



Supplement of

Single- versus two-stage revision surgery in the case of fracture-related infection: a systematic review

Jonathan Sliepen et al.

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Table S1 Search string per database.

Source	Search string
Pubmed	(1 OR (2 AND 3)) AND 4 <i>Concept 1:</i> "IAFF"[tiab] OR "osteomyelitis"[Mesh:NoExp] OR osteomyelit*[tiab] <i>Concept 2 AND 3:</i> ("Infections"[Mesh:NoExp] OR "infect*" [tiab] OR "Bone Diseases, Infectious"[Mesh:NoExp] OR "surgical wound infection"[Mesh] OR "SSI" [tiab]) AND (nonunion[tiab] OR "non union"[tiab] OR "Pseudarthrosis"[Mesh] OR pseudoarthro* [tiab] OR pseudarthro* [tiab] OR "pseudo arthro*" [tiab] OR "Fractures, Bone"[Mesh] OR "fracture*" [tiab]) <i>Concept 4:</i> "Reoperation"[Mesh] OR "reoperation"[tiab] OR "surgical revision"[tiab] OR "revision surger*" [tiab] OR "single stage"[tiab] OR "one stage"[tiab] OR "1 stage"[tiab] OR "one phase"[tiab] OR "single phase"[tiab] OR "2 stage"[tiab] OR "two stage"[tiab] OR "PMMA" [tiab] OR "polymethyl methacrylate" [tiab] OR "polymethyl-methacrylate" [tiab] OR "polymethylmethacrylate" [tiab] OR "antibiotic cement rod"[tiab] OR "cement rod"[tiab] OR "interlocking intramedullary nail*" [tiab] OR "bone cement" [tiab] OR "antibiotic cement*" [tiab] OR "antibiotic nail"[tiab] OR "antibiotic impregnated*" [tiab] OR "antibiotic-impregnated*" [tiab] OR "nail cement" [tiab]
Embase	#1 'fracture infection'/exp OR 'posttraumatic osteomyelitis'/exp OR 'IAFF':ti,ab,kw OR 'osteomyelitis'/de OR 'osteomyelit':ti,ab,kw #2 ('infection'/de OR 'infect*':ti,ab,kw OR 'bone infection'/de OR 'surgical infection'/exp OR 'SSI':ti,ab,kw) AND ('fracture nonunion'/exp OR nonunion:ti,ab,kw OR 'non union':ti,ab,kw OR 'pseudarthrosis'/de OR 'pseudoarthro*':ti,ab,kw OR 'pseudarthro*':ti,ab,kw OR 'pseudo arthro*':ti,ab,kw OR 'fracture'/exp OR 'fracture*':ti,ab,kw) #3: #1 OR #2 #4 'reoperation'/exp OR 'reoperation':ti,ab,kw OR 'revision surgery'/exp OR 'surgical revision':ti,ab,kw OR 'revision surger*':ti,ab,kw OR 'one-stage revision'/exp OR 'single stage':ti,ab,kw OR 'one stage':ti,ab,kw OR '1 stage':ti,ab,kw OR 'one phase':ti,ab,kw OR 'single phase':ti,ab,kw OR 'two-stage revision'/exp OR '2 stage*':ti,ab,kw OR 'two stage*':ti,ab,kw OR 'PMMA':ti,ab,kw OR 'polymethyl methacrylate':ti,ab,kw OR 'polymethyl-methacrylate':ti,ab,kw OR 'polymethylmethacrylate':ti,ab,kw OR 'antibiotic cement rod':ti,ab,kw OR 'cement rod':ti,ab,kw OR 'interlocking intramedullary nail*':ti,ab,kw OR 'bone cement':ti,ab,kw OR 'antibiotic cement*':ti,ab,kw OR 'antibiotic nail':ti,ab,kw OR 'antibiotic impregnated*':ti,ab,kw OR 'antibiotic-impregnated*':ti,ab,kw OR 'nail cement':ti,ab,kw #5: #3 AND #4 NOT ('conference abstract':it OR preprint:it)
Web of science Core Collection	Science Citation Index Expanded (SCI-EXPANDED)--1955-present Social Sciences Citation Index (SSCI)--1956-present Arts & Humanities Citation Index (AHCI)--1975-present Conference Proceedings Citation Index – Science (CPCI-S)--1990-present Emerging Sources Citation Index (ESCI)--2017-present Concept 1 TS=("IAFF" OR osteomyelit*) Concept 2 AND 3 TS=((("infect*" OR "SSI") AND ("nonunion" OR "non union" OR pseudoarthro* OR pseudarthro* OR "pseudo arthro*" OR "fracture*")) Concept 4 TS=(("reoperation" OR "surgical revision" OR "revision surger*" OR "single stage" OR "one stage" OR "1 stage" OR "one phase" OR "single phase" OR "2 stage" OR "two stage" OR "PMMA" OR "polymethyl methacrylate" OR "polymethyl-methacrylate" OR "polymethylmethacrylate" OR "antibiotic cement rod" OR "cement rod" OR "interlocking intramedullary nail*" OR "bone cement" OR "antibiotic cement*" OR "antibiotic nail" OR "antibiotic impregnated*" OR "antibiotic-impregnated*" OR "nail cement")
Grey literature	
Cochrane Library (CENTRAL)	#1 ([mh ^"osteomyelitis"] OR ("IAFF" OR osteomyelit*):ti,ab,kw) #2 ([mh ^"Infections"] OR [mh ^"Bone Diseases, Infectious"] OR [mh "surgical wound infection"] OR (infect* OR "SSI"):ti,ab,kw) AND ([mh "Pseudarthrosis"] OR [mh "Fractures, Bone"] OR (nonunion OR "non union" OR pseudoarthro* OR pseudarthro* OR (pseudo NEXT arthro*) OR fracture*):ti,ab,kw) #3: #1 OR #2 #4 [mh "Reoperation"] OR ("reoperation" OR "surgical revision" OR (revision NEXT surger*) OR "single stage" OR "one stage" OR "1 stage" OR "one phase" OR "single phase" OR "2 stage" OR "two stage" OR "PMMA" OR "polymethyl methacrylate" OR "polymethyl-methacrylate" OR "polymethylmethacrylate" OR "antibiotic cement rod" OR "cement rod" OR "interlocking intramedullary nail*" OR "bone cement" OR "antibiotic cement*" OR "antibiotic nail" OR "antibiotic impregnated*" OR "antibiotic-impregnated*" OR "nail cement"):ti,ab,kw #5: #3 AND #4
ICTRP	Fracture-related infection Infected non-union

Table S2 Quality assessment using the McMaster critical appraisal.

	Amorosa et al. (2013)	Amorosa et al. (2018)	Hackl et al. (2024)	Wagner et al. (2024)	Prasann et al. (2009)	Amorosa et al. (2014)	Klemm (1986)	Shah et al. (2009)	Unsworth et al. (2024)	Wu and Chen (2003)	Babulkar et al. (2005)	Wu et al. (2007)	Bakshi et al. (2022)	Bhatia et al. (2017)	Bidolegui et al. (2023)	Chavan et al. (2019)	Chavan et al. (2019)	Conway et al. (2014)
Categories																		
1. Study purpose																		
Was the study purpose clearly stated?	1	1	1	1	1	1	0	0	1	1	0	1	1	1	0	1	1	1
2. Literature review																		
Was relevant background literature reviewed?	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1
3. Study design																		
4. Sample																		
Was the sample described in detail?	1	1	1	1	1	0	0	1	0	1	0	1	1	1	1	0	0	0
Was the sample justified?	1	1	1	1	1	1	0	1	1	1	1	1	0	0	0	0	0	1
Were the groups randomized?	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	1	NA	NA	NA	NA	NA
Was randomizing appropriate done?	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA
5. Outcomes																		
Were the outcome measures reliable?	1	1	0	1	0	0	0	0	1	0	0	0	0	0	1	0	0	0
Were the outcome measures valid?	1	1	1	1	1	1	1	1	1	1	1	1	0	1	0	1	0	1
6. Intervention																		
Intervention was described in detail?	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Contamination was avoided?	1	1	1	1	NA	1	NA	NA	1	NA	NA	NA	1	0	0	NA	NA	1
Cointervention was avoided?	0	0	1	0	0	1	NA	NA	0	0	NA	NA	0	1	0	NA	NA	1
7. Results																		
Results were reported in terms of statistical significance?	1	1	1	1	0	1	0	0	1	0	0	1	1	0	0	0	0	0
Were the analysis method(s) appropriate?	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	0	1
Clinical importance was reported?	1	1	1	0	0	1	1	1	1	1	1	0	0	1	1	0	0	1
Drop-outs were reported?	1	1	1	1	1	1	0	1	1	1	1	1	0	0	0	0	0	1
8. Conclusions and implications																		
Conclusions were appropriate given study methods and results?	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	0	0	1
Total points	13	13	13	11	9	12	4	9	12	9	8	10	9	9	7	5	3	11
Max points	14	14	14	14	13	14	12	12	14	13	12	12	16	14	14	12	12	14
Score (%)	93%	93%	93%	79%	69%	86%	42%	33%	86%	69%	67%	83%	56%	64%	50%	42%	25%	79%
Study quality interpretation	E	E	E	G	M	G	P	P	G	M	M	G	M	M	M	P	P	G

NA: Not applicable; CS: Case series; RCS: retrospective cohort study; PCS: prospective cohort study; RPS: randomised prospective study. E: excellent; G: good; M: moderate; P: poor

	Dar et al. (2017)	Gao et al. (2019)	Johio et al. (2021)	Manikumar et al. (2024)	Pradhan et al. (2017)	Reddy et al. (2023)	Rice et al. (2021)	Saravanan et al. (2017)	Selhi et al. (2012)	Solanki et al. (2023)	Thomson and Conway (2008)	Kumar and Shankar (2023)	Zaitka et al. (2023)	Klemm and Hess (1995)	Quang et al. (2007)	Reilly et al. (2016)	Wang (2011)
Categories																	
1. Study purpose																	
Was the study purpose clearly stated?	0	0	0	1	1	1	0	0	1	1	0	1	1	0	1	1	1
2. Literature review																	
Was relevant background literature reviewed?	1	1	1	0	1	1	1	1	1	1	1	1	1	0	1	1	0
3. Study design																	
4. Sample																	
Was the sample described in detail?	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1
Was the sample justified?	1	0	0	0	1	1	0	0	0	0	1	0	1	0	0	1	1
Were the groups randomized?	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Was randomizing appropriate done?	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
5. Outcomes																	
Were the outcome measures reliable?	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	1	0
Were the outcome measures valid?	1	0	1	1	1	0	1	1	1	1	1	0	1	1	0	1	1
6. Intervention																	
Intervention was described in detail?	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Contamination was avoided?	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	0	0	0	0	0	0	NA
Cointervention was avoided?	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	1	0	1	0	NA	0	NA
7. Results																	
Results were reported in terms of statistical significance?	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	1	0
Were the analysis method(s) appropriate?	0	1	0	0	1	0	0	0	1	0	1	1	1	0	1	1	1
Clinical importance was reported?	0	1	1	1	1	0	0	0	1	1	1	1	1	1	1	1	1
Drop-outs were reported?	0	0	0	0	1	0	0	0	0	0	1	0	1	0	0	1	0
8. Conclusions and implications																	
Conclusions were appropriate given study methods and results?	0	1	0	0	1	1	1	0	1	1	1	1	1	0	1	1	1
Total points	5	6	5	5	10	5	5	4	8	8	10	9	13	4	7	12	8
Max points	12	12	12	12	12	12	12	12	12	12	14	14	14	14	12	14	12
Score (%)	42%	50%	42%	42%	83%	42%	42%	33%	67%	67%	71%	64%	93%	29%	58%	86%	67%
Study quality interpretation	P	M	P	P	G	P	P	P	M	M	M	M	E	P	M	G	M

NA: Not applicable; CS: Case series; RCS: retrospective cohort study; PCS: prospective cohort study; RPS: randomised prospective study. E: excellent; G: good; M: moderate; P: poor

Table S3 Additional data.

Author (year of publication)	Country of publication	Definition of infection	Age in years mean (range)	Initial implant	Implant at revision	Coated implant	Core of implant	Local antimicrobials	Bone graft	Pathogens cultured
Studies on presumed aseptic non-union*										
Amorosa et al. (2013)	USA	No	Not specified	Not specified	Plate or IMN	No	-	-	-	<i>C. acnes</i> 3x, CoNS 17x, MSSA 1x, Mixed flora 2x
Arsoy et al. (2018)	USA	No	47 (18-96) ¹	Not specified	Plate or IMN	No	-	-	50/51 (Autograft; allograft; biocomposite; bone morphogenic protein; demineralized bone matrix)	<i>C. acnes</i> , CoNS, <i>S. epidermidis</i> , <i>S. aureus</i> , <i>S. saccharolyticus</i> , <i>S. intermedius</i> , <i>Strep. viridans</i>
Hackl et al. (2024)	Germany	Yes	43 (18-74)	Femoral nail (n=25)	Interlocking nail	No	-	-	-	<i>S. epidermidis</i> 10x, <i>S. capitis</i> 3x, <i>S. lugdunensis</i> 3x, <i>S. haemolyticus</i> 2x, <i>S. warneri</i> 2x, <i>S. hominis</i> 1x, <i>S. aureus</i> 1x, <i>Streptococcus alactolyticus</i> 1x, <i>Enterococcus faecalis</i> 2x, <i>Pseudomonas aeruginosa</i> 1x, <i>Pseudomonas fluorescences</i> 1x, <i>C. acnes</i> 2x
Wagner et al. (2024)	The Netherlands	Yes	* 53 (not specified)	Not specified	Intramedullary nail / plate	No	-	-	-	CoNS 10x, <i>C. acnes</i> 8x, mixed flora 4x
Studies with confirmed or suspected infection										
Prasarn et al. (2009)	USA	No	53	Plate (n=8) IMN (n=3)	Dynamic condylar screw plate (n=4) Blade plate (n=5) IMN (n=2)	No	-	-	ICBG (n=2), Demineralized bone matrix (n=3), None (n=6)	<i>S. epidermidis</i> 4x, Mixed flora 2x, MRSA 2x, <i>Enterococcus faecalis</i> , Culture negative 2x
Amorosa et al. (2014)	USA	No	Not specified	Not specified	95-degree angled blade plate	No	-	-	ICBG/Demineralized bone matrix	Not specified
Klemm (1986)	Germany	No	27 (not specified)	Plate (n=28) IMN (n=36)	IMN	No	-	-	-	Not specified
Shah et al. (2009)	Nepal	Yes	Not specified	Not specified	IMN (SIGN)	No	-	-	-	Not specified
Unsworth et al. (2024)	United Kingdom	Yes	Group 1: median 57 (IQR: 40-66) Group 2: median 52 (IQR: 37-62)	Not specified	Not specified	No	Not specified	Vancomycin/gentamicin/tobramycin or combination	-	Not specified
Wu and Chen (2003)	Taiwan	No	Median: 37 (18-72)	Sliding hip screw	Sliding hip screw	No	-	Vancomycin (+ gentamycin)	CBG from medial tibial condyle	MRSA 8x, MSSA 1x, <i>Pseudomonas aeruginosa</i> 2x, Mixed flora 2x
Babhulkar et al. (2005)	India	No	Not specified	Not specified	Not specified	Yes, (n=4)	Interlocking IMN	Gentamycin	Yes, (n=6) not specified	Not specified
Wu et al. (2007)	Taiwan	No	48 (16-82)	Sliding hip screw (n=22) Gamma nail (n=1)	1 st stage: antibiotic loaded beads + external fixation or buck traction 2 nd stage: plating	No	-	Not specified	CBG	MRSA 4x, MSSA 4x, <i>Enterococcus</i> spp. 2x, <i>Pseudomonas aeruginosa</i> 1x, <i>Enterobacter cloacae</i> 1x, <i>Acinetobacter</i> 1x, Mixed flora 8x, Culture negative 2x
PMMA-coated implant studies**										
Bakshi et al. (2022)	India	No	Not specified (21-40)	Plate (n=5) IMN (n=8)	Cement coated interlocking IMN	Yes	Interlocking IMN	Vancomycin (+ gentamycin)	Yes, (n=7) not specified	<i>S. aureus</i> 15x, <i>Pseudomonas aeruginosa</i> 2x, <i>E. coli</i> 1x, Mixed flora 2x
Bhatia et al. (2017)	India	No	39 (22-61)	Not specified	Cement coated K-nail	Yes	K-nail	Vancomycin + teicoplanin	-	<i>S. aureus</i> 12x, culture negative 8x
Bidolegui et al. (2023)	Brasil	No	53 (24-72)	Plate (n=12) IMN (n=3)	Cement coated plate	Yes	Plate	Vancomycin (+ gentamycin)	Yes, not specified	MSSA 8x, <i>Enterobacter cloacae</i> 2x, <i>Proteus mirabilis</i> 1x, <i>Streptococcus viridans</i> 1x, <i>E. coli</i> 1x, Culture negative 2x

Charan et al. (2022)	India	No	Not specified	Not specified	Cement coated interlocking IMN	Yes	Interlocking IMN	Vancomycin	-	Not specified
Chavan et al. (2019)	India	No	Not specified	Not specified	Cement coated K-nail	Yes	K-nail	Vancomycin + clindamycin	-	Not specified
Conway et al. (2014)	USA	No	37 (15-74) ¹	Not specified	Cement coated intramedullary locking rod	Yes	Locking rod	Vancomycin + tobramycin	-	MRSA in 15x, Mixed flora 18x, Culture negative 10x
Dar et al. (2017)	India	No	34 (21-64)	Not specified	Cement coated threaded Ilizarov rod	Yes	Threaded Ilizarov rod	Tobramycin (5x) Gentamycin + Vancomycin (2x) Gentamycin (2x) Amikacin (2x)	-	<i>S. aureus</i> 5x, <i>E. coli</i> 2x, <i>Pseudomonas</i> spp. 1x, Mixed flora 1x, Culture negative 2x
Gao et al. (2019)	China	No	45 (19-79)	IMN (n=4) Plate (n=7)	Cement coated k-wire or pedicle	Yes	K-wire or pedicle	Vancomycin + gentamicin	-	<i>S. aureus</i> 7x, <i>Acinetobacter baumannii</i> 1x, <i>Enterobacter aerogenes</i> 1x, <i>S. haemolyticus</i> 1x, culture negative 3x
Jokhio et al. (2021)	Pakistan	No	Not specified (22-61)	IMN	Cement coated K-nail	Yes	K-nail	Vancomycin + Teicoplanin	-	<i>S. aureus</i> 16x Not further specified
Manikumar et al. (2024)	India	No	Not specified (20-70)	Not specified	Cement coated interlocking IMN	Yes	Interlocking IMN	Vancomycin	-	Not specified
Pradhan et al. (2017)	India	No	34 (20-63)	IMN (n=18) Plate (n=2) External fixator (n=1)	Cement coated K-nail	Yes	K-nail	Vancomycin + gentamycin	-	MSSA: 10x, MRSA: 5x, CoNS 1x, <i>Enterobacter</i> 1x, <i>Pseudomonas aeruginosa</i> 1x, <i>Klebsiella</i> 1x, Mixed flora 1x, Culture negative 1x
Reddy et al. (2023)	India	No	43 (18-72)	Not specified	Cement coated Ender's nail/titanium IMN	Yes	Cement coated Ender's nail/titanium IMN	Vancomycin + gentamicin	-	Not specified
Rice et al. (2021)	USA	Yes	47 (not specified)	Not specified	Cement coated interlocking IMN	Yes	Interlocking IMN	Vancomycin + tobramycin, + gentamicin	-	Not specified
Saravanan et al. (2017)	India	No	Not specified (21-65)	Not specified	Cement coated locked K-nail	Yes	Locked K-nail		-	Not specified
Selhi et al. (2012)	India	No	39 (18-54)	IMN (n=8) External fixator (n=5) Plate (n=3)	Cement coated K-nail, guidewire, interlocking IMN	Yes	K-nail (n=11) Guidewire (n=4) Interlocking IMN (n=1)	Vancomycin + gentamycin	-	<i>S. aureus</i> 5x, <i>Enterobacter</i> 3x, Culture negative 8x
Solanki et al. (2023)	India	No	40 (23-67)	Not specified	Cement coated locked K-nail	Yes	Locked K-nail	Not specified	-	Not specified
Thonse and Conway (2008)	USA	No	46 (16-86) ¹	Not specified	Cement coated interlocking IMN	Yes	Interlocking IMN	Vancomycin + tobramycin	-	Not specified
Kumar and Shankar (2023)	India	No	36 (23-50)	Not specified	Polymer coated nail or cement coated interlocking IMN	Yes	Polymer coated nail or cement coated interlocking IMN	Vancomycin + gentamicin	-	MRSA 8x, <i>Pseudomonas</i> 1x, mixed flora 7x, culture negative 4x
Zalikha et al. (2023)	USA	Yes	39 (20-66)	IMN (n=41)	1 st stage: cement coated interlocking nail 2 nd stage: exchange cement coated interlocking IMN	Yes	Interlocking IMN	Vancomycin + tobramycin	-	<i>S. aureus</i> 22x, Mixed flora 9x, Culture negative 3x, Other 7x

Klemm and Hess (1995)	Germany	No	38 (17-58)	Not specified	1 st stage: external fixator + gentamicin cement beads 2 nd stage: interlocking IMN with cement coated surgical wire inside	Yes	Multistrand ed surgical wire	Gentamicin	Yes (n=12), not specified	Not specified
Qiang et al. (2007)	China	No	38 (22-78)	IMN (n=18)	1 st stage: cement coated guidewire 2 nd stage: Interlocking IMN	Yes	Guidewire	Vancomycin	Yes, (n=6) not specified	<i>S. aureus</i> 8x, Culture negative 11x
Reilly et al. (2016)	USA	Yes	41 (15-78)	IMN (n=41)	1 st stage: cement coated guidewire or threaded Ilizarov wire 2 nd stage: Interlocking IMN	Yes	Ilizarov rod or ball-tipped guidewire	Not specified	-	<i>S. aureus</i> 27x, Other 13x
Wang (2011)	China	No	40 (26-53)	IMN (n=12)	1 st stage: cement coated K-wire 2 nd stage: locking plate	Yes	K-wire	Vancomycin	ICBG 10x	MRSA 8x, Streptococcus spp. 2x, Culture negative 2x
C.: Cutibacterium; CBG: Cancellous bone graft; CoNS: Coagulase negative staphylococci; E.: Escherichia; ICBG: Iliac crest bone graft; IMN: intramedullary nail; K-wire: Kirschner-wire; K-nail: Kuntscher nail; MRSA: methicillin resistant staphylococcus aureus; MSSA: methicillin sensitive staphylococcus aureus; S.: staphylococcus; Spp: species; UTN: unreamed tibia nail; USA: United States of America; ¹ number is based on the entire population or the subpopulation closest related to the patients relevant to our study. * Only the patients with positive cultures were included. ** All studies conducted on PMMA-coated implants were concerned with confirmed or suspected cases of infection.										

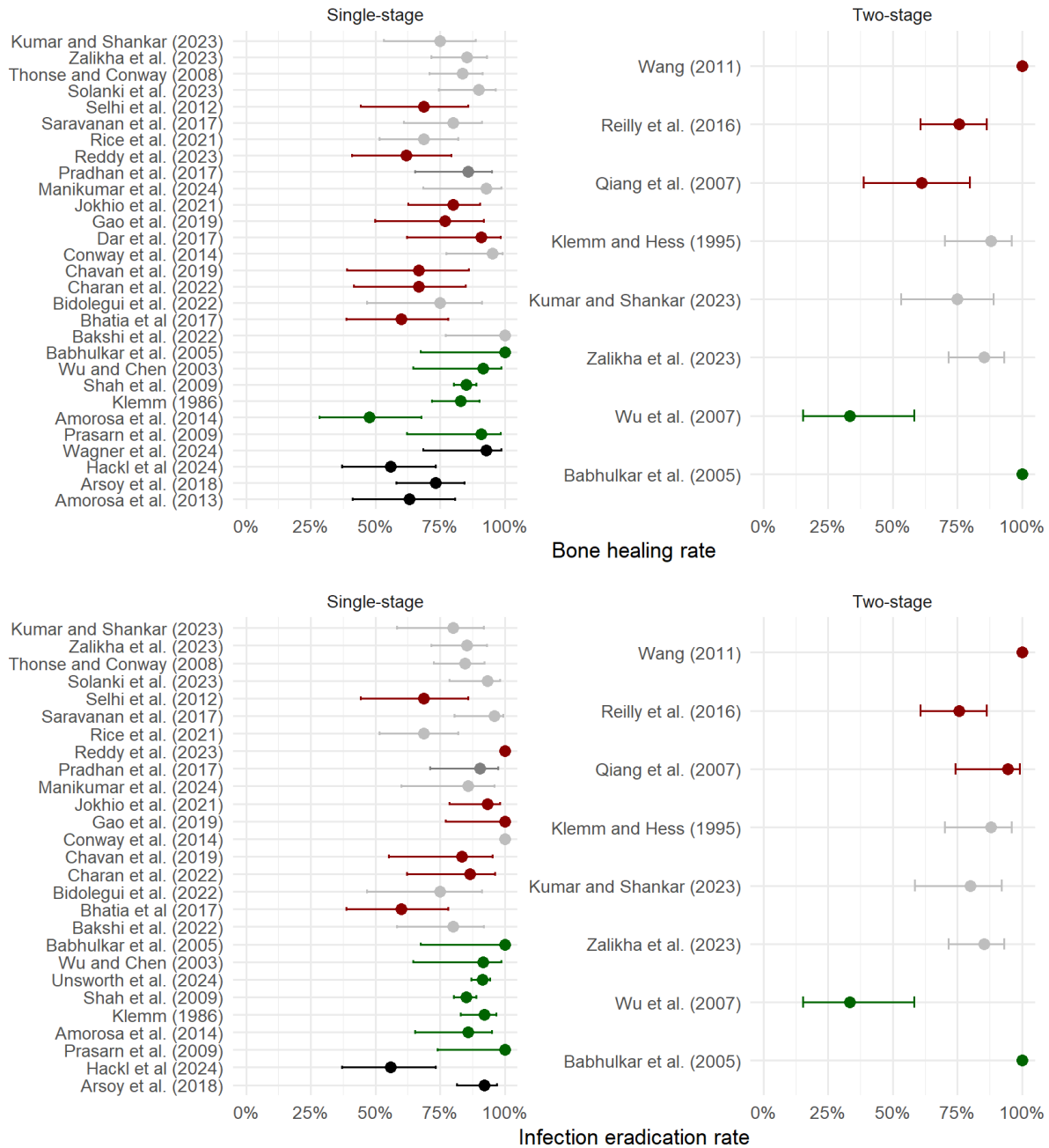


Figure S1 A forest plot displaying the bone healing rate and infection eradication rate of single-stage and two-stage revision per study. Black: studies on presumed patients with an aseptic fracture non-union; Green; studies that used conventional implants without a PMMA coating; Red: : the studies that used PMMA-coated non-conventional implants Grey: the studies that used PMMA-coated conventional implants.