: 70 (30-94)
Holm, 2015[30] Retrospective chart review Follow-up: mean 30 months (range 12-61)	NR	NR	NR	NR	AOFAS Ankle-Hindfoot Score Mean (SD) 81.3 (3.5) (n=3)	AOFAS Ankle-Hindfoot Score Mean (SD) 74.5 (11.6) (n=6)
Lechler, 2012[31] Prospective case series Follow-up: 15.8 months (range 6-24)	NR	NR	NR	NR	Improvement in mean AOFAS not significantly influenced by autologous bone grafting (P=.62)	

Author Year Study Design Follow-up	Functional Outcome Clinically Meaningful Differences (describe measure)		Quality of Life Clinically Meaningful Differences (describe measure)		Function or Quality of Life Scale Scores (mean, SD) (describe measure)	
	Orthobiologic(s)	Non-Orthobiologic(s)	Orthobiologic(s)	Non-Orthobiologic(s)	Orthobiologic(s)	Non-Orthobiologic(s)
Plaass, 2009[33] Prospective case series Follow-up: 12 months	NR	NR	NR	NR	AOFAS Total (range 0-92) DBM only (n=7) Pre: 44.0 (12.6) Post: 66.1 (15.0) Platelet Only (n=1) Pre: 28 Post: 54 DBM+Platelet (n=3) Pre: 59.0 (5.3) Post: 62.3 (9.8)	AOFAS Total (range 0-92) Pre: 33.0 (15.7) Post: 70.8 (12.1)
Sun, 2019[36] Prospective case series Follow-up: 21 months	NR	NR	NR	NR	AOFAS Outcome 50% (2/4) “good” 50% (2/4) “excellent”	AOFAS Outcome 45% (5/11) “good” 55% (6/11) “excellent”
Yildirim, 2015[40] Retrospective chart review Follow-up: 36.8 months	NR	NR	NR	NR	AOFAS No significant difference in mean scores between graft and no-graft groups	

AOFAS=American Orthopedic Foot and Ankle Society (Ankle-Hindfoot score for function, pain, & alignment: maximum of 92-94 points (full function, no pain) depending on site of fusion); DBM=demineralized bone matrix; NR=not reported; SD=standard deviation

[a]Morgan et al (1985) clinical outcomes ratings: Excellent (solid fusion, no pain, no limp, no job restriction, esthetic appearance); Good (solid fusion, mild pain, mild occasional limp, same job with some restrictions, acceptable appearance); Fair (solid fusion, moderate pain, constant limp, job change, poor appearance); Poor (failure of fusion or severe pain)

Table 5. Intermediate and Cost Outcomes

Author Year Study Design Follow-up	Radiographic Fusion % (n/N)		Mean Time to Fusion (weeks)		Patient Costs (describe measure)		Facility Costs (describe measure	
	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobio-logic(s)
Abd-Ella, 2017[20] Prospective case series Follow-up: 23 months (range 12-60)	Solid osseous union 89% (8/9)* (2 smokers, 6 non-smokers) (9th patient, a smoker, had painless fibrous union) *Bridging trabeculae included 50% or more of the joint surface on CT scan	Solid osseous union 0% (0/3) (1 smoker, 2 non-smokers)	NR	NR	NR	NR	NR	NR
Anderson, 2013[21] Retrospective chart review Follow-up: weekly (for first 2 weeks) then biweekly until clinical union	Total radiographic Non-Unions: 7% (4/62 patients), P=NS % of Radiographic Fusion: 94.1%	Total radiographic Non-Unions: 4% (2/52 patients) % of Radiographic Fusion: 96.0%	Time to Clinical Union (weeks) Mean (SD) 6.52 (1.46) P=NS Time to Radiographic Union: Mean (SD) 6.69 (1.70) P=NS	Time to Clinical Union (weeks) Mean (SD) 6.46 (1.31) Time to Radiographic Union: Mean (SD) 6.76 (1.31)	NR	NR	NR	NR
Bibbo, 2009[22] Retrospective chart review Follow-up: every 2-4 weeks	NR	NR	Ankle joint fusions (n=8): Mean 13.3 weeks P=.267 Subtalar joint fusions (n=8): Mean 13.2 weeks P=.116	Ankle joint fusions (n=24): Mean 9.1 weeks Subtalar joint fusions (n=27): Mean 10.4 weeks	NR	NR	NR	NR

Author Year Study Design Follow-up	Radiographic Fusion % (n/N)		Mean Time to Fusion (weeks)		Patient Costs (describe measure)		Facility Costs (describe measure	
	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobio-logic(s)
			Calcaneo-cuboid joint fusions (n=1): Mean 12 weeks P NR *Union: mini-mum of 50% bony bridging across arthro-desis site, or multiple spot welding areas equaling 50% of fusion site	Calcaneo-cuboid joint fusions (n=14): Mean 11 weeks				
Buda, 2018[23] Retrospective chart review Follow-up: 77.5 months	Non-union* 7% (5/70) OR 0.22 (95%CI 0.1, 0.6; P=.005) *presence of radiolucent line through TMT joint, sealing off of medullary cavity with sclerosis at edge of TMT join, and bony resorption or regional osteoporosis above and below TMT joint	Non-union 28% (5/18)	NR	NR	NR	NR	NR	NR
Cao, 2017[24] Retrospective chart review Follow-up: 39.8 months	All feet fused solidly (at 3 or 6 months post-surgery) per radiographs.		NR	NR	NR	NR	NR	NR

Author Year Study Design Follow-up	Radiographic Fusion % (n/N)		Mean Time to Fusion (weeks)		Patient Costs (describe measure)		Facility Costs (describe measure	
	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobio-logic(s)
Chahal, 2006[25] Retrospective chart review Follow-up: 35.5 months (mean)	Union* 84.8% (39/46), P<.107 OR for non-union: 0.32 (95%CI 0.12, 1.29) (adj for age, sex) *Complete bridging callus or trabeculation across subtalar joint with no pain when stress applied to joint (from lateral view of foot, 2 oblique radiographs of hindfoot, and axial view of hindfoot)	Union 65.0% (13/20)	NR	NR	NR	NR	NR	NR
Chen, 1996[26] Retrospective Chart Review Follow-up: 4 years (mean)	Nonunion: 0% (0/15 feet) Delayed union: 7% (1/15 feet)	Nonunion: 4% (1/25 feet) Delayed union: 0% (0/25 feet)	Mean 15 weeks (12-20)	NR	NR	NR	NR	NR
Easley, 2000[27] Retrospective chart review Follow-up: 51 months (mean)	Union* 85% (80/94) P=NS *Clinical or radiographic evidence of non-union. Clinical union based on pain when stress applied. Radiographic	Union 87% (34/39)	Weeks Mean (range) 11 (8-20) P=NS	Weeks Mean (range) 11 (8-24)	NR	NR	NR	NR

Author Year Study Design Follow-up	Radiographic Fusion % (n/N)		Mean Time to Fusion (weeks)		Patient Costs (describe measure)		Facility Costs (describe measure	
	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobio-logic(s)
	union based on lateral radio-graph and 2 Broden radiographs							
Fourman, 2014[28] Retrospective chart review Follow-up: 43 months	Initial Union (3 months): 92% (39/42) P<.001 OR 11.76 (95%CI 3.12, 44.41) Final Union (at time of frame removal – mean 124 days)): 92% (40/42) P=.08 Bridging bone (CT at 3 months) Mean (SD) 48% (4.18) P=.04	Initial Union (3 months): 53% (21/40) Final Union (at time of frame removal – mean 161 days)): 82% (33/40) Bridging bone (CT at 3 months) Mean (SD) 32% (5.90)	NR	NR	NR	NR	NR	NR
Grunander, 2012[29] Retrospective chart review Follow-up: 23 months (mean)	Non-union*: 29% (2/7 patients) P=.36 (calculated) *Evaluated on radiographs (AP, lateral, and oblique). CT scan used occasionally and union defined as > 50% bone union	Non-union: 56% (5/9 patients)	NR	NR	NR	NR	NR	NR

Author Year Study Design Follow-up	Radiographic Fusion % (n/N)		Mean Time to Fusion (weeks)		Patient Costs (describe measure)		Facility Costs (describe measure	
	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobio-logic(s)
Holm, 2015[30] Retrospective chart review Follow-up: mean 30 months (range 12-61)	"Osseous union was achieved in all patients" (osseous union not defined)		NR	NR	NR	NR	NR	NR
Lechler, 2012[31] Prospective case series Follow-up: 15.8 months (range 6-24)	NR	NR	Time to osseous union not significantly influenced by autologous bone grafting (P=.38)		NR	NR	NR	NR
Patil, 2011[32] Retrospective chart review Follow-up: 12 months	Union 100% (4/4) Plain radiographs	Union 100% (13/13) Plain radiographs	NR	NR	NR	NR	NR	NR
Plaass, 2009[33] Prospective case series Follow-up: 12 months	100% in all groups (16/16) *Presence of bridging trabeculae at the level of the arthrodesis on standard x-ray; CT used if doubt about union	100% (5/5)	DBM Only (n=7) Weeks 12.7 (6.1) Platelet Only (n=1) Weeks 8.0 DBM+Platelet (n=3) Weeks 13.0 (7.8)	No Orthobiologic (n=5) Weeks 12.0 (7.8)	NR	NR	NR	NR
Rearick, 2014[34] Retrospective chart review Follow-up: until union	Non-union 21% (3/14 sites) 2 tibiotalar fusions, 1 midfoot fusion	Nonunion 0% (0/60 sites)	Tibiotalar: 16.9 weeks Subtalar: 14.3 weeks Talonavicular: 16.3 weeks Midfoot: N/A All P=NS	Tibiotalar: 17.0 weeks Subtalar: 16.9 weeks Talonavicular: 16.7 weeks Midfoot: 13.0 weeks	NR	NR	NR	NR

Author Year Study Design Follow-up	Radiographic Fusion % (n/N)		Mean Time to Fusion (weeks)		Patient Costs (describe measure)		Facility Costs (describe measure	
	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobio-logic(s)
Rungprai, 2016[35] Retrospective Chart Review Follow-up: 25.8 months	Union* Cancellous autograft: 83% (10/12) DBM+cancel-lous autograft: 92% (11/12) BMP+cancel-lous autograft: 83% (10/12) Platelet concentrator + cancellous autograft: 86% (6/7) All P=NS	Union* 100% (6/6) *Appearance of osseous trabeculae across the subtalar arthrodesis site on a lateral weight-bearing radiograph	Time (weeks) Cancellous autograft: 16.7 (11.0) DBM+cancel-lous autograft: 16.2 (9.4) BMP+cancel-lous autograft: 14.3 (2.7) Platelet concentrator + cancellous autograft: 16.0 (4.0) All P=NS	Time (weeks) 14.6 (0.9)	NR	NR	NR	NR
Sun, 2019[36] Prospective case series Follow-up: 21 months	Bone fusion confirmed (radiographs or CT scans) in all patients		Fusion within 3-5 months (range 2-4 months)		NR	NR	Operation time[a] Mean (SD) 83.8 (4.8) minutes (range 40-85) P<.01	Operation time[a] Mean (SD) 50.9 (7.0) minutes (range 40-60)
Weinraub, 2010[37] Retrospective Chart Review Follow-up: NR	No non-unions observed		Time (weeks) Mean (SD) PRP (n=7 patients): 7.9 (1.2) DBM (n=5): 7.4 (0.9) PRP/DBM (n=6): 8.5 (1.2) BMP (n=1): 20 PGC (n=1): 8 PRP/SC (n=1): 8	Time (weeks) Mean (SD) 8.4 (1.7)	NR	NR	Duration of surgery (minutes) Mean (SD) PRP (n=7 patients): 84.6 (13.3) DBM (n=5): 82.6 (12.4) PRP/DBM (n=6): 81.7 (15.7) BMP (n=1): 164 PGC (n=1): 98	Duration of surgery (minutes) Mean (SD) 82.9 (11.8)

Author Year Study Design Follow-up	Radiographic Fusion % (n/N)		Mean Time to Fusion (weeks)		Patient Costs (describe measure)		Facility Costs (describe measure	
	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobio-logic(s)
			DBM/SC (n=1): 10				PRP/SC (n=1): 93 DBM/SC (n=1): 91	
Wheeler, 2009[38] Retrospective chart review Follow-up: 6 and 12 weeks	Bridging bone (mean % of healing) *AP view* 6 weeks: 94.1%, P=.0099 12 weeks: 98.1%, P=.026 *Lateral view** 6 weeks: 89.7%, P=.2 12 weeks: 91.3%, P=.14 *Substantial challenges noted in interpretation of lateral radiographs	Bridging bone (mean % of healing) *AP view* 6 weeks: 76.4% 12 weeks: 85.7% *Lateral view** 6 weeks: 80.9% 12 weeks: 82.9% *Substantial challenges noted in interpretation of lateral radiographs	NR	NR	NR	NR	NR	NR
Yavuz, 2014[39] Retrospective chart review Follow-up: 43 months (mean)	Non-union: 0% (0/11 patients)	Non-union: 11% (1/9 patients)	No significant difference in time required for unification between patients that did and did not receive bone grafting, P=.544		NR	NR	NR	NR
Yildirim, 2015[40] Retrospective chart review Follow-up: 36.8 months	Non-union 5.3% (1/19 feet)	Non-union 7.1% (1/14 feet)	14.4 (1.7) weeks n=19 P<.05	17.5 (2.8) weeks n=14	NR	NR	NR	NR

AP=anteroposterior; BMP=bone morphogenic protein; CI=confidence interval; CT=computed tomography; DMB=demineralized bone matrix; N/A=not applicable; NR=not reported; NS=not statistically significant; OR=odds ratio; PGC=platelet gel concentrate; PRP=platelet-rich plasma; rhBMP-2=recombinant human BMP-2; SC=stem cell; SD=standard deviation; TMT=tarsometatarsal

[a]Time from cutting skin to stitching wound

Table 6. Harms – Post-operative Complications

Author Year Study Design Follow-up	Wound Complications (describe); % (n/N)		Mortality % (n/N)		Amputation % (n/N)		Infection/Other (describe) % (n/N)	
	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobio-logic(s)
Abd-Ella, 2017[20] Prospective case series Follow-up: 23 months (range 12-60)	NR	NR	NR	NR	NR	NR	NR	NR
Chen, 1996[26] Retrospective Chart Review Follow-up: 4 years (mean)	NR	NR	NR	NR	0% (0/15 feet)	4% (1/25 feet)	Infection 13% (2/15 feet) Subtalar varus: 7% (1/15 feet) Reflex sympathetic dystrophy: 7% (1/15 feet)	Infection 0% (0/25 feet) Subtalar varus: 0% (0/25 feet) Reflex sympathetic dystrophy: 0% (0/25 feet)
Fourman, 2014[28] Retrospective chart review Follow-up: 43 months	No compartment syndrome or wound breakdown in either group		NR	NR	2.4% (1/42) (for infection)	0% (0/40)	Infection, pin site 14.3% (6/42) P=NS	Infection, pin site 12.5% (5/40)
Weinraub, 2010[37] Retrospective Chart Review Follow-up: NR	No reported wound complications	6% (1/18) Incision dehiscence	NR	NR	NR	NR	PRP/DBM: 17% (1/6) Lateral column pain 17% (1/6) Elevated first ray BMP: 100% (1/1) Poor exposure (abandoned procedure)	6% (1/18) Painful fixation 6% (1/18) Talar fracture
Yavuz, 2014[39] Retrospective chart review Follow-up: 43 months (mean)	NR	NR	NR	NR	NR	NR	Infection 12.5% (1/8 patients who received autograft) 33% (1/3 patients who received allograft)	Infection 0% (0/9 patients)

BMP=bone morphogenic protein; DBM=demineralized bone matrix; NR=not reported; NS=not statistically significant; PRP=platelet-rich plasma

Table 7. Harms – Donor Site Morbidity

Author Year Study Design Follow-up	Hematoma Formation % (n/N)		Donor Site Infection % (n/N)		Chronic Pain % (n/N)		Other (describe) % (n/N)	
	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobio-logic(s)	Orthobio-logic(s)	Non-Orthobi-ologic(s)
Abd-Ella, 2017[20] Prospective case series Follow-up: 23 months (range 12-60)	NR	NR	NR	NR	NR	NR	No donor site morbidity was encountered	

NR=not reported