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APPENDICES:

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Appendix A: Search Strategies

Updated Searches
2018 Aug 7

Ovid Multifile

Database: Embase Classic+Embase <1947 to 2018 August 06>, Ovid MEDLINE(R) ALL <1946 to August 06, 2018>
Search Strategy:
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1 Prosthesis-Related Infections/ (190992)
2 exp Joint Prosthesis/ae and (infect* or sepsis or septic*).tw,kw. (2674)
3 ((periprosthetic* or peri-prosthetic*) adj3 (infect* or sepsis or septic)).tw,kw. (3959)
4 (PJI or PJIs).tw,kw. (1948)
5 (((prosthe* or periprosthetic* or peri-prosthetic*) adj3 (joint$1 or knee$1 or hip or hips or shoulder$1 or wrist$1 or ankle$1 or elbow$1)) and (infect* or sepsis or septic)).tw,kw. (9874)
6 (((arthroplas* or replacement*) adj3 (joint$1 or knee$1 or hip or hips or shoulder$1 or wrist$1 or ankle$1 or elbow$1)) and (infect* or sepsis or septic)).tw,kw. (21507)
7 ((replacement* adj3 arthroplas*) and (infect* or sepsis or septic)).tw,kw. (416)
8 or/1-7 (212967)
9 Prosthesis-Related Infections/di [Diagnosis] (6684)
10 exp Sepsis/di [Diagnosis] (31123)
11 exp Arthritis, Infectious/di (8337)
12 Diagnosis/ (1508876)
13 Clinical Decision-Making/ (33752)
14 Delayed Diagnosis/ (14174)
15 Diagnosis, Differential/ (711821)
16 "Diagnostic Techniques and Procedures"/ (83402)
17 exp Clinical Laboratory Techniques/ (2593362)
18 Early Diagnosis/ (122374)
19 diagnos*.tw,kw. (5341486)
20 exp Biomarkers/an, bl (273977)
21 (biomarker* or marker?).tw,kw. (1957361)
22 Interleukin-6/an, bl (19656)
23 ((Interleukin-6 or "IFN-beta 2" or "IL-6" or IL6 or "MGI-2" or myeloid differentiation-inducing protein? or plasmacytoma growth factor? or B cell stimulatory factor? or B cell differentiation factor? or hepatocyte-stimulating factor? or hybridoma growth factor?) and (analys* or biomarker* or marker? or serum or blood or tissue?)).tw,kw. (183315)
24 Synovial Fluid/ (30259)
25 (((synovia* or synovium or articular or joint?) adj1 fluid?) and (analys* or biomarker* or marker? or serum or blood or tissue?)).tw,kw. (20264)
26 ((serum or blood or tissue?) adj3 (sampl* or screen* or test or tests or testing)).tw,kw. (739561)
27 or/9-26 (10716656)
28 8 and 27 (42599)
29 exp animals/ not (exp animals/ and humans/) (16087057)
30 28 not 29 (38080)
31 (comment or editorial or interview or news).pt. (1791395)
32 (letter not (letter and randomized controlled trial)).pt. (1957132)
33 30 not (31 or 32) (37258)

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34 limit 33 to yr="2004-current" (12932)
35 (2016* or 2017* or 2018*).dt. (3151131)
36 34 and 35 (1090)
37 36 use medall [MEDLINE records] (1090)
38 periprosthetic joint infection/di (239)
39 periprosthetic joint infection/ (1115)
40 exp joint prosthesis/ and exp prosthesis infection/ (2233)
41 ((periprosthetic* or peri-prosthetic*) adj3 (infect* or sepsis or septic)).tw,kw. (3959)
42 (PJI or PJIs).tw,kw. (1948)
43 (((prosthe* or periprosthetic* or peri-prosthetic*) adj3 (joint$1 or knee$1 or hip or hips or shoulder$1 or wrist$1 or ankle$1 or elbow$1)) and (infect* or sepsis or septic)).tw,kw. (9874)
44 (((arthroplas* or replacement*) adj3 (joint$1 or knee$1 or hip or hips or shoulder$1 or wrist$1 or ankle$1 or elbow$1)) and (infect* or sepsis or septic)).tw,kw. (21507)
45 ((replacement* adj3 arthroplas*) and (infect* or sepsis or septic)).tw,kw. (416)
46 or/39-45 (27575)
47 exp prosthesis infection/di (1061)
48 exp Sepsis/di (31123)
49 exp infectious arthritis/di (8337)
50 diagnosis/ (1508876)
51 Clinical Decision-Making/ (33752)
52 Delayed Diagnosis/ (14174)
53 Diagnosis, Differential/ (711821)
54 "Diagnostic Techniques and Procedures"/ (83402)
55 exp Clinical Laboratory Techniques/ (2593362)
56 Early Diagnosis/ (122374)
57 diagnos*.tw,kw. (5341486)
58 (biomarker* or marker?).tw,kw. (1957361)
59 ((Interleukin-6 or "IFN-beta 2" or "IL-6" or IL6 or "MGI-2" or myeloid differentiation-inducing protein? or plasmacytoma growth factor? or B cell stimulatory factor? or B cell differentiation factor? or hepatocyte-stimulating factor? or hybridoma growth factor?) and (analys* or biomarker* or marker? or serum or blood or tissue?)).tw,kw. (183315)
60 (((synovia* or synovium or articular or joint?) adj1 fluid?) and (analys* or biomarker* or marker? or serum or blood or tissue?)).tw,kw. (20264)
61 ((serum or blood or tissue?) adj3 (sampl* or screen* or test or tests or testing)).tw,kw. (739561)
62 or/47-61 (10624356)
63 46 and 62 (7601)
64 38 or 63 (7601)
65 exp animal experimentation/ or exp models animal/ or exp animal experiment/ or nonhuman/ or exp vertebrate/ (46306698)
66 exp humans/ or exp human experimentation/ or exp human experiment/ (36406260)
67 65 not 66 (9902138)
68 64 not 67 (7481)
69 editorial.pt. (997376)
70 letter.pt. not (letter.pt. and randomized controlled trial/) (1952456)
71 68 not (69 or 70) (7378)
72 limit 71 to yr="2004-current" (5483)
73 (2016* or 2017* or 2018*).dc. (3524148)
74 72 and 73 (785)
75 74 use emczd [EMBASE RECORDS] (785)
76 37 or 75 [BOTH DATABASES] (1875) [TOTAL UNIQUE RECORDS]
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77 remove duplicates from 76 (1554)
78 77 use medall [MEDLINE UNIQUE RECORDS] (1087)
79 77 use emczd [EMBASE UNIQUE RECORDS] (467)

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2018 Aug 13

Cochrane Library
Search Name: Periprosthetic Joint Infections - Update2 - Final
Date Run: 13/08/2018 14:43:16
Comment: 2018 Aug 8 - Updates Jan 2016 search

ID	Search	Hits
#1	MeSH descriptor: ["Prosthesis-Related Infections"] explode all trees	164
#2	[mh "Joint Prosthesis"/AE] and (infect* or sepsis or septic):ti,ab,kw	37
#3	((periprosthetic* or (peri next prosthetic*)) near/3 (infect* or sepsis or septic)):ti,ab,kw	81
#4	(PJI or PJIs):ti,ab,kw	52
#5	(((prosthes* or periprosthetic* or (peri next prosthetic*)) near/3 (joint or joints or knee or knees or hip or hips or shoulder or shoulders or elbow or elbows or wrist or wrists or ankle or ankles)) and (infect* or sepsis or septic)):ti,ab,kw	447
#6	(((arthroplas* or replacement*) near/3 (joint or joints or knee or knees or hip or hips or shoulder or shoulders or elbow or elbows or wrist or wrists or ankle or ankles)) and (infect* or sepsis or septic)):ti,ab,kw	897
#7	((replacement* near/3 arthroplas*) and (infect* or sepsis or septic)):ti,ab,kw	317
#8	{or #1-#7}	1088
#9	MeSH descriptor: ["Prosthesis-Related Infections"] explode all trees and with qualifier(s): [DI - DI]	27
#10	MeSH descriptor: [Sepsis] explode all trees and with qualifier(s): [DI - DI]	236
#11	MeSH descriptor: ["Arthritis, Infectious"] explode all trees and with qualifier(s): [DI - DI]	5
#12	MeSH descriptor: [Diagnosis] explode all trees	66
#13	MeSH descriptor: ["Clinical Decision-Making"] explode all trees	120
#14	MeSH descriptor: ["Delayed Diagnosis"] explode all trees	25
#15	MeSH descriptor: ["Diagnosis, Differential"] explode all trees	1443
#16	Any MeSH descriptor	28
#17	MeSH descriptor: ["Clinical Laboratory Techniques"] explode all trees	41637
#18	MeSH descriptor: ["Early Diagnosis"] explode all trees	1422
#19	diagnos*:ti,ab,kw	161906
#20	MeSH descriptor: [Biomarkers] explode all trees and with qualifier(s): [AN - AN, BL - BL]	12433
#21	(biomarker* or marker or markers):ti,ab,kw	55052
#22	MeSH descriptor: ["Interleukin-6"] explode all trees and with qualifier(s): [AN - AN, BL - BL]	2226
#23	("Interleukin-6" or "IFN-beta 2" or "IL-6" or IL6 or "MGI-2" or ("myeloid differentiation-inducing" next protein*) or ("plasmacytoma growth" next factor*) or ("B cell stimulatory" next factor*) or ("B cell differentiation" next factor*) or ("hepatocyte-stimulating" next factor*) or ("hybridoma growth" next factor*)):ti,ab,kw	11212
#24	MeSH descriptor: ["Synovial Fluid"] explode all trees	145
#25	((synovia* or synovium or articular or joint or joints) next (fluid or fluids)):ti,ab,kw	466
#26	{or #9-#25}	242338
#27	#8 and #26 with Cochrane Library publication date between Jan 2016 and Aug 2018	113

Search Strategy Method:
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Electronic search strategies were developed and tested through an iterative process by an experienced medical information specialist in consultation with the review team. Using the OVID platform, we searched Ovid MEDLINE®, Ovid MEDLINE® In-Process & Other Non-Indexed Citations and Embase on May 20, 2014. We searched the Cochrane Library on Wiley (including Cochrane Database of Systematic Reviews, DARE, CENTRAL, HTA, and NHS EED) on May 19, 2014. We also searched for grey literature using the checklist from CADTH's Grey Matters Light (http://www.cadth.ca/en/resources/finding-evidence-is/grey-matters/grey-matters-light). The database searches were updated on January 20, 2016 and again in August, 2018 (the Ovid searches were updated on August 8 and the Cochrane Library searches on August 13).

Strategies utilized a combination of controlled vocabulary (e.g., "Prosthesis-Related Infections", "Joint Prosthesis/adverse effects", "Arthritis, Infectious/diagnosis") and keywords (e.g., "periprosthetic joint infection", "replacement joint infection", "PJI"). Vocabulary and syntax were adjusted across databases. Animal-only studies and opinion pieces were removed, and the results were limited to the publication years 2004 to the present. Additional references were also sought through hand-searching the bibliographies of relevant items (Appendix A).

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Quality Assessment Method:

We created a custom PJI-specific approach to the three domains of the QUADAS-2 tool (patient selection, reference standard, flow and timing) to determine risk of bias. For rating population applicability, we developed a list of clinical risk factors that determined the risk status of the patients in a given study after consulting clinical experts and literature. We rated the patients' applicability based on the risk status considering the number of risk factors observed, proportion of patients with the risk factor, and type of risk factors classified into low, high, or unclear concern. Under the flow and timing domain, if patients in a given study received antibiotics and/or chemotherapy before administration of index and/or reference standard tests, we judged the bias for this domain as "high risk". Both screening and quality assessment were carried out independently by two reviewers and disagreements were resolved through consensus or third-party adjudication.

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Table A1: Quality Assessment of the individual studies using QUADAS-II tool

Author, Publication Year	Patient Selection					Index Test				Reference Test				Flow and Timing					Overall Judgment	
	Consecutive or random sample?	Case-control design avoided?	Avoid inappropriate exclusions?	Risk of Bias Judgment	Applicability Judgment	Index test interpreted without knowledge of reference standard?	If a threshold was used, was it prespecified?	Risk of Bias Judgment	Applicability Judgment	Reference standard to correctly classify the target condition?	Reference standard interpreted without knowledge of index test?	Risk of Bias Judgment	Applicability Judgment	Appropriate interval between index tests and reference standard?	A patients receive a reference standard?	Did all patients receive the same reference standard?	All patients included in the analysis?	Risk of Bias Judgment	OVERALL Risk of Bias Judgment	OVERALL Applicability Judgment
Ghanem, 2008[201]	Y	Y	Y	LRB	LC	Y	NA	LRB	LC	N	Y	HRB	LC	U	Y	Y	Y	URB	HRB	LC
Ronde-Oustau, 2014[59]	U	Y	U	HRB	LC	U	N	HRB	lC	N	U	HRB	LC	Y	Y	Y	Y	LRB	HRB	LC
Milone, 2014[61]	Y	Y	Y	LRB	HC	N	N	HRB	HC	N	Y	HRB	LC	Y	N	N	Y	HRB	HRB	HC
Randau, 2014[90]	Y	Y	Y	LRB	lC	N	N	HRB	UC	N	Y	HRB	lC	Y	Y	Y	Y	LRB	HRB	UC
Chalmers, 2014[185]	Y	Y	N	HRB	UC	N	N	HRB	LC	N	Y	HRB	LC	U	Y	N	Y	HRB	HRB	UC
Cross, 2014[130]	U	Y	Y	LRB	LC	N	NA	HRB	LC	Y	N	HRB	LC	Y	Y	Y	Y	LRB	HRB	UC
Muller, 2008[62]	U	Y	Y	URB	UC	U	NA	URB	LC	N	U	HRB	LC	Y	Y	Y	Y	LRB	HRB	UC
Metso, 2014[221]	Y	Y	Y	LRB	UC	U	U	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Miyamae, 2013[63]	U	Y	Y	URB	LC	U	Y	URB	lC	Y	U	URB	lC	Y	Y	Y	Y	HRB	HRB	LC
Alijanipour, 2013[64]	U	Y	Y	URB	UC	Y	Y	LRB	lC	N	Y	HRB	lC	Y	Y	Y	Y	LRB	HRB	UC
Aggarwal, 2013[223]	Y	Y	Y	LRB	UC	U	U	URB	lC	N	U	HRB	lC	U	Y	Y	Y	URB	HRB	UC
Vanderstappen, 2013[199]	U	Y	N	HRB	UC	U	Y	URB	lC	N	U	HRB	lC	U	Y	Y	N	HRB	HRB	UC

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Glehr, 2013[65]	Y	Y	Y	LRB	UC	Y	NA	LRB	LC	N	Y	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Rak, 2013[224]	Y	N	Y	HRB	UC	U	NA	URB	LC	N	U	HRB	lC	Y	Y	Y	Y	LRB	HRB	UC
Janz, 2013[66]	Y	Y	Y	LRB	UC	U	NA	URB	LC	N	U	HRB	UC	Y	Y	Y	Y	LRB	HRB	UC
Gollwitzer, 2013[67]	Y	N	Y	HRB	HC	U	Y	URB	LC	N	U	HRB	lC	U	Y	Y	Y	URB	HRB	HC
Dinneen, 2013[186]	Y	Y	Y	LRB	lC	U	N	HRB	lC	Y	U	URB	lC	Y	Y	Y	Y	LRB	HRB	LC
Fink, 2013[68]	Y	Y	Y	LRB	HC	U	NA	URB	LC	Y	U	URB	UC	Y	Y	Y	Y	LRB	URB	HC
Zmistowski, 2012[187]	U	Y	Y	URB	UC	U	U	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Schwartz, 2012[69]	U	Y	Y	URB	LC	U	Y	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	LC
Toossi, 2012[70]	U	Y	Y	URB	UC	U	U	URB	LC	N	U	HRB	HC	U	Y	Y	Y	URB	HRB	UC
Wetters, 2012[151]	U	Y	Y	URB	UC	U	Y	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Parvizi, 2012[188]	Y	Y	Y	LRB	UC	U	U	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Titecat, 2012[210]	Y	Y	Y	LRB	UC	U	Y	URB	LC	Y	U	URB	LC	Y	Y	Y	Y	LRB	URB	UC
Corona, 2012[225]	Y	Y	Y	LRB	UC	U	Y	URB	LC	N	U	HRB	LC	Y	Y	Y	Y	LRB	HRB	UC
Costa, 2012[71]	Y	Y	Y	LRB	HC	U	NA	URB	LC	N	U	HRB	LC	U	Y	Y	U	URB	HRB	HC
Cipriano, 2012[72]	Y	Y	Y	LRB	LC	U	U	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	LC
Marin, 2012[211]	Y	Y	Y	LRB	LC	U	NA	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	LC
Parvizi, 2012[124]	Y	Y	Y	LRB	UC	Y	N	HRB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Parvizi, 2011[152]	U	Y	Y	URB	UC	U	Y	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Johnson, 2011[73]	U	Y	Y	URB	LC	Y	U	URB	LC	N	U	HRB	LC	Y	Y	Y	Y	LRB	HRB	UC
Zywiel, 2011[212]	U	Y	Y	URB	UC	Y	Y	lRB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Jacovides, 2011[162]	Y	Y	U	URB	UC	U	Y	URB	LC	N	U	HRB	LC	U	Y	Y	U	URB	HRB	UC
Bori, 2011[226]	Y	Y	U	URB	UC	U	Y	URB	LC	N	U	HRB	LC	Y	Y	Y	U	URB	HRB	UC
Buttaro, 2010[74]	Y	Y	Y	LRB	UC	U	Y	URB	LC	N	U	HRB	LC	Y	Y	Y	Y	LRB	HRB	UC

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Johnson, 2010[213]	U	Y	Y	URB	UC	U	NA	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Worthington, 2010[75]	U	U	Y	URB	UC	U	U	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	LC
Deirmengian, 2010[76]	Y	Y	U	URB	HC	U	U	URB	LC	Y	U	URB	LC	Y	Y	Y	Y	LRB	URB	HC
Font-Vizcarra, 2010[208]	U	Y	Y	URB	UC	U	NA	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Meermans, 2010[131]	Y	Y	Y	LRB	UC	U	NA	LRB	LC	Y	U	URB	LC	U	Y	Y	Y	URB	URB	UC
Piper, 2010[77]	U	Y	U	URB	UC	U	Y	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Tohtz, 2010[78]	Y	Y	Y	LRB	UC	U	Y	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Ghanem, 2009[121]	U	Y	Y	URB	UC	U	Y	URB	LC	N	U	HRB	LC	Y	Y	Y	Y	LRB	HRB	UC
Morgan, 2009[123]	Y	Y	Y	LRB	UC	U	N	HRB	LC	N	U	URB	LC	U	Y	Y	Y	URB	HRB	UC
Morawietz, 2009[227]	U	Y	U	URB	UC	U	U	URB	LC	N	U	HRB	LC	U	Y	Y	U	URB	HRB	UC
Ghanem, 2009[214]	U	Y	N	HRB	UC	U	Y	URB	LC	N	U	HRB	LC	U	Y	Y	N	HRB	HRB	UC
Schinsky, 2008[79]	Y	Y	Y	LRB	UC	U	Y	URB	LC	N	U	HRB	LC	Y	Y	Y	Y	LRB	HRB	UC
Kanner, 2008[80]	U	Y	Y	URB	UC	U	NA	URB	LC	Y	U	URB	LC	Y	Y	Y	Y	LRB	URB	UC
Ghanem, 2008[189]	Y	Y	Y	LRB	LC	U	Y	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	LC
Picado, 2008[228]	U	Y	Y	URB	UC	U	NA	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Fink, 2008[81]	Y	Y	Y	LRB	UC	U	NA	URB	LC	Y	U	URB	LC	Y	Y	Y	Y	LRB	URB	UC
Gallo, 2008[132]	Y	Y	N	HRB	UC	U	Y	LRB	LC	N	U	HRB	LC	Y	Y	Y	N	HRB	HRB	UC
Austin, 2008[82]	U	Y	Y	URB	UC	U	NA	URB	LC	N	U	HRB	LC	Y	Y	Y	Y	LRB	HRB	UC
Nilsdotter-Augustinsson, 2007[83]	U	Y	Y	HRB	HC	Y	Y	LRB	LC	N	N	HRB	LC	Y	Y	Y	Y	LRB	HRB	HC
Della Valle, 2007[120]	Y	Y	Y	LRB	UC	U	Y	URB	LC	N	U	HRB	LC	Y	Y	Y	Y	LRB	HRB	UC
Greidanus, 2007[84]	Y	Y	Y	LRB	lC	U	Y	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	LC
Nunez, 2007[229]	U	Y	Y	URB	UC	U	NA	URB	LC	Y	U	URB	LC	Y	Y	Y	Y	LRB	URB	UC

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Borrego, 2007[230]	U	Y	U	URB	UC	U	NA	URB	LC	Y	U	URB	LC	Y	Y	Y	Y	LRB	URB	UC
Bottner, 2007[85]	Y	Y	Y	LRB	UC	U	NA	URB	LC	Y	U	URB	LC	Y	Y	Y	Y	LRB	URB	UC
van den Bekerom, 2006[168]	U	Y	Y	URB	UC	U	NA	URB	LC	N	U	HRB	LC	Y	Y	Y	Y	LRB	HRB	UC
Mikkelsen, 2006[231]	U	Y	Y	URB	UC	U	NA	URB	LC	N	Y	HRB	UC	N	Y	U	Y	HRB	HRB	UC
Bori, 2006[215]	U	Y	Y	URB	UC	U	Y	URB	LC	Y	U	URB	LC	Y	Y	Y	Y	LRB	URB	UC
Bare, 2006[86]	Y	Y	Y	LRB	UC	U	NA	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Ali, 2006[169]	U	Y	U	URB	UC	U	NA	URB	LC	Y	U	URB	LC	Y	Y	Y	Y	LRB	URB	UC
Wong, 2005[232]	U	Y	U	URB	UC	U	NA	URB	LC	N	U	HRB	LC	Y	Y	Y	Y	LRB	HRB	UC
Panousis, 2005[87]	Y	Y	Y	URB	UC	U	NA	URB	LC	N	U	HRB	LC	Y	Y	Y	Y	LRB	HRB	UC
Di Cesare, 2005[88]	U	U	U	URB	UC	U	NA	URB	LC	Y	U	URB	LC	Y	Y	Y	U	URB	URB	UC
Sadiq, 2005[233]	Y	Y	Y	LRB	UC	Y	NA	LRB	LC	N	U	HRB	LC	Y	Y	Y	U	URB	HRB	UC
Ko, 2005[216]	U	Y	Y	URB	UC	U	NA	URB	LC	Y	U	URB	LC	Y	Y	Y	Y	LRB	URB	UC
Trampuz, 2004[190]	Y	Y	Y	LRB	UC	U	N	HRB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Bernard, 2004[89]	Y	Y	U	URB	UC	U	N	URB	LC	Y	U	URB	LC	U	Y	Y	U	URB	URB	UC
Williams, 2004[133]	Y	Y	Y	LRB	UC	Y	NA	LRB	LC	Y	Y	LRB	LC	Y	Y	Y	Y	LRB	LRB	UC
Malhotra, 2004[183]	Y	Y	U	LRB	HC	U	NA	URB	LC	N	U	HRB	LC	U	Y	Y	U	URB	HRB	HC
Randau, 2011[90]	Y	Y	U	URB	UC	U	U	URB	LC	N	U	HRB	LC	U	Y	Y	U	URB	HRB	UC
Mason, 2003[191]	Y	Y	U	URB	HC	U	Y	URB	LC	N	U	HRB	LC	U	Y	Y	U	URB	HRB	HC
Fehring, 1994[217]	Y	Y	Y	LRB	UC	U	NA	URB	LC	Y	U	URB	LC	U	Y	Y	Y	URB	URB	UC
Lonner, 1996[234]	Y	Y	Y	LRB	HC	U	NA	URB	LC	Y	U	URB	LC	U	Y	Y	Y	URB	URB	HC
Atkins, 1998[260]	Y	Y	Y	LRB	LC	U	U	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Abdul-Karim, 1998[218]	U	Y	U	URB	UC	U	Y	URB	LC	Y	U	URB	LC	Y	Y	Y	Y	LRB	URB	UC

http://dx.doi.org/10.2106/JBJS.18.00632

Alijanipour, 2015[200]	U	Y	Y	URB	UC	U	NA	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Athanasou, 1995[256]	U	Y	U	URB	LC	U	NA	URB	LC	Y	U	URB	UC	Y	Y	N	U	HRB	HRB	LC
Banit, 2002[257]	Y	Y	Y	LRB	UC	U	U	URB	LC	Y	U	URB	LC	Y	Y	Y	Y	LRB	URB	UC
Barrack, 1993[147]	Y	Y	U	URB	UC	U	NA	URB	LC	N	U	HRB	LC	N	Y	Y	N	HRB	HRB	UC
Bemer, 2014[235]	Y	Y	U	URB	UC	U	NA	URB	LC	N	U	HRB	LC	N	Y	Y	N	HRB	HRB	UC
Bingham, 2014[91]	Y	Y	Y	LRB	UC	U	NA	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	LC
Borde, 2015[236]	Y	Y	Y	LRB	UC	U	Y	URB	LC	Y	U	URB	LC	Y	Y	Y	Y	LRB	URB	UC
Buttaro, 2015[146]	Y	Y	Y	LRB	UC	U	Y	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Cansu, 2014[92]	Y	Y	U	URB	UC	U	NA	URB	LC	N	U	HRB	LC	U	Y	Y	Y	HRB	HRB	UC
Chalmers, 2015[192]	Y	N	Y	HRB	HC	U	Y	URB	LC	N	U	HRB	LC	U	U	U	N	HRB	HRB	HC
Chimento, 1996[258]	U	Y	Y	URB	UC	U	Y	URB	UC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Cipriano, 2014[93]	Y	Y	Y	LRB	UC	U	NA	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Claassen, 2014[94]	U	Y	Y	LRB	UC	U	Y	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Colvin, 2015[153]	U	Y	Y	URB	LC	U	Y	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	LC
Deirmengian, 2014[164]	Y	Y	Y	LRB	LC	U	N	HRB	LC	N	N	HRB	LC	N	Y	Y	U	HRB	HRB	LC
Deirmengian, 2014[207]	Y	Y	U	URB	HC	U	Y	URB	LC	N	U	HRB	LC	N	Y	Y	Y	HRB	HRB	HC
Deirmengian, 2015[154]	Y	Y	Y	LRB	LC	U	Y	URB	LC	N	U	HRB	LC	Y	Y	Y	Y	HRB	HRB	LC
Della Valle, 1999[259]	U	Y	U	LRB	HC	Y	NA	LRB	LC	N	U	HRB	LC	Y	Y	Y	Y	LRB	HRB	HC
Duff, 1996[170]	Y	Y	U	URB	HC	U	NA	URB	LC	Y	U	URB	LC	U	Y	Y	N	HRB	HRB	HC
Elgeidi, 2014[95]	Y	Y	Y	LRB	LC	U	N	HRB	LC	N	U	HRB	LC	Y	Y	Y	U	URB	HRB	LC
Ettinger, 2015[96]	Y	Y	Y	LRB	UC	U	N	HRB	LC	N	U	HRB	LC	Y	Y	Y	U	URB	HRB	UC
Fehring, 1996[126]	Y	Y	Y	LRB	UC	U	NA	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC

http://dx.doi.org/10.2106/JBJS.18.00632

Feldman, 1995[219]	Y	Y	Y	LRB	UC	U	Y	URB	LC	N	U	HRB	LC	Y	Y	Y	Y	LRB	HRB	UC
Friedrich, 2014[97]	Y	Y	Y	LRB	LC	U	N	HRB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	LC
Itasaka, 2001[98]	U	Y	U	URB	LC	U	Y	URB	LC	Y	U	URB	LC	U	Y	Y	Y	URB	URB	LC
Janz, 2015[127]	Y	Y	U	URB	UC	U	NA	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Johnson, 1988[171]	Y	Y	Y	LRB	UC	Y	NA	LRB	LC	Y	N	HRB	LC	U	Y	Y	N	HRB	HRB	UC
Jordan, 2014[237]	Y	Y	U	URB	UC	U	NA	URB	LC	N	U	HRB	LC	U	Y	Y	U	URB	HRB	UC
Klatte, 2013[172]	Y	Y	U	URB	UC	U	NA	URB	LC	Y	U	URB	LC	U	Y	Y	U	URB	URB	UC
Kraemer, 1993[128]	U	Y	Y	URB	UC	U	NA	URB	LC	Y	U	URB	LC	Y	Y	Y	Y	LRB	URB	UC
Lachiewicz, 1996[173]	Y	Y	Y	LRB	LC	U	NA	URB	LC	N	U	HRB	LC	Y	Y	Y	Y	LRB	HRB	LC
Lenski, 2014[99]	U	Y	U	URB	UC	U	Y	URB	LC	N	U	HRB	LC	U	Y	Y	U	URB	HRB	UC
Levine, 2001[209]	U	Y	Y	URB	UC	U	NA	URB	LC	N	U	HRB	LC	Y	Y	Y	Y	LRB	HRB	UC
Levitsky, 1991[174]	Y	Y	U	URB	UC	Y	NA	LRB	LC	N	Y	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Liu, 2014[100]	Y	Y	Y	LRB	HC	U	Y	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	HC
Lourtet-Hascoett, 2015[238]	Y	Y	U	LRB	UC	U	NA	URB	LC	Y	Y	LRB	LC	Y	Y	Y	Y	LRB	URB	UC
Melendez, 2014[134]	U	Y	U	URB	UC	U	N	HRB	LC	N	Y	HRB	LC	N	Y	U	Y	HRB	HRB	UC
Mihalic, 2012[193]	Y	Y	U	URB	UC	Y	Y	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Musso, 2003[220]	U	Y	U	URB	HC	U	Y	URB	LC	Y	U	URB	LC	U	Y	Y	Y	URB	URB	UC
Omar, 2015[101]	U	Y	U	URB	HC	U	Y	URB	LC	Y	U	URB	LC	U	Y	Y	Y	URB	URB	HC
Pace, 1997[239]	Y	Y	U	URB	LC	U	Y	URB	LC	Y	U	URB	LC	Y	Y	Y	Y	LRB	URB	UC
Padgett, 1995[240]	Y	Y	U	URB	HC	U	NA	URB	LC	N	Y	HRB	LC	Y	Y	Y	Y	LRB	HRB	HC
Petti, 2015[102]	Y	Y	Y	LRB	HC	U	U	URB	HC	N	U	HRB	LC	N	Y	N	U	HRB	HRB	HC
Pons, 1999[129]	Y	Y	Y	LRB	UC	Y	Y	LRB	LC	Y	N	HRB	LC	U	Y	Y	Y	LRB	HRB	UC
Portillo, 2014[241]	Y	Y	U	URB	UC	U	NA	URB	LC	N	U	HRB	LC	N	Y	Y	Y	HRB	HRB	UC

http://dx.doi.org/10.2106/JBJS.18.00632

Portillo, 2015[242]	Y	Y	Y	LRB	HC	U	NA	URB	LC	N	U	HRB	LC	N	Y	Y	Y	HRB	HRB	HC
Ramsingh, 2010[103]	Y	Y	U	URB	UC	U	U	URB	LC	Y	U	URB	LC	U	Y	Y	U	URB	URB	UC
Ryu, 2014[135]	Y	Y	U	URB	UC	U	NA	URB	LC	N	N	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Shafafy, 2015[155]	Y	Y	Y	LRB	LC	Y	N	HRB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	LC
Shen, 2015[175]	Y	Y	Y	LRB	UC	U	NA	URB	LC	N	N	HRB	LC	N	Y	Y	Y	HRB	HRB	UC
Smith, 2014[221]	Y	Y	Y	LRB	UC	U	NA	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Somme, 2003[176]	Y	Y	Y	LRB	LC	U	NA	URB	LC	N	U	HRB	LC	N	Y	Y	Y	HRB	HRB	LC
Spangehl, 1999[104]	Y	Y	Y	LRB	HC	Y	NA	LRB	LC	N	N	HRB	LC	Y	Y	Y	Y	LRB	HRB	HC
Taylor, 1995[202]	Y	Y	Y	LRB	UC	Y	NA	LRB	LC	N	U	HRB	LC	U	Y	N	Y	HRB	HRB	UC
Teller, 2000[122]	Y	Y	U	URB	LC	Y	Y	LRB	LC	N	U	HRB	LC	U	Y	Y	N	HRB	HRB	LC
Tetreault, 2014[105]	Y	Y	Y	LRB	LC	U	Y	URB	LC	N	Y	HRB	LC	U	Y	Y	Y	URB	HRB	LC
Tigges, 1993[177]	U	Y	Y	URB	UC	Y	NA	LRB	LC	Y	N	HRB	LC	Y	Y	Y	Y	LRB	HRB	UC
Tischler, 2014[194]	Y	Y	Y	LRB	UC	U	Y	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Virolainen, 2002[106]	U	Y	U	URB	UC	U	NA	URB	LC	Y	U	URB	LC	U	Y	Y	U	URB	URB	UC
Wu, 2014[125]	Y	Y	Y	LRB	LC	Y	N	HRB	LC	N	Y	HRB	LC	U	Y	Y	Y	URB	HRB	LC
Yuan, 2015[107]	Y	Y	Y	LRB	LC	U	N	HRB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	LC
Zegaer, 2014[243]	Y	Y	U	URB	UC	U	NA	URB	LC	N	U	HRB	LC	U	Y	U	Y	URB	HRB	UC
Frangiamore, 2016[108]	Y	Y	Y	LRB	UC	U	Y	URB	LC	N	U	HRB	LC	Y	Y	Y	Y	LRB	HRB	UC
Kelly, 2018[158]	Y	Y	Y	HRB	HC	U	U	URB	LC	N	U	HRB	HC	Y	Y	Y	Y	LRB	HRB	HC
Huang, 2018[139]	Y	Y	Y	LRB	UC	U	Y	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Zahar, 2018[159]	Y	Y	U	URB	UC	U	U	URB	UC	N	U	HRB	LC	UY	Y	Y	Y	URB	HRB	LC
Li, 2018[205]	N	Y	Y	HRB	UC	Y	Y	LRB	UC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC

http://dx.doi.org/10.2106/JBJS.18.00632

Gallo, 2018[109]	Y	Y	Y	LRB	HC	Y	N	HRB	UC	N	U	HRB	LC	N	Y	Y	N	HRB	HRB	HC
De Saint Vincent, 2018[167]	U	Y	N	HRB	HC	U	U	URB	LC	N	U	HRB	LC	N	Y	Y	N	HRB	HRB	HC
Yan, 2018[255]	Y	Y	Y	LRB	HC	U	Y	URB	LC	N	U	HRB	HC	N	Y	Y	Y	HRB	HRB	HC
Balato, 2018[143]	Y	Y	Y	LRB	LC	U	Y	URB	LC	N	U	HRB	LC	Y	Y	Y	Y	LRB	HRB	UC
Larsen, 2018[145]	U	Y	Y	URB	HC	U	Y	URB	LC	N	U	HRB	LC	N	N	Y	N	HRB	HRB	HC
Ottink, 2018[252]	Y	Y	N	HRB	UC	Y	Y	LRB	LC	N	U	HRB	UC	Y	Y	Y	Y	LRB	HRB	HC
Renz, 2018[166]	Y	Y	Y	LRB	HC	Y	U	URB	LC	N	U	HRB	LC	N	Y	Y	U	HRB	HRB	HC
Li, 2018[161]	Y	Y	Y	HRB	HC	Y	U	URB	LC	N	U	HRB	LC	Y	Y	U	U	URB	HRB	HC
Wouthuyzen-Bakker, 2018[111]	Y	Y	U	URB	HC	U	Y	URB	LC	N	U	HRB	LC	N	Y	Y	Y	HRB	HRB	HC
Omar, 2018[253]	Y	Y	U	URB	HC	U	U	URB	LC	N	U	HRB	LC	U	Y	Y	U	URB	HRB	HC
Sebastian, 2018[112]	Y	Y	Y	LRB	HC	N	Y	HRB	LC	N	U	HRB	LC	N	Y	Y	Y	HRB	HRB	HC
Fang, 2018[184]	U	Y	Y	URB	HC	N	Y	HRB	LC	N	N	HRB	LC	N	Y	Y	Y	HRB	HRB	HC
Janz, 2018[261]	U	Y	U	URB	UC	U	N	HRB	LC	N	U	HRB	LC	U	Y	Y	N	HRB	HRB	UC
Sambri, 2018[251]	U	Y	Y	URB	UC	U	Y	URB	LC	N	U	HRB	LC	Y	Y	Y	Y	LRB	HRB	UC
Tani, 2018[113]	U	Y	U	URB	LC	N	Y	HRB	LC	N	U	HRB	LC	Y	Y	Y	Y	LRB	HRB	LC
Tarabichi, 2018[254]	Y	Y	Y	LRB	HC	N	Y	HRB	LC	N	N	HRB	LC	Y	Y	Y	N	HRB	HRB	HC
Gehrke, 2018[165]	Y	Y	Y	LRB	UC	U	Y	URB	LC	N	U	HRB	LC	Y	Y	Y	N	HRB	HRB	UC
Lausmann, 2017[142]	U	Y	Y	URB	LC	U	NA	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	LC
Bicart-See, 2017[180]	Y	Y	U	URB	HC	U	U	URB	LC	N	U	HRB	LC	Y	Y	Y	Y	LRB	HRB	HC
Balato, 2018[181]	Y	Y	Y	LRB	UC	U	N	HRB	LC	N	N	HRB	LC	Y	Y	Y	Y	LRB	HRB	UC
Galloa, 2017	Y	Y	Y	LRB	LC	U	N	HRB	LC	N	Y	HRB	LC	N	Y	Y	Y	HRB	HRB	LC
Renz, 2017[244]	U	Y	Y	URB	UC	U	Y	URB	LC	N	N	HRB	LC	Y	Y	Y	Y	LRB	HRB	UC

http://dx.doi.org/10.2106/JBJS.18.00632

Li, 2017[138]	Y	Y	Y	LRB	HC	U	Y	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	HC
Kawamura, 2017[245]	U	Y	U	URB	LC	U	Y	URB	LC	N	N	HRB	LC	N	Y	Y	Y	HRB	HRB	LC
Suren, 2017[248]	Y	Y	Y	LRB	UC	U	U	URB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Morgenstern, 2018[136]	Y	Y	Y	LRB	UC	U	Y	URB	LC	N	U	HRB	LC	Y	Y	Y	Y	LRB	HRB	UC
Randelli, 2018[178]	U	Y	U	URB	UC	U	U	URB	LC	N	N	HRB	UC	Y	Y	Y	Y	LRB	HRB	UC
Koh, 2017[157]	Y	Y	Y	LRB	UC	U	Y	URB	UC	N	U	HRB	UC	U	Y	Y	Y	URB	HRB	UC
Kwiecien 2017[262]	Y	Y	Y	LRB	UC	Y	Y	LRB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Suda, 2017[141]	Y	Y	U	URB	UC	N	U	HRB	LC	N	Y	HRB	LC	N	Y	Y	N	HRB	HRB	UC
Wimmer, 2017[249]	U	Y	U	URB	UC	N	U	HRB	UC	N	N	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Fernandez-Sampedro 2018 [114]	Y	Y	Y	LRB	UC	U	Y	URB	UC	N	U	HRB	UC	N	Y	Y	N	HRB	HRB	UC
Kasparek, 2016[137]	Y	Y	Y	LRB	UC	U	Y	URB	UC	N	U	HRB	LC	Y	Y	Y	Y	LRB	HRB	UC
Ruangsomboon, 2017[149]	U	Y	U	URB	UC	Y	N	HRB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Berger, 2017[115]	U	Y	Y	URB	UC	U	Y	URB	LC	N	Y	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Higuera, 2017[204]	U	Y	Y	URB	LC	U	N	HRB	LC	N	U	HRB	LC	Y	Y	Y	N	HRB	HRB	LC
Rothenberg, 2017[12]	U	Y	Y	URB	UC	U	Y	URB	LC	N	U	HRB	LC	U	Y	Y	N	HRB	HRB	UC
Pohlig, 2017[116]	Y	Y	Y	LRB	UC	Y	Y	LRB	LC	N	Y	HRB	LC	Y	U	Y	U	URB	HRB	UC
Sousa, 2017[195]	Y	Y	Y	LRB	UC	Y	N	HRB	LC	N	Y	HRB	LC	N	Y	Y	Y	HRB	HRB	UC
Wang, 2017[156]	U	Y	U	URB	UC	U	Y	URB	LC	N	U	HRB	LC	U	Y	Y	N	HRB	HRB	UC
Sigmund, 2017[117]	U	Y	Y	URB	UC	U	Y	URB	LC	N	U	HRB	LC	U	Y	Y	N	HRB	HRB	UC
Bonanzinga, 2017[206]	Y	Y	Y	LRB	LC	Y	Y	LRB	LC	N	Y	HRB	LC	Y	Y	Y	Y	LRB	HRB	LC
Claassen, 2016[118]	Y	Y	N	HRB	HC	N	Y	HRB	LC	N	N	HRB	LC	U	N	N	N	HRB	HRB	HC
Choi, 2016[196]	Y	Y	Y	LRB	LC	N	N	HRB	LC	N	N	HRB	LC	Y	Y	Y	Y	LRB	HRB	LC

http://dx.doi.org/10.2106/JBJS.18.00632

Wimmer, 2016[163]	U	Y	N	HRB	UC	U	U	URB	LC	N	U	HRB	LC	U	N	Y	N	HRB	HRB	UC
Rak, 2016[246]	U	Y	U	URB	UC	U	NA	URB	LC	N	U	HRB	LC	N	Y	Y	Y	HRB	HRB	UC
De Vecchi, 2016[160]	Y	Y	U	URB	UC	Y	Y	LRB	LC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Stylianakis, 2018[119]	Y	Y	Y	LRB	UC	U	Y	URB	LC	N	U	HRB	LC	N	Y	Y	N	HRB	HRB	UC
Kawamura, 2017[197]	U	Y	U	URB	UC	U	N	HRB	UC	N	U	HRB	LC	U	Y	Y	Y	URB	HRB	UC
Melendez, 2016[148]	Y	Y	Y	LRB	UC	N	Y	HRB	LC	N	Y	HRB	LC	N	Y	Y	Y	HRB	HRB	UC
Hischebeth, 2016[247]	U	Y	U	URB	UC	U	U	URB	LC	N	U	HRB	LC	N	Y	Y	Y	HRB	HRB	UC
Deirmengian, 2013[198]	N	N	U	HRB	HC	N	N	HRB	UC	N	N	HRB	LC	U	Y	Y	U	URB	HRB	HC
Fink, 2018[81]	Y	Y	U	URB	LC	Y	U	URB	LC	Y	U	URB	LC	Y	Y	Y	Y	LRB	URB	LC
Boettner, 2016[144]	U	Y	U	URB	UC	U	Y	URB	LC	Y	U	URB	LC	Y	Y	Y	Y	LRB	URB	UC
Wing, 2017[140]	U	Y	U	URB	UC	U	U	URB	UC	U	U	URB	UC	U	Y	U	Y	URB	URB	UC
Radhakrishnan, 2015[179]	Y	Y	Y	LRB	UC	Y	U	URB	LC	Y	U	URB	LC	U	Y	Y	Y	URB	URB	UC
Partridge, 2018[182]	U	Y	Y	URB	U	Y	U	URB	LC	Y	U	URB	LC	Y	Y	Y	N	HRB	HRB	UC
Di Benedetto, 2016[250]	U	Y	Y	URB	U	U	Y	URB	LC	Y	U	URB	LC	N	Y	Y	N	HRB	HRB	UC
Martin, 2015[150]	Y	Y	Y	LRB	UC	U	U	URB	UC	U	U	URB	UC	U	Y	Y	Y	URB	URB	UC

Abbreviations: U=unclear, URB=unclear risk of bias; Y=yes; N=no; H=high, HRB=high risk of bias; L=low, LRB=low risk of bias; LC=low concern; HC=high concern; UC=unclear concern; NA=not applicable; Bolded fonts: new studies during the update or correcting errors

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Appendix B: Additional details of the meta-analyses

Details about the statistical analyses

We started with modeling the true positive (TP) and false positive (FP) counts as binomial distributed,

$$y_d^i \sim \text{Binom}\left(n_d^i, p_d^i\right), \quad d = 0, 1,$$

where n_d^i is the number of non-infected ($d = 0$) or infected ($d = 1$) subjects/joints, among which y_d^i is the number of subjects/joints with positive test results. We did not perform univariate meta-analysis for sensitivity or specificity alone (unless one of them is not of concern), in accordance with the recommendation of *Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy* [17].

Instead of directly modeling the logit-transformed reported sensitivity and specificity, the preference to use true positive (TP), true negative (TN), false positive (FP) and false negative (FN) counts was for the following reasons: 1) this approach of modeling permits variability of sensitivity and 1-specificity parameters around the reported estimates at the study level; 2) this approach accounts for the sample size (with and without the condition) of each study; 3) this approach permits sensitivity and specificity to reach 0% or 100% without having to apply continuity correction. Unfortunately, due to most of the studies providing only the parameter estimates such as sensitivity and specificity rather than the exact counts, TP and FP counts were calculated, followed by verification of their agreement with declared sensitivity and specificity.

For a study to enter meta-analysis, it was required to have TP, TN, FP, FN counts, either directly reported from the article or calculated from other reported information such as declared sensitivity and specificity. If a study reported $(sens_i, spec_i)$ but no clues about the true positive and false positive counts, we use $sens_i \times n_1^i$ or $(1 - spec_i) \times n_0^i$ rounded to the closest integer, as long as the resulting integer divided by n_1^i or n_0^i does not contradict the reported sensitivity or specificity to the second place after the decimal point (0.01, or 1%). If discrepancies were observed during this "agreement verification" process at the second place after the decimal point (0.01, or 1%), we contacted the authors for the exact the TP, TN, FP and FN counts, and excluded such studies from quantitative analysis if the authors did not reply. We emailed each author three times that included an initial contact followed by two reminders of at least one week apart. If the email address for the corresponding author was not functional, we searched for email addresses for other study authors and contacted them instead.

As shown by Harbord et al. (2007) [25], a transformation exists between the bivariate model (Reitsma et al. 2005, Chu and Cole 2006) [22-23] and the hierarchical summary ROC model (Rutter and Gatsonis 2001) [24], both without covariate adjustment. Therefore, the two models are equivalent, and we can obtain the mean/median summary points as well as hierarchical summary ROC (HSROC) curve by fitting a bivariate model,

$$\begin{pmatrix} \text{logit}\left(p_1^i\right) \\ \text{logit}\left(p_0^i\right) \end{pmatrix} \sim N\left(\begin{pmatrix} \mu_1 \\ \mu_0 \end{pmatrix}, \begin{pmatrix} \sigma_1^2 & \sigma_{01} \\ \sigma_{01} & \sigma_0^2 \end{pmatrix}\right)$$

where μ_1 and μ_0 are the mean logit-transformed sensitivity and 1-specificity, respectively. The mean/median summary sensitivity and specificity are given by the posterior mean/median of $\frac{\exp(\mu_1)}{1+\exp(\mu_1)}$ and $\frac{\exp(\mu_0)}{1+\exp(\mu_0)}$, respectively, after running the Bayesian hierarchical model using JAGS (Plummer 2016)[26]. The fitted HSROC curve, given by

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$$\mathrm{sens}(x) = 1/(1 + \exp(-\Lambda \exp(\beta/2) - \mathrm{logit}(x)\exp(\beta)))$$

where $\beta = \log(\sigma_0/\sigma_1)$ and $\Lambda = \mu_1 \exp(\beta/2) - \mu_0 \exp(-\beta/2)$, is a functional curve of x (1-specificity) with the posterior mean estimates $\hat{\mu}_1$, $\hat{\mu}_0$, $\hat{\sigma}_1^2$, and $\hat{\sigma}_0^2$ plugged in. In addition, we could obtain the 95% credible region by connecting the posterior 2.5% and 97.5% quantiles of $\mathrm{sens}(x)$ at point wise values of (1-specificity).

For each test with more than 5 records of data, we fitted a regression of $\log_{10}$ diagnostic odds ratio (DOR) against the explanatory variable 1/sqrt(ESS) weighted by ESS, where $ESS_i = 2/\left(\frac{1}{n_0^i} + \frac{1}{n_1^i}\right)$ is the effective sample size of the i^{th} study, and checked whether the p-value for the slope indicates significant small-study effect. If the small-study effect was detected, it might attribute to publication bias.

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Small study effect (as a signal of publication bias)

Regression of log10(DOR) against the explanatory variable 1/sqrt(ESS), weighted by ESS		
Tests with small study effects detected by p-value < 0.05 for the slope of 1/sqrt(ESS):		
α-defensin lateral flow test	9 records (in meta-analysis) from 9 studies	p-value: 0.0019
Tests with small study effects detected by p-value < 0.1 for the slope of 1/sqrt(ESS):		
Swab culture	6 records (in meta-analysis) from 4 studies	p-value: 0.0502
Serum ESR	40 records (in meta-analysis) from 33 studies	p-value: 0.0866

α-defensin lateral flow test 9 records (in meta-analysis) from 9 studies, p-value: 0.0019

By fitting a regression of log10 diagnostic odds ratio (DOR) against the explanatory variable 1/sqrt(ESS), weighted by ESS, we have found that the p-value for the slope of 1/sqrt(ESS) is 0.0019. Also, the smaller value of effective sample size (ESS), the larger 1/sqrt(ESS), the smaller the log10(DOR), as is shown in the effective sample size funnel plot. In other words, studies with a smaller effective sample sizes tend to have smaller diagnostic odds ratios. This small-study effect might attribute to publication bias.

Other possible reasons: α-defensin lateral flow test had no records of data with tissue culture as the reference standard (among the total of 9 records that entered meta-analysis).

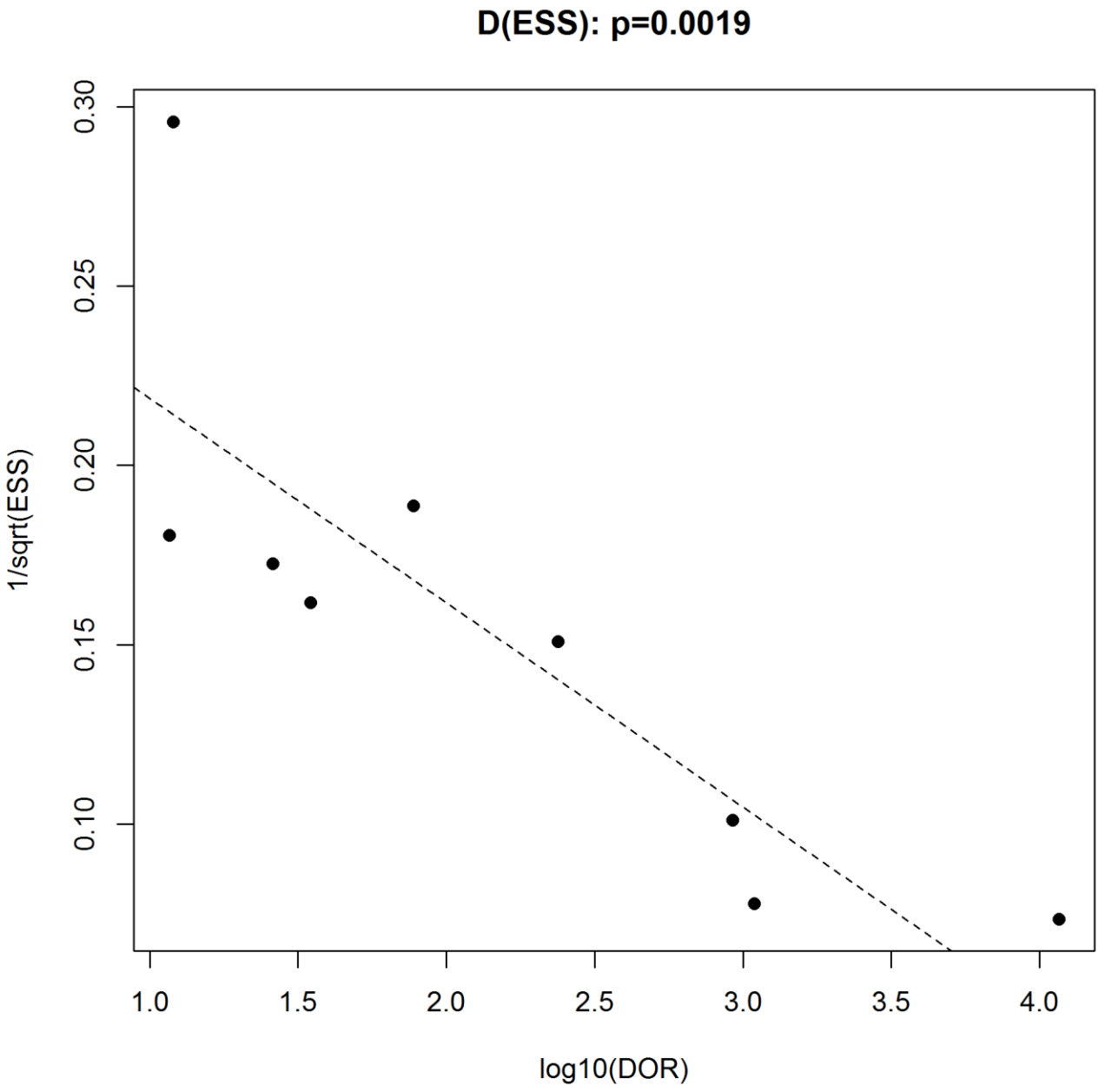

Figure A1: Effective sample size funnel plot for α-defensin lateral flow test

Swab culture 6 records (in meta-analysis) from 4 studies, p-value: 0.0502

By fitting a regression of log10 diagnostic odds ratio (DOR) against the explanatory variable 1/sqrt(ESS), weighted by ESS, we have found that the p-value for the slope of 1/sqrt(ESS) is 0.0502. Also, the smaller value of effective sample size (ESS), the larger 1/sqrt(ESS), the larger the log10(DOR), as is shown in the effective

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sample size funnel plot. In other words, studies with a smaller effective sample sizes tend to have larger diagnostic odds ratios. This small-study effect might attribute to publication bias.

Other possible reasons: swab culture had no records of data with tissue culture as the reference standard (among the total of 6 records that entered meta-analysis).

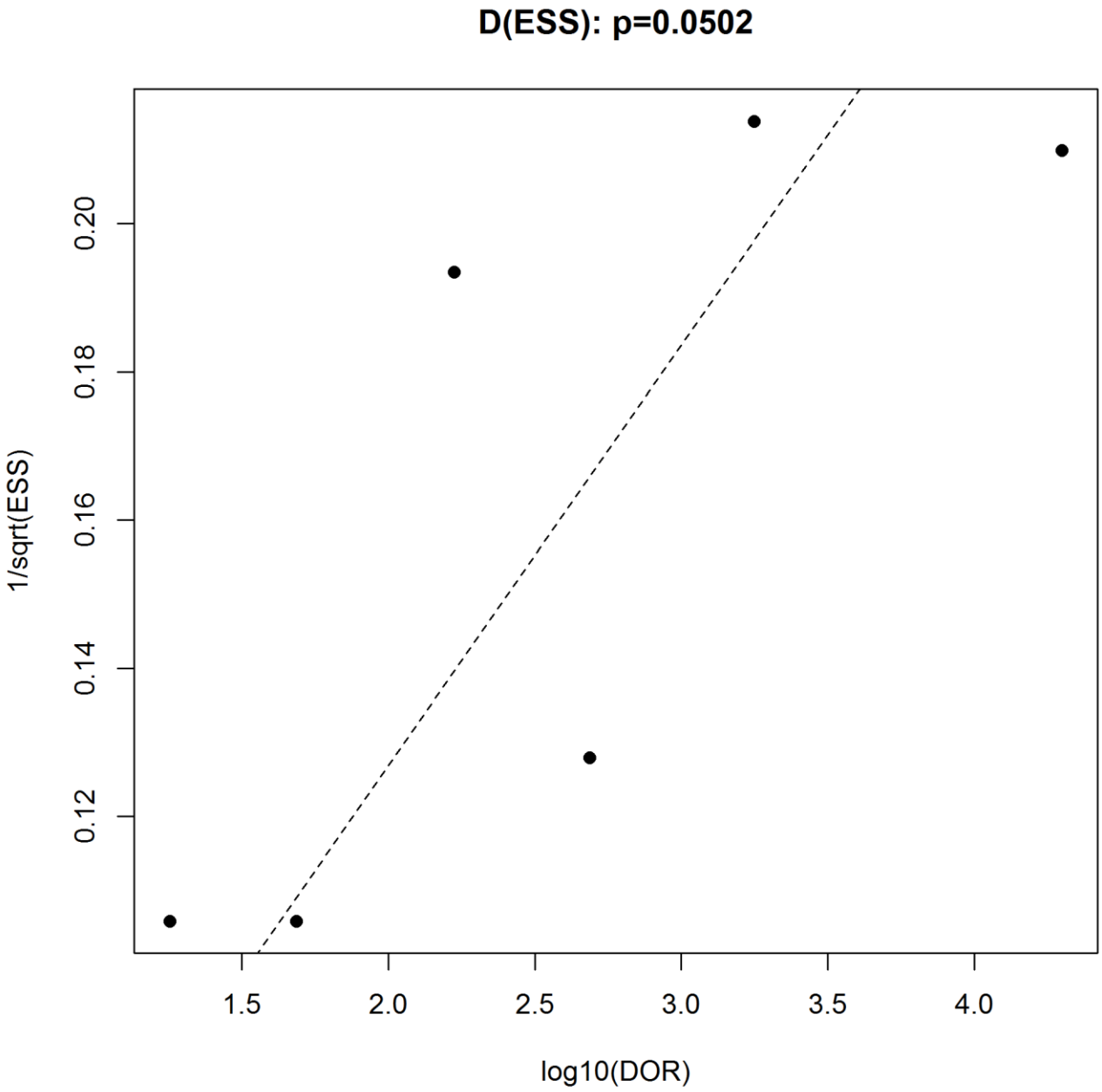

Figure A2: Effective sample size funnel plot for swab culture

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Serum ESR 40 records (in meta-analysis) from 33 studies, p-value: 0.0866

By fitting a regression of log10 diagnostic odds ratio (DOR) against the explanatory variable 1/sqrt(ESS), weighted by ESS, we have found that the p-value for the slope of 1/sqrt(ESS) is 0.0502. Also, the smaller value of effective sample size (ESS), the larger 1/sqrt(ESS), the larger the log10(DOR), as is shown in the effective sample size funnel plot. In other words, studies with a smaller effective sample sizes tend to have larger diagnostic odds ratios. This small-study effect might attribute to publication bias.

Other possible reasons: swab culture had no records of data with tissue culture as the reference standard (among the total of 6 records that entered meta-analysis).

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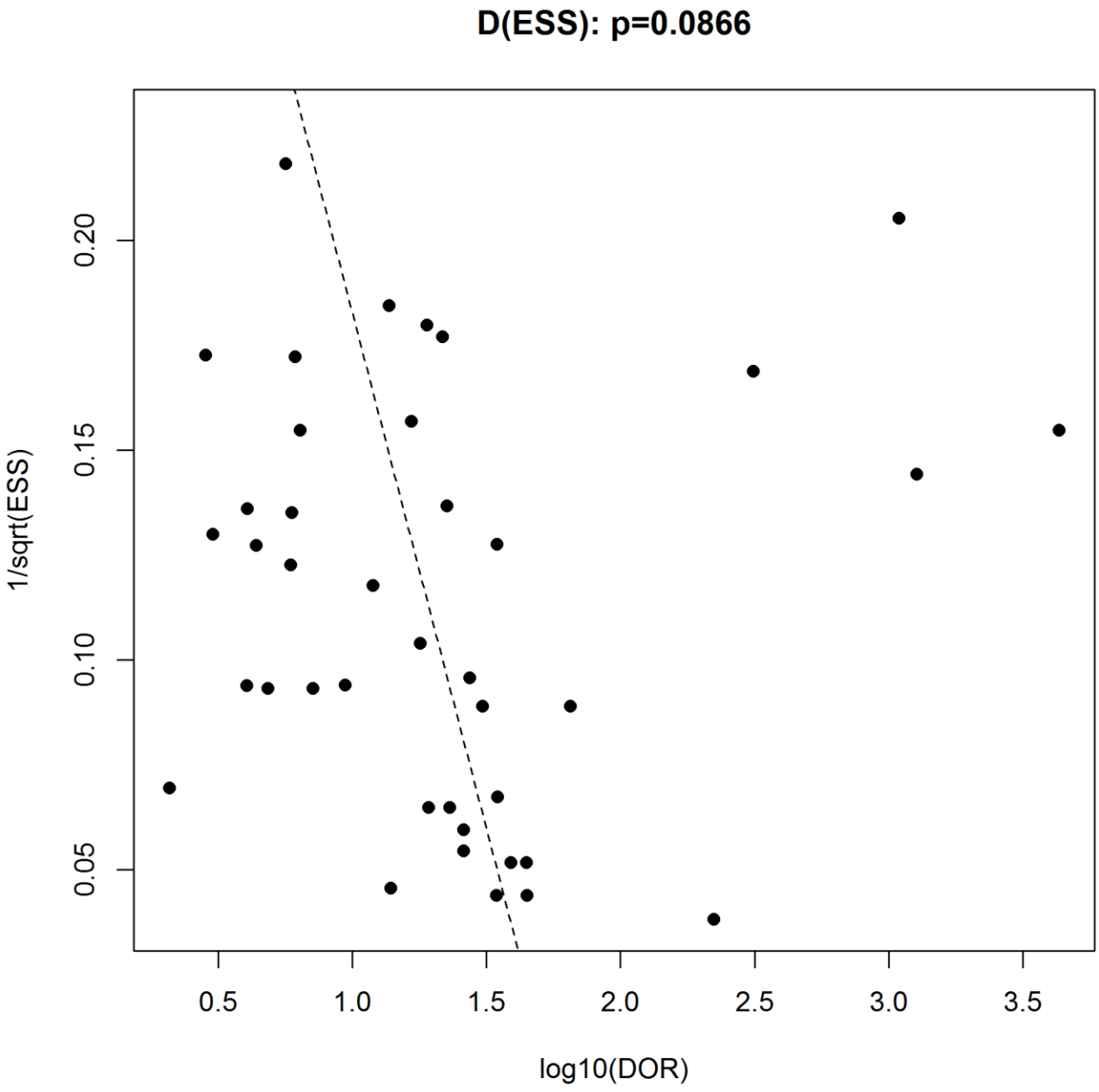

Figure A3: Effective sample size funnel plot for serum ESR

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Part I. Serum Tests

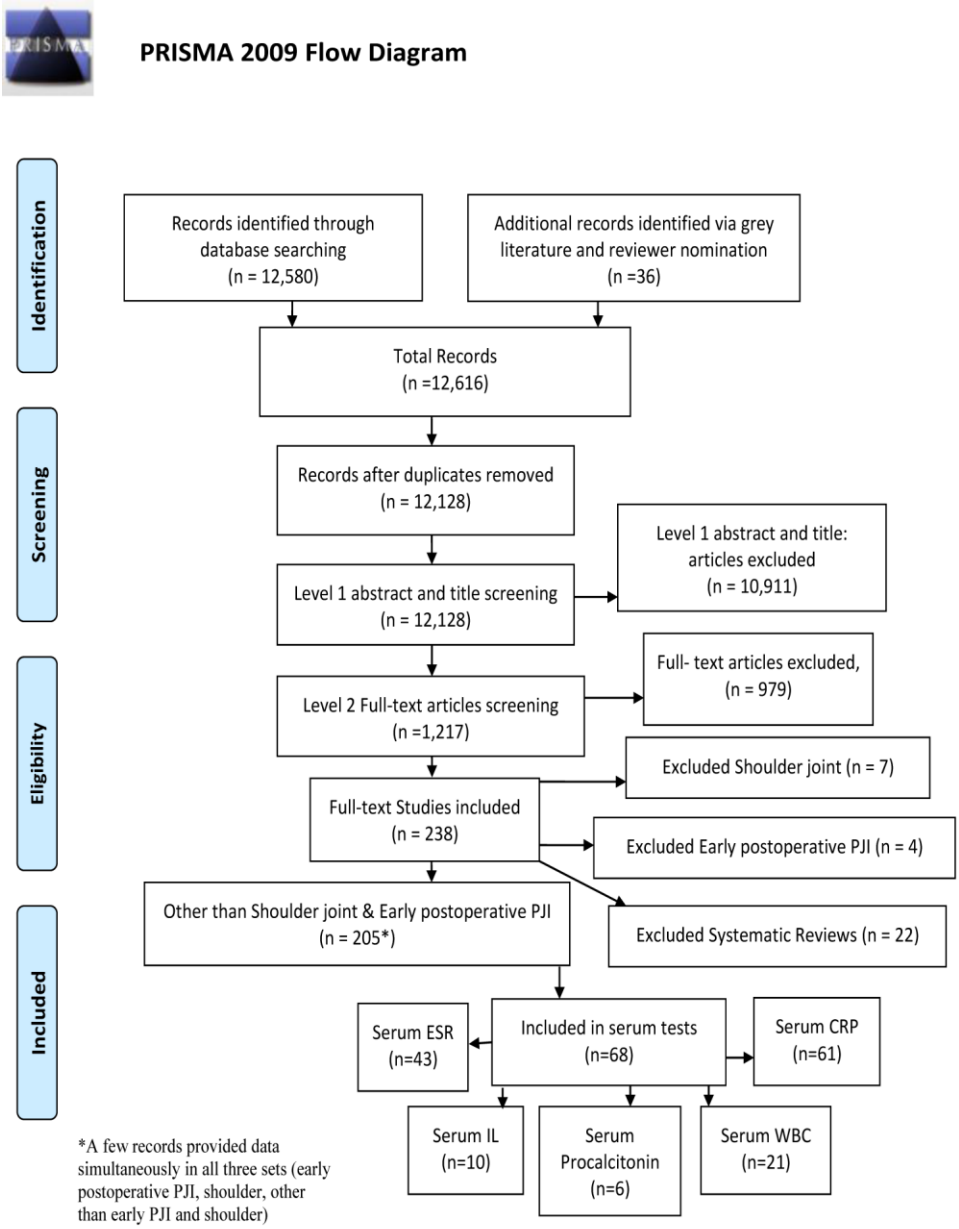

Figure A4: PRISMA for Serum Tests

When analyzing serum test performance in studies that used tissue culture as the reference standard, only CRP and ESR had sufficient data for fitted HSROC curves; serum CRP had a higher mean summary specificity than ESR (Figure A5).

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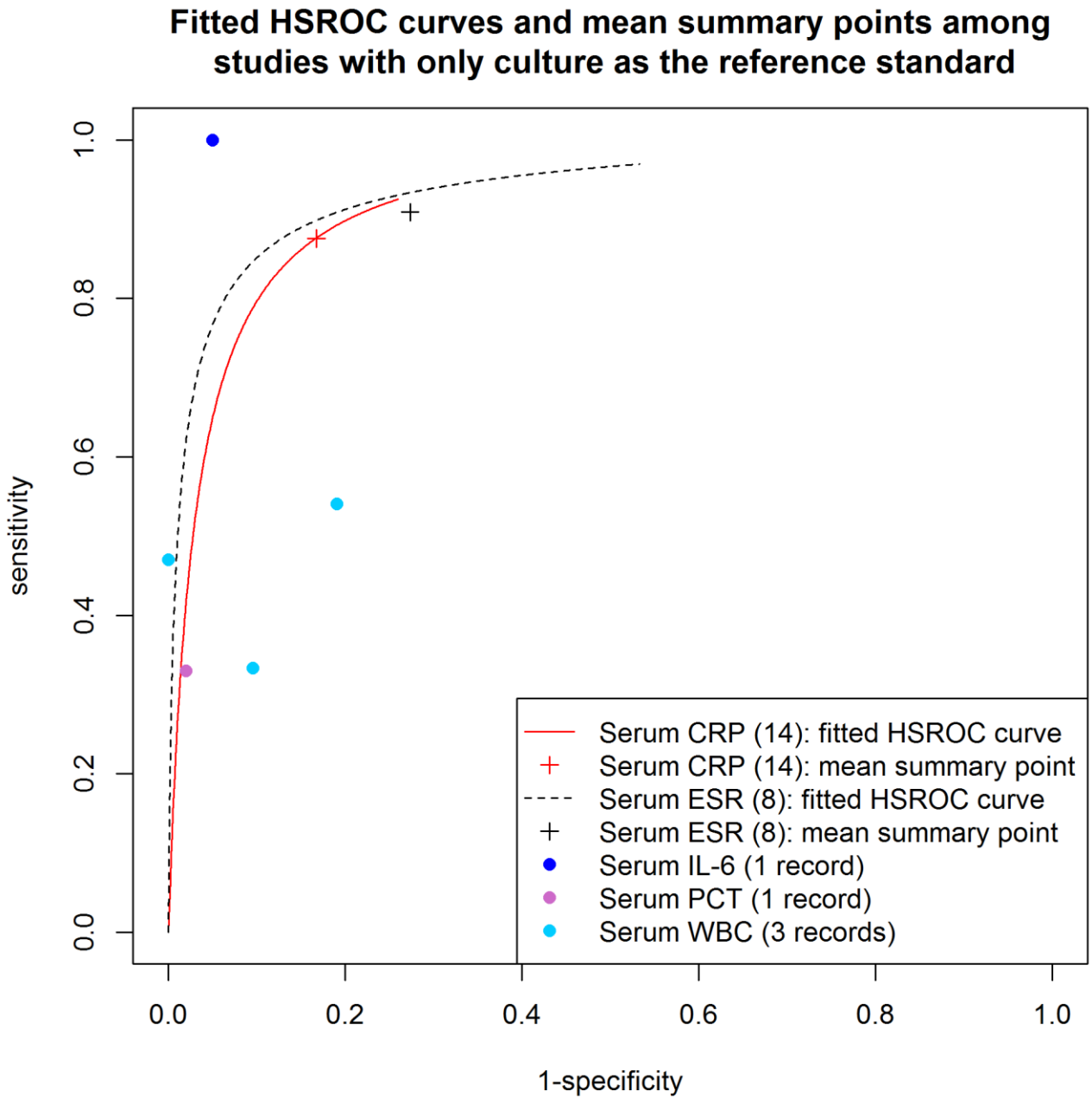

Figure A5: Fitted HSROC curves and mean summary points for serum tests among studies with tissue culture as reference standard. The number inside the parenthesis is the records of data corresponding to each test.

Serum CRP

Of the 68 studies on serum tests, 61 provided data on serum CRP [12,59,60,62–66,68,69,71–92,94–96,98–108,110–121,123–125], 46 were included in the meta-analysis, and 16 studies were not because three of them did not report sufficient data

needed for analyses [1,99,106] , and 12 had contradiction during the "agreement verification" process of the reported sensitivity and/or specificity[59,60,69,73,79,91,96,100-102,125,108].

Serum ESR

Of the 68 studies on serum tests, 43 provided data on serum ESR[12,59,61,64,69,71–80,82–89,91,92,95,98,100–102,104,108,111–113,115,116,119–123,1255], and 33 were included in the meta-analysis. Nine studies were not included in the meta-analysis, one for having insufficient information [71]{, and eight for having contradiction during the "agreement verification" process of the reported sensitivity and/or specificity[69,73,74,79,91,100,101,102,116].

Serum IL-6

Of the 68 studies on serum tests, 10 reported data on serum IL-6[60,67,74,75,85,88,90,95,96,109]. Among them, seven studies were included in the meta-analysis and three were not due to contradiction during the "agreement verification" process of the reported sensitivity and/or specificity[60,85,90].

Serum Procalcitonin

Of the 68 studies on serum tests, six reported data on serum procalcitonin and were all included in the meta-analysis[60,65,85,90,96,107].

Serum WBC

Of the 68 studies on serum tests, 21 reported data on serum WBC[60–62,65,70,78,85,88–91,94,95,98,99,104,106,108,118,119,123]. Of these, 16 were included in the meta-analysis and five were not for either having insufficient information[99,106] having contradiction during the "agreement verification" process of the reported sensitivity and/or specificity[85,90,91].

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Table A2: Diagnostic accuracy of serum tests with <=4 studies for which meta-analyses (bivariate model) were not performed

Author name (publication year); sample size	Index Test	Reference Standard	Cut off	Joints	Sensitivity (95% CI)	Specificity (95% CI)	Risk of Bias
Worthington (2010)[75] n=46	Serum sICAM-1 (Sica)	Institution's specific definition (combination of clinical findings and markers); Presurgical imagine, elevated presurgical ESR and/or CRP, positive intraoperative swab and tissue cultures - same organism from two or more clinical samples	250 ng/mL	Hip	0.94	0.74	High
Gollwitzer (2013)[67] n=35	Serum IL-1B	Institution's specific definition (combination of clinical findings and markers); Morawweitz et al.: (1) demonstration of open sinus tracts, (2) two positive major criteria (positive intraoperative microbiological culture and positive histopathological grading of infection), or (3) one positive major criterion (positive intraoperative microbiological culture or histopathological grading of infection) and one positive minor criterion (CRP > 1.0 mg/dL and/or positive microbiological culture of the aspirate)	4.4	Mix of Knee and Hip	0.67	1	High
	Serum IL-2		3.14	Mix of Knee and Hip	0.67	1	High
	Serum IL-4		13.5	Mix of Knee and Hip	0.60	0.90	High
	Serum IL-17A		8.55	Mix of Knee and Hip	0.67	0.1	High
	Serum LL-37		1	Mix of Knee and Hip	0.733	0.50	High
	Serum HBD-2		78	Mix of Knee and Hip	0.80	0.70	High
	Serum HBD-3		68	Mix of Knee and Hip	0.333	0.95	High
Ramsingh(2010)[103] n=53	Plasma Viscosity test	Tissue culture	NR	Mix of knee and hip	1.00	0.43	Unclear
Ettinger (2015)[96] n=98	Lipopolysaccharide binding protein	2011 MSIS criteria	6.35	Mix of all three	0.842	0.724	High
Friedrich (2014)[97] n=120	Lipopolysaccharide-binding protein level	At least one of: -Purulent synovial fluid, or greater than or equal to 1700 leukocytes/microliter, or greater than or equal to 65% neutrophils in the joint aspirate (TKA); greater than or equal to 3600 leukocytes/microliter, or greater than or equal to 80% neutrophils (THA) -Histological confirmation of a PJI (periprosthetic membrane type II or III according to histopathological consensus classification of the periprosthetic inteface)	>7	Mix of knee and hip	0.656 (0.468, 0.814)	0.707 (0.591, 0.806)	High

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		-Pathogen detection in sterile joint aspiration and identical positive intraoperative tissue specimen, or in at least two intra-operative tissue specimens after incubation -definite signs of PJI clinically or intra-operatively (e.g sinus tract, presnece of purulence in the affected joint)					
Milone (2014)[61] n=98	serum hs-CRP (hs stands for high-sensitivity)	Aspiration or operation culture, clinical follow-up and serologic evaluation (for cases without culture)	28.6	Mix of Knee and Hip	1.00	0.97	High
Milone (2014) [61] n=98	serum hs-CRP (hs stands for high-sensitivity)		7.3	Mix of Knee and Hip	1.00	0.59	High
Milone (2014) [61] n=98	serum ls-CRP (ls stands for low-sensitivity)		2.6	Mix of Knee and Hip	1.00	0.97	High
Milone (2014) [61] n=98	serum ls-CRP (ls stands for low-sensitivity)		0.8	Mix of Knee and Hip	1.00	0.62	High
Milone (2014) [61] n=40	Neutrophil differential (%)		71	Mix of Knee and Hip	1.00	0.89	High
Toossi (2012) [70]n=930	serum neutrophil%	One of the following criteria: 1. Positive culture: a. More than 5 colonies on 1 plate b. Light growth and greater in a single culture c. Very light growth on 2 cultures if pathogen has the same resistance profile d 3 positive cultures in broth 2. Intraoperative purulence 3. Draining sinus tract or 3 of the following 4: a. ESR greater than 30 mm/h b. CRP greater than 10 mg/L c. Synovial WCC greater than 1760 cells/μL or 10700 cells/μL acute postoperative (from synovial fluid) d. Synovial neutrophils percentages greater than 73% or 89% acute postoperative (from synovial fluid)	69%	Mix of Knee and Hip	0.530 (0.476, 0.577)	0.750 (0.719, 0.782)	High
Cipriano (2014)[93] n=50	Toll-like receptors (TLR) 1	MSIS 2011	0.0065	Mix of Knee and Hip	1	0.9	High
			0.0372		0.952	0.931	
			0.0924		0.952	1	
	Toll-like receptors (TLR) 6	MSIS 2011	0.0056		0.905	0.621	
			0.0215		0.857	0.828	
			0.0316		0.762	0.862	

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Part II. Synovial Tests

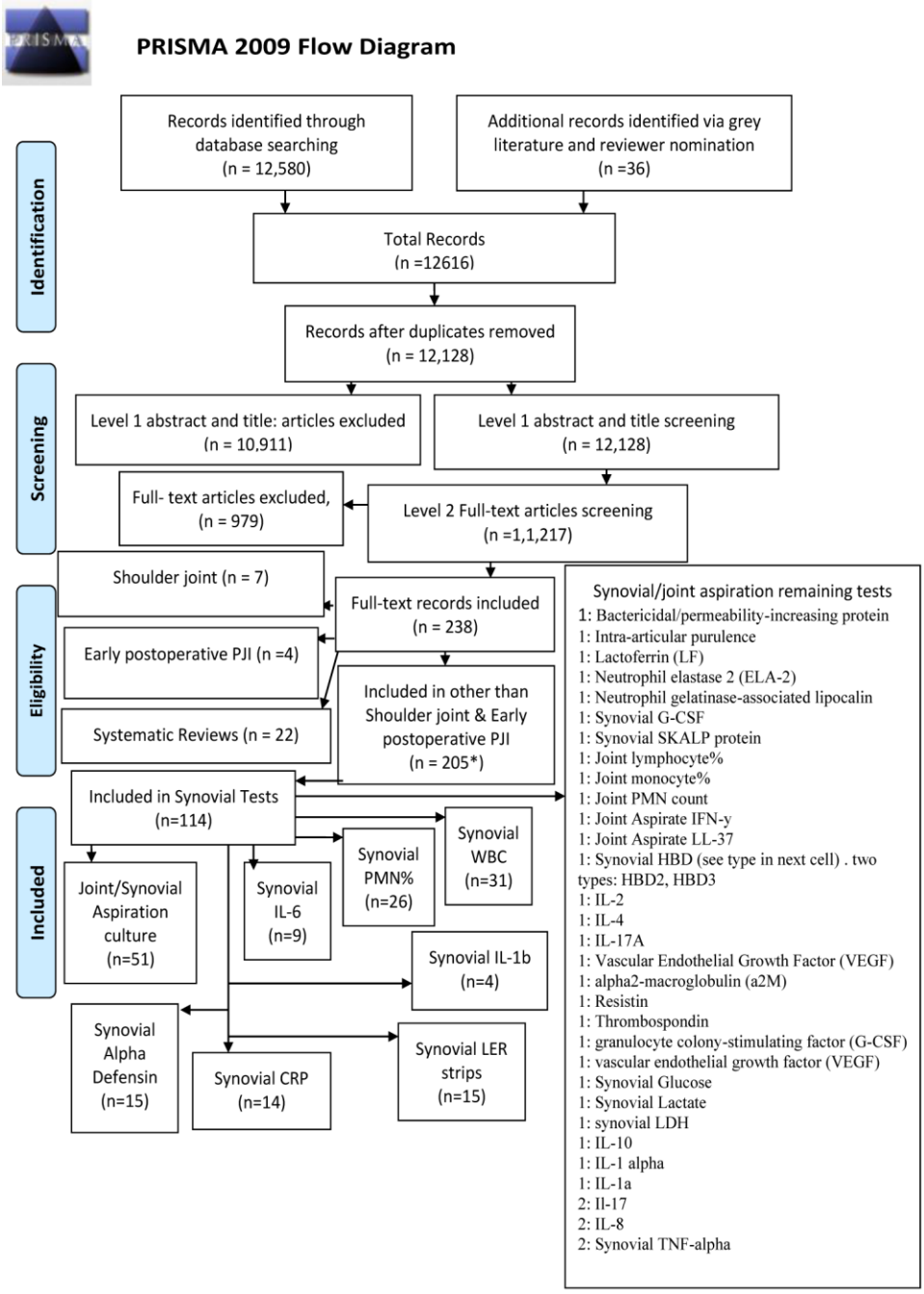

Figure A6: PRISMA for Synovial Tests

We plot the fitted HSROC curve and mean summary point of synovial IL-6 (5 records of data) along with other synovial tests in Figure A7. Synovial IL-6 has fitted HSROC curve very close to synovial CRP, WBC and PMN%, and may have slightly higher mean summary specificity but lower mean summary sensitivity but has too few studies to reach any affirmative conclusion.

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Comparison of synovial tests with studies that used tissue culture as the reference standard was not possible due to insufficient number of studies.

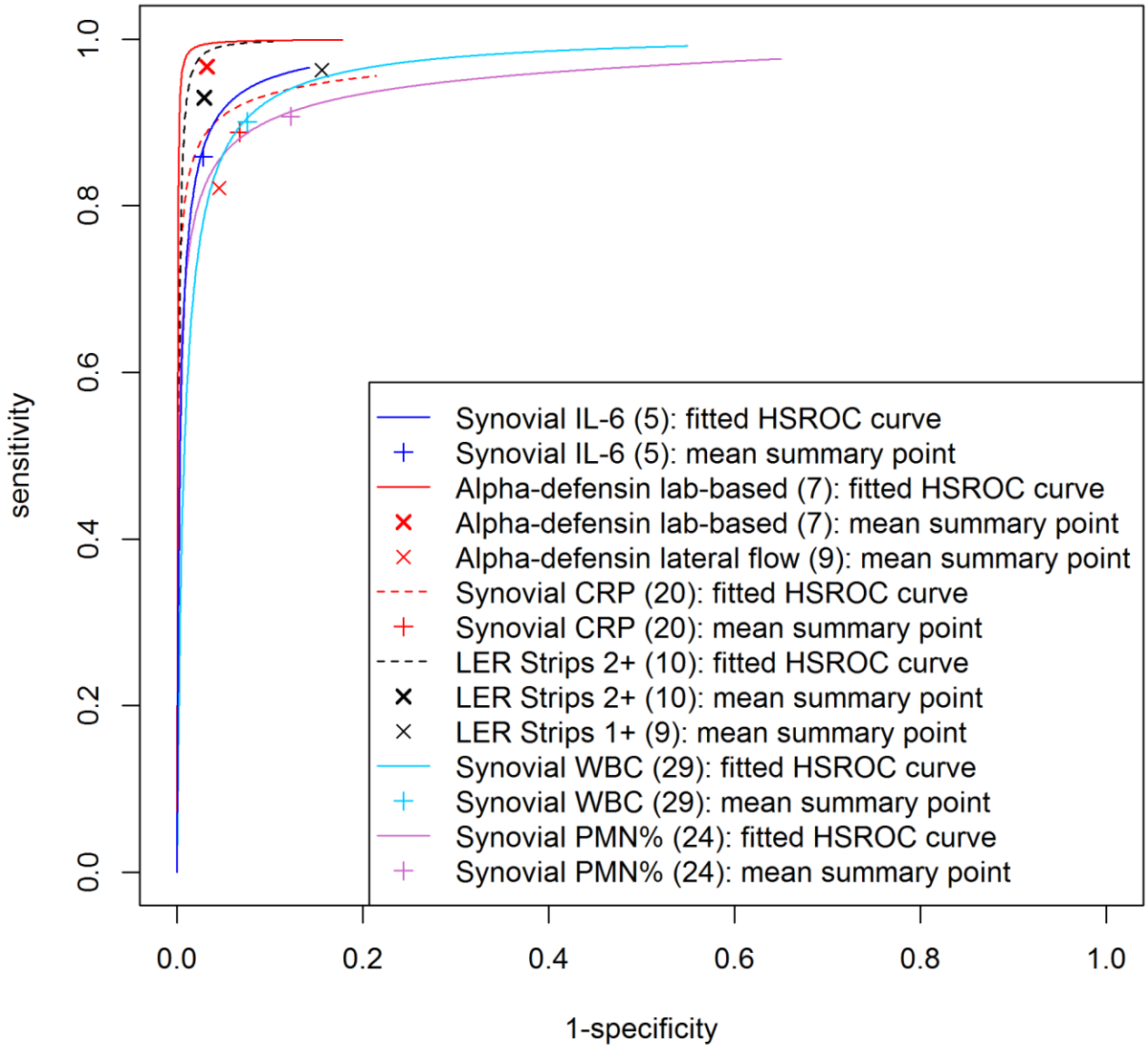

Figure A7: Fitted HSROC curve and mean summary points for synovial tests (synovial IL-6 added). The number inside the parenthesis is the records of data corresponding to each test.

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We only had 2 records of data for synovial TNF-alpha, IL-1b and IL-8 each (another 2 records of data for IL-1b had contradiction during the "agreement verification" process of reported sensitivity and/or specificity). Figures A8-A10 provides scatterplots along with the fitted HSROC curves and mean summary points of other synovial tests.

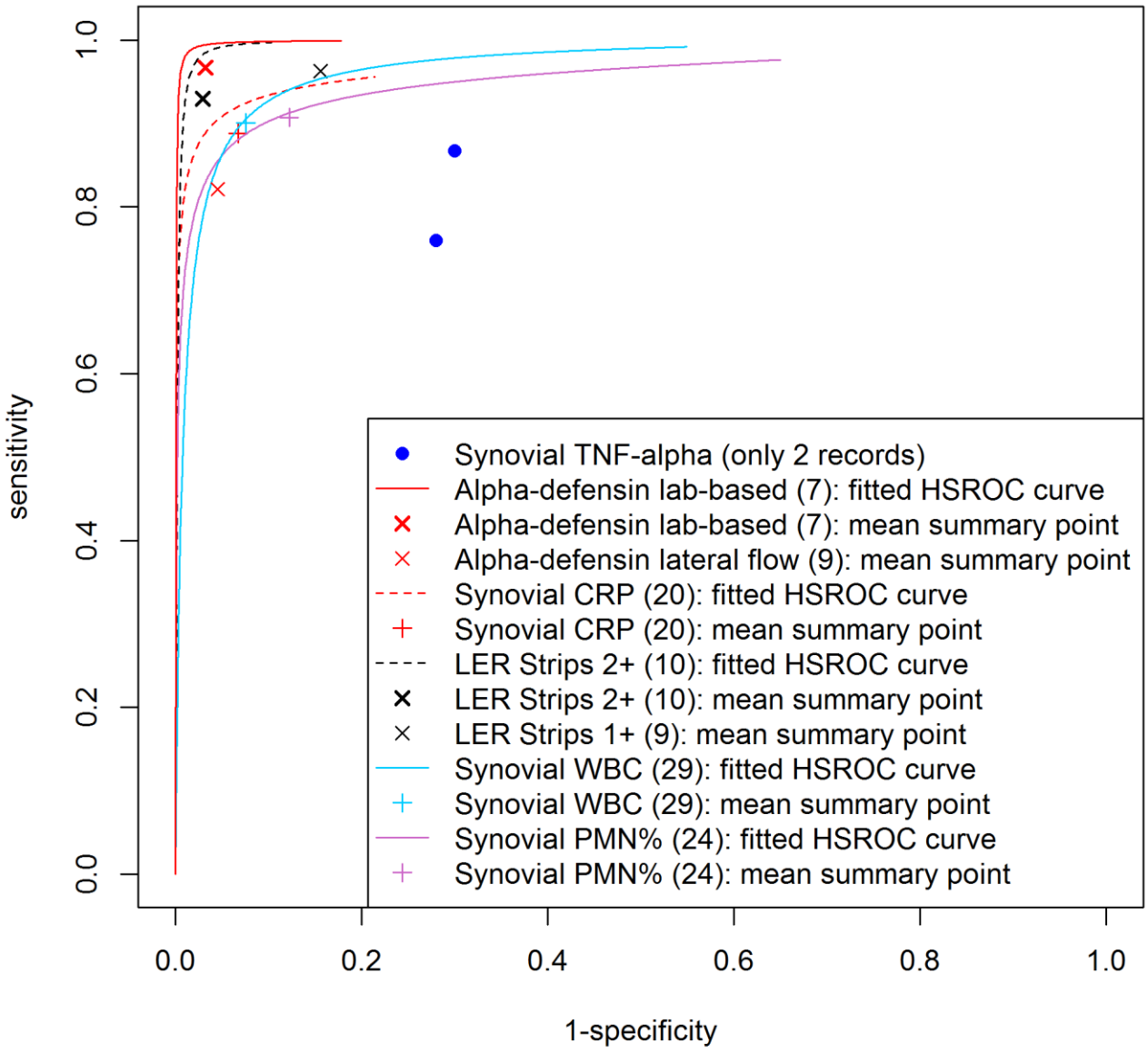

Figure A8: Fitted HSROC curve and mean summary points for synovial tests (synovial TNF-alpha added). The number inside the parenthesis is the records of data corresponding to each test.

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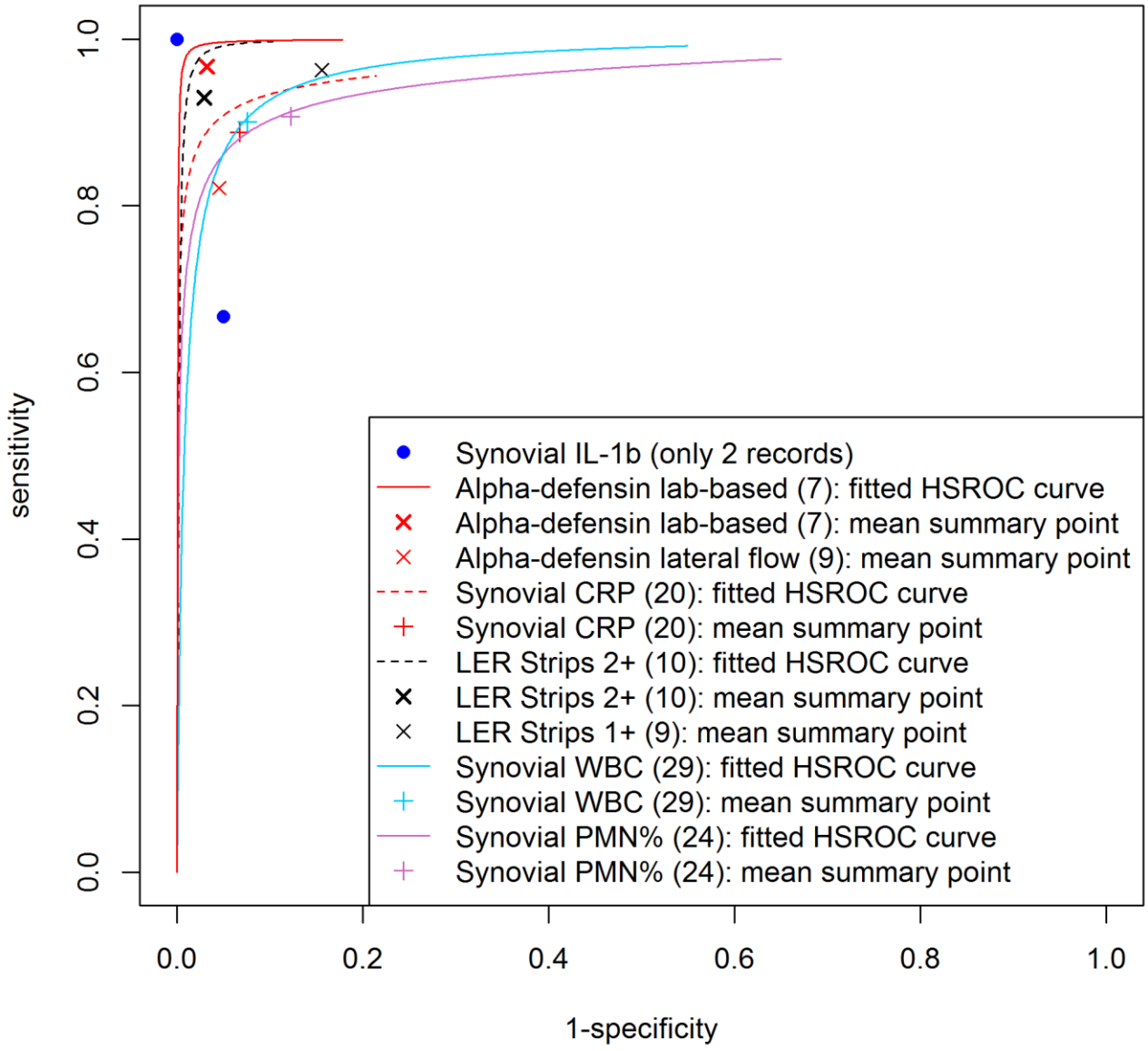

Figure A9: Fitted HSROC curve and mean summary points for synovial tests (synovial IL-1b added). The number inside the parenthesis is the records of data corresponding to each test.

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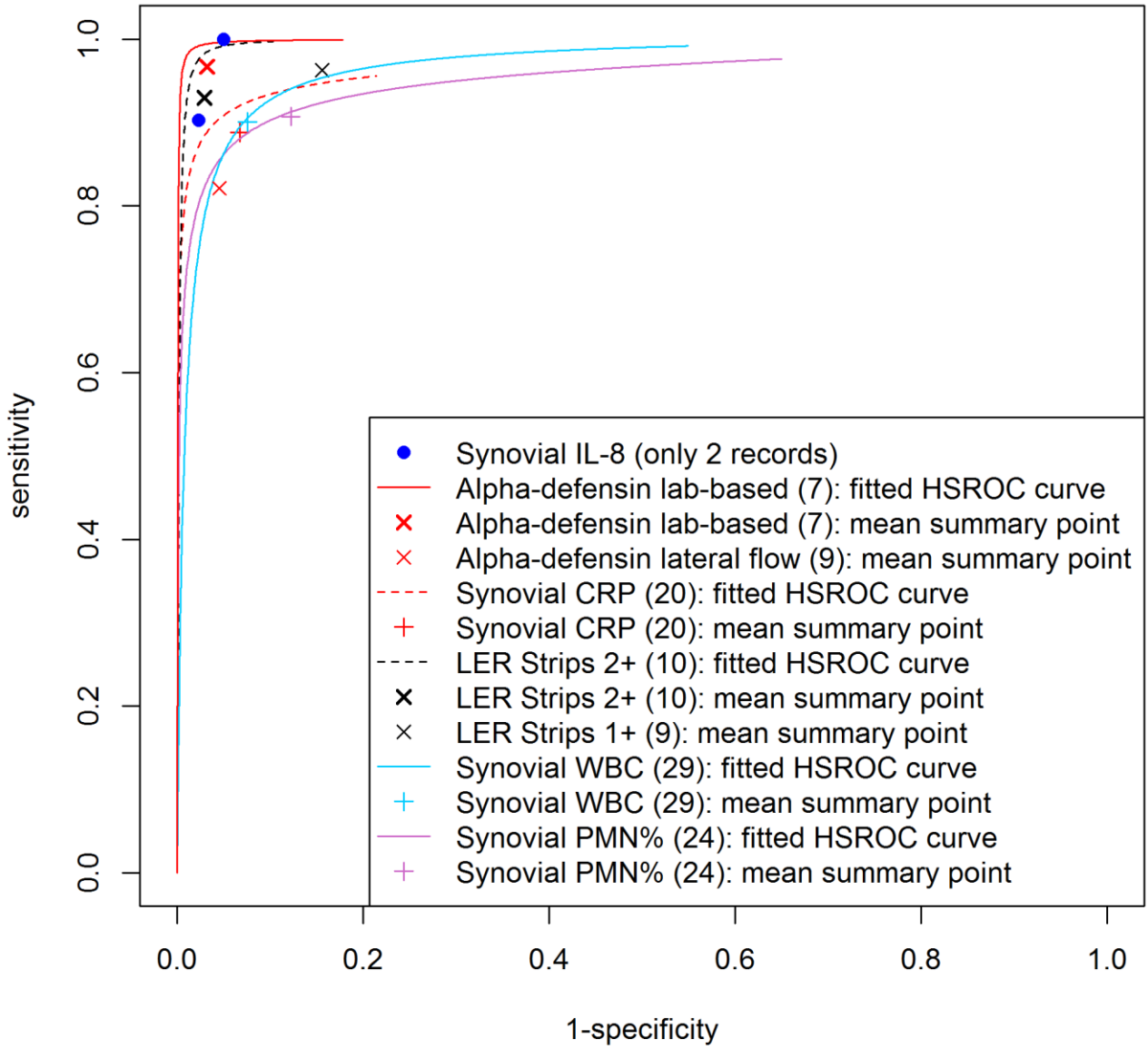

Figure A10: Fitted HSROC curves and mean summary points for synovial tests (synovial IL-8 added). The number inside the parenthesis is the records of data corresponding to each test.

Alpha-Defensin

Of the 114 studies on synovial tests, 15 provided data on synovial alpha-defensin[91,108,115,117,137,141,143,150,154,158,165–167,206,207.] Seven of these studies which contributed data about lab-based alpha-defensin enzyme-linked immunosorbent assay (ELISA) and nine which contributed data about alpha-

defensin lateral flow test (Table A14) were meta-analyzed separately. One study was not included in the meta-analysis because it was a re-analysis of previously published samples[154].

Synovial IL-1b

Of the 114 studies on synovial tests, four provided data on synovial IL-1b[67,76,122,164] but two records had contradiction during the "agreement verification" process of the reported sensitivity and/or specificity[122,164]. As such, we were unable to perform meta-analysis using the bivariate model. Further detail on this test is presented in Table A16.

Synovial IL-6

Of the 114 studies on synovial tests, nine reported data on synovial IL-6[60,67,76,83,99,109,162–164]. However, four studies were not included in the meta-analysis due to insufficient information [99] contradiction during the "agreement verification" process of the reported sensitivity and/or specificity[164,83]or on a different technique (IL-6 lateral flow immunoassay)[163].

Synovial CRP

Of the 114 studies on synovial tests, 14 provided data on CRP[59,101,105,109,124,146,160,162,164,188,195,197,199,207]. Among them, 13 studies were included in the meta-analysis, but one was not due to contradiction during the "agreement verification" process of the reported sensitivity and/or specificity[197].

Synovial PMN%

Of the 114 studies on synovial tests, 26 reported data on PMN%[12,69,72,76,79,101,104,115,120,143,159,161,181,185–187,189–193,195,197,198,203,204] Among them, 22 studies were included in the meta-analysis and four were not due to contradiction during the "agreement verification" process of the reported sensitivity and/or specificity[186,69,191,197].

Synovial WBC

Of the 114 studies on synovial tests, 31 provided data on WBC[12,69,72,76,79,83,99,101,104,115,120,143,144,159,161,181,185–187,189–193,195–198,201,203,204], and 26 studies were included in the meta-analysis. Five studies were not included in the meta-analysis, four due to contradiction during the "agreement verification" process of the reported sensitivity and/or specificity[186,69,101,204], and one due to insufficient information[99].

LER Strips

Of the 114 studies on synovial tests, 15 reported data on LER strips[138,142,149,151–157,159–161,194,205], 14 studies were included in the meta-analysis, but one was not due to insufficient information[159]. Ten of these studies which contributed data about LER strip with "++" or above and nine which contributed data about "+" or above (Table A13) were meta-analyzed separately.

Joint Aspiration / Synovial Fluid Culture

Of the 114 studies on synovial tests, 51 provided data on joint aspiration / synovial fluid culture [12,62,68,78,87,89,91,98,104,106,110,114–116,120,122,126–136,139,140,142,145,147,148,168–180,182–184,202,208]. Among them, 45 studies were included in the meta-analysis and 6 were not (two for insufficient information[172,106], three for contradiction during the "agreement verification" process of the reported sensitivity and/or specificity[62,91,127], and one for having reported sensitivity and/or specificity that did not agree with the reported counts for chronic PJI[208].

Synovial IL-8

Of the 114 studies on synovial tests, two provided data on synovial IL-8[162,164] so we were unable to conduct meta-analysis using the bivariate model. Further detail on this test is presented in Table A18.

Synovial TNF-α

Of the 114 studies on synovial tests, two provided data on synovial TNF-α[67,83] so we were unable to conduct meta-analysis using the bivariate model. Further detail on this test is presented in Table A20.

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Table A3: Diagnostic accuracy of synovial tests with <=4 studies for which meta-analyses (bivariate model) were not performed

Author name (publication year); sample size	Index Test	Reference Standard	Cut off	Joints	Sensitivity (95% CI)	Specificity (95% CI)	Risk of Bias
Deirmengian (2010)[76] n=51	Synovial IL-1β	Institution's specific definition (combination of clinical findings and markers); One or more positive cultures on solid medium; OR a chronic draining sinus communicating with the synovial fluid	112 pg/ml	Mix of Knee and Hip	1.00	1.00	Unclear
	Synovial G-CSF		35 pg/ml	Mix of Knee and Hip	1.00	0.95	Unclear
	Synovial IL-1α		1 pg/ml	Mix of Knee and Hip	0.86	0.97	Unclear
	Synovial IL-17		7.2 pg/ml	Mix of Knee and Hip	0.86	0.97	Unclear
	Synovial SKALP protein		1880 pg/ml	Mix of Knee and Hip	0.79	0.89	Unclear
Zmistowski (2012)[187] n=150	Synovial lymphocyte %	3 of the following: 1) positive culture from aspirate 2) positive culture from intraoperative tissue 3) purulence 4) ESR > 30 mm/h 5) serum CSR > 1 mg/dL	<=7%	Knee	0.87	0.84	High
	Synovial monocyte %		<=16%	Knee	0.96	0.73	High
	Synovial PMN count		>=2950 cells/uL	Knee	0.93	0.96	High
Gollwitzer (2013)[67] n=35	Synovial IL-1β	Morawweitz et al criteria.: (1) demonstration of open sinus tracts, (2) two positive major criteria (positive intraoperative microbiological culture and positive histopathological grading of infection), or (3) one positive major criterion (positive intraoperative microbiological culture or histopathological grading of infection) and one positive minor criterion (CRP > 1.0 mg/dL and/or positive microbiological culture of the aspirate)	27.57	Mix of Knee and Hip	0.667	0.950	High
	Joint Aspirate IL-2		12.04	Mix of Knee and Hip	0.133	1.000	High
	Joint Aspirate IL-4		7.79	Mix of Knee and Hip	0.933	0.850	High
	Synovial IL-17A		12.43	Mix of Knee and Hip	0.40	1.000	High
	Joint Aspirate IFN-γ		6.9	Mix of Knee and Hip	0.867	0.650	High
	Joint Aspirate TNF-α		4.04	Mix of Knee and Hip	0.867	0.700	High
	Joint Aspirate LL-37		5	Mix of Knee and Hip	0.80	0.85	High
	Joint Aspirate HBD-2		37	Mix of Knee and Hip	0.867	0.400	High
	Joint Aspirate HBD-3		195	Mix of Knee and Hip	0.60	0.85	High
Jacovides (2011)[162] n=74	Vascular Endothelial Growth Factor (VEGF)	One of: 1) sinus tract or open wound in communication with joint OR purulence found in joint intraoperatively	9745	Mix of Knee and Hip	0.774	0.915	High
	alpha2-macroglobulin (α2M)		0.262	Mix of Knee and Hip	0.806	0.956	High

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	IL-8	2) positive pre- or intra-operative fluid or tissue culture 3) combination of serologic and aspiration analyses was positive	8790	Mix of Knee and Hip	0.903	0.977	High
Alijanipour (2015)[200] n=557	Purulence	2011 MSIS criteria	Subjective interpretation	Mix of Knee and Hip	0.82	0.32	High
Deirmengian (2014)[164] n=95	ELA-2	2011 MSIS criteria	2	Mix of Knee and Hip	1.00 (0.88, 1.00)	1.00 (0.95, 1.00)	High
	BPI		2.2	Mix of Knee and Hip	1.00 (0.88, 1.00)	1.00 (0.95, 1.00)	High
	NGAL		2.2	Mix of Knee and Hip	1.00 (0.88, 1.00)	1.00 (0.95, 1.00)	High
	Lactoferrin		7.5	Mix of Knee and Hip	1.00 (0.88, 1.00)	1.00 (0.95, 1.00)	High
	Synovial IL-8		6.5	Mix of Knee and Hip	1.00 (0.87, 1.00)	0.95 (0.87, 0.99)	High
	Resistin		340	Mix of Knee and Hip	0.97 (0.82, 0.99)	1.00 (0.95, 1.00)	High
	Thrombospondin		1061	Mix of Knee and Hip	0.90 (0.73, 0.98)	0.97 (0.90, 1.00)	High
	Synovial IL-1β		3.1	Mix of Knee and Hip	0.96 (0.82, 1.00)	0.95 (0.87, 0.99)	High
	Synovial IL-10		32	Mix of Knee and Hip	0.89 (0.72, 0.98)	0.89 (0.79, 0.96)	High
	Interleukin-1α		4	Mix of Knee and Hip	0.82 (0.63, 0.94)	0.91(0.81, 0.97)	High
	Synovial IL-17		3.1	Mix of Knee and Hip	0.82 (0.63, 0.94)	0.99 (0.92, 1.00)	High
	granulocyte colony-stimulating factor (G-CSF)		15.4	Mix of Knee and Hip	0.82 (0.62, 0.94)	0.92 (0.82, 0.97)	High
	vascular endothelial growth factor (VEGF)		2.3	Mix of Knee and Hip	0.75 (0.55, 0.89)	0.77 (0.65, 0.87)	High
Lenski (2014)[99] n=69	Synovial Glucose	2011 MSIS criteria	44	Mix of Knee and Hip	0.792 (0.595, 0.908)	0.796 (0.605, 0.898)	High
	Synovial Lactate		8.3	Mix of Knee and Hip	0.714 (0.500, 0.862)	0.880 (0.700, 0.958)	High
	Synovial LDH		1423	Mix of Knee and Hip	0.840 (0.654, 0.936)	0.621 (0.44, 0.73)	High
Nilsdotter-Augustinsson (2007)[83]	Joint Aspirate TNF-α	Criteria for infection: -orthopedic surgeon preoperatively classified the prosthetic loosening as being due to deep	>=60	Hip	0.76	0.72	High
	Synovial IL-1β		>=60	Hip	0.59	0.83	High

n=78		infection of device, based on clinical symptoms, laboratory and radiographic findings, preoperative cultures of synovial fluid aspiration, or occurrence of fistulas AND/OR -surgeon deemed the patient infected because significant bacterial grwoth wass observed in cultures from tissue samples taken at revision surgery and th surgeion decided to treat the patient as being infected					
Gallo (2017)[203]	Synovial lymphocyte %	PJI was diagnosed according to the following criteria: 1) presence of a sinus tract communicating with a joint and/or intra-articular pus; 2) coincidentally positive results of histological examination (5 or more neutrophils per high power field) and culture of intraoperative samples; 3) if only intraoperative culture or histological results were positive, then at least two of the following signs had to be present: high clinical suspicion of infection (acute onset, fever, erythema, edema, persistent local pain, early prosthetic failure, wound healing disturbances, etc.), erythrocyte sedimentation rate > 30 mm/h, or C-reactive protein elevated more than 1.5 times above the laboratory reference value	14.60%	Mix of Knee and Hip	0.917	0.903	High

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Part III. Tissue Tests

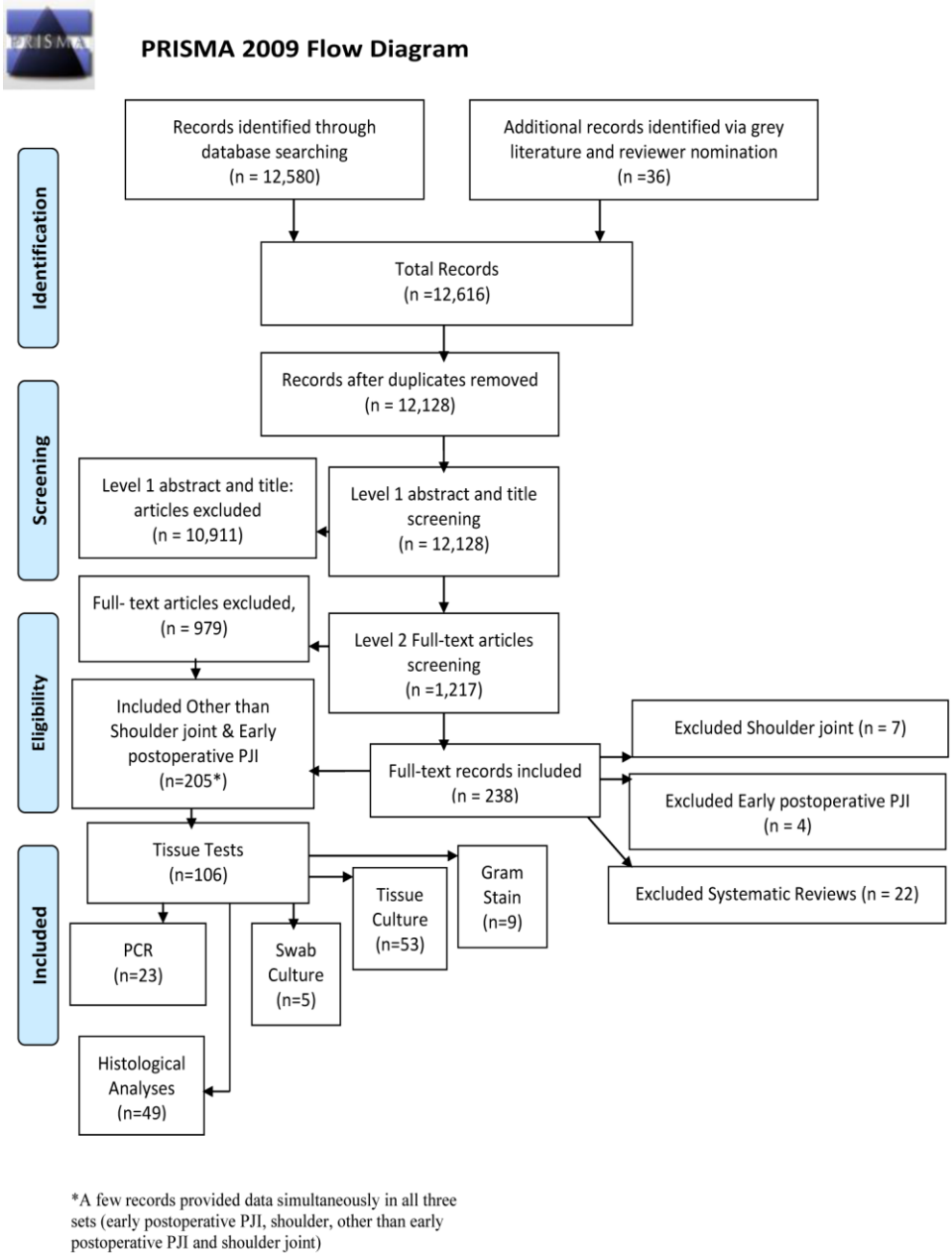

Figure A11: PRISMA for Tissue-based Tests

http://dx.doi.org/10.2106/JBJS.18.00632

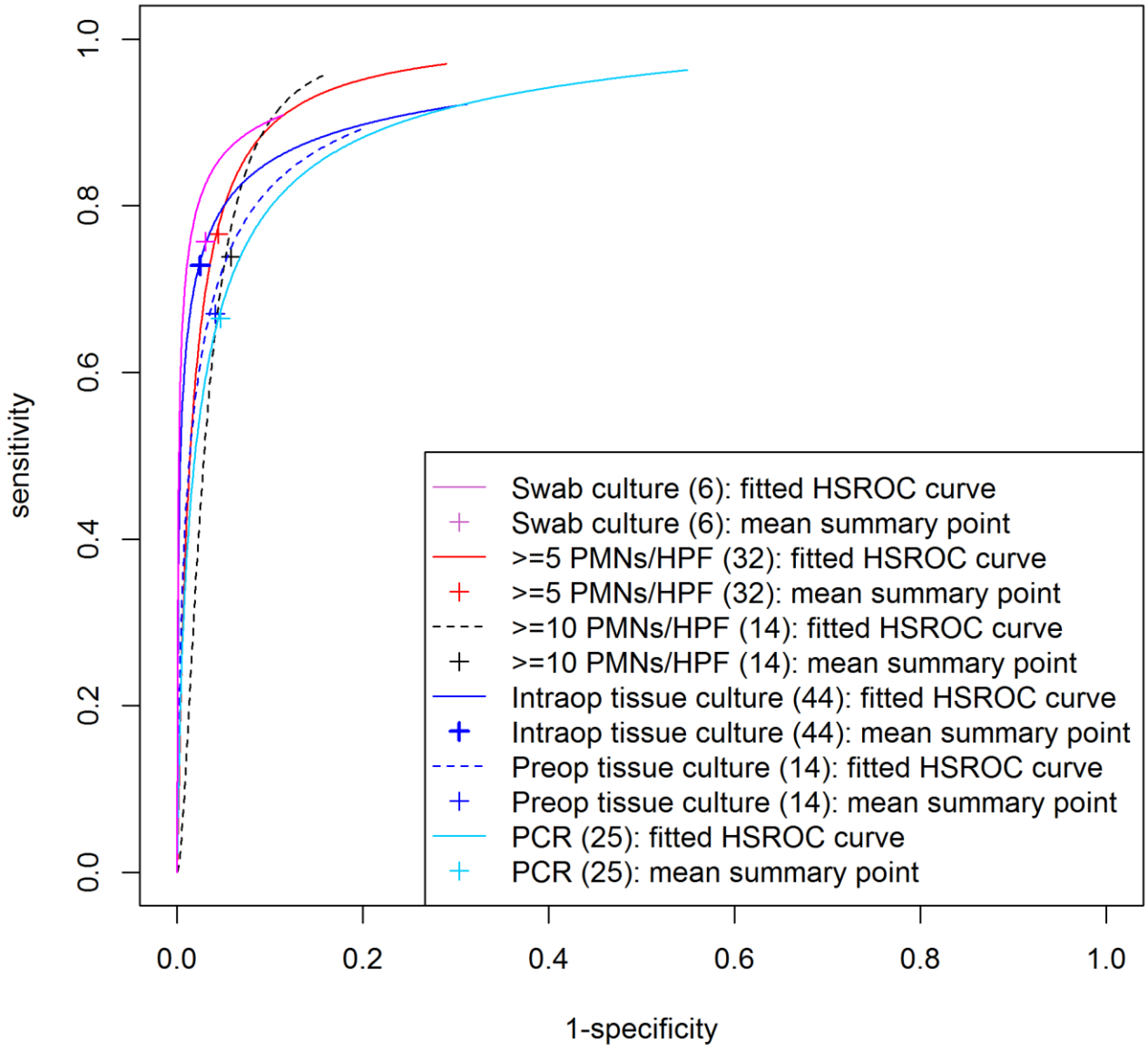

Figure A12: Fitted HSROC curves and mean summary points for tissue tests (swab culture added). The number inside the parenthesis is the records of data corresponding to each test.

In studies that utilized tissue culture as the reference standard, only preoperative tissue culture, histological analysis and PCR had sufficient data for fitted HSROC curves; they had equivalent performance (Figure A13).

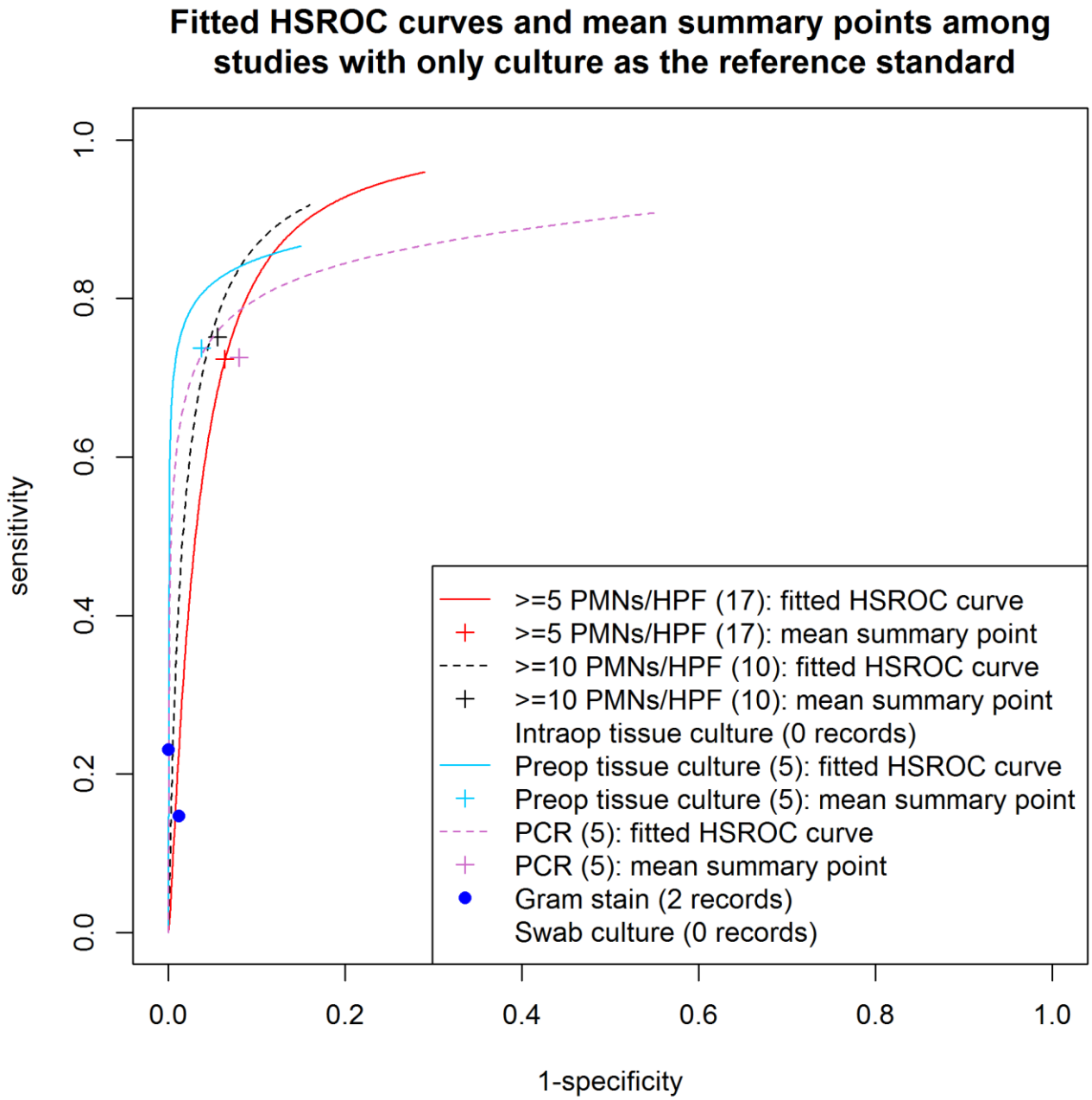

Figure A13: Fitted HSROC curves and mean summary points for synovial tests among studies with tissue culture as the reference standard. The number inside the parenthesis is the records of data corresponding to each test.

PCR:

Of the 106 studies on tissue tests, 23 reported data on PCR[63,87,110,132,135,136,139,141,142,145,148,184,211,222,224,235,236,238,243,245,246,253,261] and 21 of them were included in the

meta-analysis. Two studies were not included in the meta-analysis due to contradiction during the "agreement verification" process of the reported sensitivity and/or specificity[238] or having used a different technique[145].

Swab Culture

Of the 106 studies on tissue tests, five provided data on swab culture[104,208,209,223,228] and four of them were included in the meta-analysis. One study was not included in the meta-analysis for having reported sensitivity and/or specificity that did not agree with the reported counts for chronic PJI [208].

Tissue Culture

Of the 106 studies on tissue tests, 53 reported on tissue culture. Among them[12,62,66,68,78,79,81,86,87,104,112–114,116–119,126,127,130,131,133,135,136,139–143,145,147,208,209,223,225,231,233,237,240–244,246–249,251–255,260], 38 studies which contributed data about intraoperative tissue culture (Table A27) and 13 which contributed data about preoperative tissue culture (Table A28) were meta-analyzed separately. Two studies were not included in the meta-analysis (one for having reported sensitivity and/or specificity that did not agree with the reported counts for chronic PJI[208], and one for contradiction during the "agreement verification" process of the reported sensitivity and/or specificity[248]).

Gram Stain

Of the 106 studies on tissue tests, nine provided data on Gram stain[104,106,123,128,212–214,259,260] and all of them were included in the meta-analysis except one[106] that did not report sufficient information.

Histological Analyses

Of the 106 studies on tissue tests, 49 reported data on histological analyses[12,62,63,66,68,74,78–81,83,87,103,104,108,114,117,118,120,125–127,129,136–138,141,144,146,214–220,226,227,229,230,232,234,239,249,250,256–258,262]. Among them, 32 studies were included in the meta-analyses of > or >=5 PMNs/HPF and > or >=10 PMNs/HPF, and 17 were not (one for insufficient information[227], one for contradiction during the "agreement verification" process of the reported sensitivity and/or specificity[74,125], and 14 for using a different/unclear criterion or technique[62,66,78,217,256,126,127,136,137,114,117,249,141,118]).

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Table A4: Diagnostic accuracy of tissue-based tests with <=4 studies for which meta-analyses (bivariate model) were not performed

Author name (publication year); sample size	Index Test	Reference Standard	Cut off	Joints	Sensitivity (95% CI)	Specificity (95% CI)	Risk of Bias
Virolainen et al. (2002)[106] n=68	joint aspiration, staining	tissue culture alone	NR	Mix of Knee and Hip	0.67	1.00	Unclear
Marin et al. (2012)[211] n=122	Tissue AND/OR synovial fluid culture	One of: 1. purulence in the synovial fluid or around the prosthesis 2. acute inflammation detected in the histological examination of periprosthetic tissue 3. a sinus tract communicating with the prosthesis	>/= 1 sample positive	Mix of Knee, Hip Shoulder, and Elbow (1)	0.878 (0.745, 0.947)	0.671 (0.563, 0.763)	Unclear
Marin et al. (2012) [211]	Tissue AND/OR synovial fluid culture		>/= 2 sample positive		0.610 (0.457, 0.743)	0.939 (0.865, 0.974)	Unclear
Marin et al. (2012) [211]	Tissue AND/OR synovial fluid culture		>/= 3 sample positive		0.463 (0.321, 0.613)	0.988 (0.934, 0.998)	Unclear
Marin et al. (2012) [211] n=497	Tissue AND/OR synovial fluid culture		Positive culture		0.759 (0.688, 0.819)	0.812 (0.767, 0.850)	Unclear
Levine et al. (2001)[209] n=34	Vial culture	Clinical diagnosis of the patient's infection status was made based on the pre-ponderance of data and in accordance with the Centers for Disease Control recommendations	NR	Mix of Knee and Hip	0.92	1.00	High
Smith et al. (2014)[221] n=190	Broth-only culture	2011 MSIS criteria	Change in Turbidity	Mix of Knee and Hip	0.19 (0.46, 0.40)	0 .88 (0.82, 0.93)	High
Titecat et al. (2012)[210] n=104	mecA gene rapid molecular assay:methicillin-resistant staphylococci (MRS) by Xpert® technology	tissue culture alone	positive	Mix of Knee and Hip	0.871	1.000	Unclear
Titecat et al. (2012) [210] n=30	mecA gene rapid molecular assay:methicillin-resistant staphylococci (MRS) by Xpert® technology	tissue culture alone	positive	Mix of Knee and Hip	0.923	1.000	Unclear
Nilsdotter-Augustinsson et al. (2007)[83]	Plasma cells	Criteria for infection: -orthopedic surgeon preoperatively classified the prosthetic loosening as being due to deep	>=1	Hip	0.48	1.00	High

n=46		infection of device, based on clinical symptoms, laboratory and radiographic findings, preoperative cultures of synovial fluid aspiration, or occurrence of fistulas AND/OR -surgeon deemed the patient infected because significant bacterial grwoth wass observed in cultures from tissue samples taken at revision surgery and th surgeion decided to treat the patient as being infected					
Nilsdotter-Augustinsson et al. (2007)[83] n=46	B-cells		>=1	Hip	0.86	0.96	High
Nilsdotter-Augustinsson et al. (2007) [83] n=46	T-helper cells		>=5	Hip	0.71	0.20	High
Nilsdotter-Augustinsson et al. (2007) [83] n=46	T-cytox cells		>=20	Hip	0.52	0.92	High

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Clinical Exams:

Only three studies provided data on the following clinical exams (Table A5):

Table A5: Diagnostic accuracy of clinical exam tests with <=4 studies for which meta-analyses (bivariate model) were not performed

Author name (publication year); sample size	Index Test	Reference Standard	Cut off	Joints	Sensitivity (95% CI)	Specificity (95% CI)	Risk of Bias
Bernard et al. (2004)[89] n=230	Fever	One intraoperative culture was positive and associated with purulence for a particularly virulent organism and for low virulence, a minimum of 3 positive intraoperative cultures with identical phenotype bacteria profile	Not applicable	Mix of Knee and Hip	0.53	0.90	Unclear
	Presence of fistula		Not applicable	Mix of Knee and Hip	0.31	0.95	Unclear
Pons et al. (1999)[129] n=80	Questionnaire and clinical exam	Tissue culture + histology; Microbiological and histological examination	At least one positive answer to: -presence of pain during interview -chronic pain -previous episode of drainage or fever for more than 48 hours in the first month after primary operation	Hip	0.625	0.980	High
Teller et al. (2000)[122] n=166	Temperature (fever)	tissue culture alone; intraoperative culture	99.5 de F	hip or knee	0.90 (0.11, 0.292)	0.96 (0.941, 0.975)	High
	erythema, warmth or edema	tissue culture alone; intraoperative culture	clinical	hip or knee	0.18 (0.52, 0.403)	1.00 (0.98,1.00)	High

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Appendix C: List of included studies with their characteristics

Note: In the tables below (A6-A28), in the "Agreement Verification" column, studies that are labeled as "rounding of counts contradicted reported se, sp" were not used in our meta-analyses (bivariate model) because they had contradiction during the "agreement verification" process of the reported sensitivity and/or specificity (Appendix B).

Serum Tests

Table A6: Serum CRP

Study	Joint	Cutoff mg/L	Ref	Total	PJI	Aseptic	sens_as_report	spec_as_report	TP	TN	FP	FN	Risk of Bias	Agreement Verification
Randau (2014) [60]	mixed	9.1	0	120	48	72	0.617	0.8261	29.616	59.4792	12.5208	18.384	high	rounding of counts contradicted reported se, sp
Worthington (2010) [75]	hips	10	0	46	16	30	0.94	0.97	15	29	1	1	high	replied by authors
Deirmengian (2010) [76]	mixed	10	1	51	14	37	0.71	0.86	9.94	31.82	5.18	4.06	unclear	rounding of counts did not contradict reported se, sp to the 1% decimal place
Fink (2008) [81]	knees	13.5	1	145	40	105	0.725	0.809	29	85	20	11	unclear	counts as reported
Janz (2013) [66]	mixed	NR	0	59	23	36	0.83	0.72	19	26	10	4	high	counts as reported
Fink (2013) [68]	hips	10	1	100	45	55	0.64	0.75	29	41	14	16	unclear	counts as reported
Buttaro (2010) [74]	hips	10	0	69	11	58	0.72	0.91	7.92	52.78	5.22	3.08	high	rounding of counts contradicted reported se, sp
Piper (2010) [77]	knees	10	0	297	82	215	0.83	0.79	68	170	45	14	high	counts as reported
Piper (2010) [77]	knees	14.5	0	297	82	215	0.79	0.88	65	189	26	17	high	counts as reported
Piper (2010) [77]	hips	10	0	221	34	187	0.74	0.78	25	146	41	9	high	counts as reported
Piper (2010) [77]	hips	10.3	0	221	34	187	0.74	0.79	25	147	40	9	high	counts as reported
Schinsky (2008) [79]	hips	100	0	201	55	146	0.94	0.71	51.7	103.66	42.34	3.3	high	rounding of counts contradicted reported se, sp

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Muller (2008) [62]	hips	5	0	50	37	13	0.95	0.62	35.15	8.06	4.94	1.85	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Miyamae (2013) [63]	mixed	10	1	81	10	71	0.9	0.85	9	60.35	10.65	1	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Alijanipour (2013) [64]	hips	13.5	0	1068	57	1011	0.9	0.88	51	888	123	6	high	replied by authors
Alijanipour (2013) [64]	knees	23.5	0	759	165	594	0.92	0.94	151.8	558.36	35.64	13.2	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Alijanipour (2013) [64]	hips	10	0	1203	108	1095	0.881	0.774	95.148	847.53	247.47	12.852	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Alijanipour (2013) [64]	knees	10	0	713	119	594	0.966	0.702	115	416	178	4	high	replied by authors
Kanner (2008) [80]	mixed	8-250	0	71	16	55	0.88	0.65	14	36	19	2	high	counts as reported
Bernard (2004) [89]	mixed	10	1	228	207	21	0.97	0.81	200	17	4	7	unclear	counts as reported
Bare (2006) [86]	knees	10	0	222	75	147	0.6	0.63	45	92.61	54.39	30	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Austin (2008) [82]	knees	10	0	296	116	180	0.94	0.74	109.04	133.2	46.8	6.96	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Cipriano (2012) [72]	mixed	15	0	810	146	664	0.858	0.834	125.268	553.776	110.224	20.732	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Della Valle (2007) [120]	knees	10	0	94	41	53	0.951	0.755	38.991	40.015	12.985	2.009	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Spangehl (1999) [104]	hips	10	0	142	26	116	0.96	0.92	25	107	9	1	high	counts as reported
Bingham (2014) [91]	mixed	10	0	61	19	42	0.79	0.66	15.01	27.72	14.28	3.99	high	rounding of counts contradicted reported se, sp
Morgan (2009) [123]	knees	10	0	697	215	482	0.3	1	58	481	1	157	high	counts as reported
Tetreault (2014) [105]	mixed	11.2	0	119	32	87	0.97	0.76	31.04	66.12	20.88	0.96	high	rounding of counts did not contradict reported se, sp to the 1% decimal place

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Tetreault (2014) [105]	hips	11.2	0	59	15	44	1	0.84	15	36.96	7.04	0	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Tetreault (2014) [105]	knees	21.2	0	60	17	43	0.88	0.84	14.96	36.12	6.88	2.04	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Ronde-Oustau (2014) [59]	knees	14.95	0	31	10	21	1	0.77	10	16.17	4.83	0	high	rounding of counts contradicted reported se, sp
Ronde-Oustau (2014) [59]	knees	51.75	0	31	10	21	0.5	0.888	5	18.648	2.352	5	high	rounding of counts contradicted reported se, sp
Wu (2014) [125]	mixed	10	0	156	37	119	0.92	0.69	34.04	82.11	36.89	2.96	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Wu (2014) [125]	mixed	15	0	156	37	119	0.92	0.84	34.04	99.96	19.04	2.96	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Wu (2014) [125]	mixed	20	0	156	37	119	0.67	0.85	24.79	101.15	17.85	12.21	high	rounding of counts contradicted reported se, sp
Cansü (2014) [92]	hips	10	1	31	8	23	NR	NR	7	17	6	1	high	counts as reported
Tohtz (2010) [78]	hips	10	0	64	19	45	0.579	0.8	11.001	36	9	7.999	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Liu (2014) [100]	knees	14	0	38	28	10	0.958	0.786	26.824	7.86	2.14	1.176	high	rounding of counts contradicted reported se, sp
Liu (2014) [100]	knees	10	0	38	28	10	0.958	0.642	26.824	6.42	3.58	1.176	high	rounding of counts contradicted reported se, sp
Ramsingh (2010) [103]	mixed	NR	1	53	9	44	0.89	0.75	8.01	33	11	0.99	unclear	rounding of counts did not contradict reported se, sp to the 1% decimal place
Elgeidi (2014) [95]	mixed	18	0	40	11	29	1	0.862	11	24.998	4.002	0	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Ettinger (2015) [96]	mixed	3	0	98	41	57	0.8	0.64	32.8	36.48	20.52	8.2	high	rounding of counts contradicted reported se, sp
Claassen (2014) [94]	knees	5	0	77	31	46	0.48	0.61	14.88	28.06	17.94	16.12	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Claassen (2014) [94]	knees	23	0	77	31	46	0.29	0.89	8.99	40.94	5.06	22.01	high	rounding of counts did not contradict reported se, sp to the 1% decimal place

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Itasaka (2001) [98]	hips	3	1	48	6	42	0.83	0.76	5	32	10	1	unclear	counts as reported
Omar (2015) [101]	hips	9.5	0	80	21	59	0.783	0.864	16.443	50.976	8.024	4.557	high	rounding of counts contradicted reported se, sp
Petti (2015) [102]	mixed	NR	0	79	41	38	0.95	0.75	38.95	28.5	9.5	2.05	high	rounding of counts contradicted reported se, sp
Parvizi (2012) [124]	knees	16.5	0	55	25	30	0.76	0.933	19	27.99	2.01	6	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Greidanus (2007) [84]	knees	10	1	151	45	106	0.93	0.83	41.85	87.98	18.02	3.15	unclear	rounding of counts did not contradict reported se, sp to the 1% decimal place
Greidanus (2007) [84]	knees	13.5	1	151	45	106	0.91	0.86	40.95	91.16	14.84	4.05	unclear	rounding of counts did not contradict reported se, sp to the 1% decimal place
Di Cesare (2005) [88]	mixed	10	1	58	17	41	0.94	0.78	15.98	31.98	9.02	1.02	unclear	rounding of counts did not contradict reported se, sp to the 1% decimal place
Glehr (2013) [65]	mixed	23.65	0	84	55	29	0.8	0.79	44	22.91	6.09	11	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Glehr (2013) [65]	mixed	10.25	0	84	55	29	0.91	0.72	50.05	20.88	8.12	4.95	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Glehr (2013) [65]	mixed	17.05	0	84	55	29	0.84	0.79	46.2	22.91	6.09	8.8	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Schwartz (2012) [69]	knees	14	0	158	28	130	0.826	0.807	23.128	104.91	25.09	4.872	high	rounding of counts contradicted reported se, sp
Johnson (2011) [73]	knees	10	0	113	105	8	0.95	0.2	99.75	1.6	6.4	5.25	high	rounding of counts contradicted reported se, sp
Randau (2011) [90]	mixed	10	0	103	32	71	0.5	0.77	16	54.67	16.33	16	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Bottner (2007) [85]	mixed	32	1	78	21	57	0.95	0.96	19.95	54.72	2.28	1.05	unclear	rounding of counts did not contradict reported se, sp to the 1% decimal place
Bottner (2007) [85]	mixed	15	1	78	21	57	0.95	0.91	19.95	51.87	5.13	1.05	unclear	rounding of counts did not contradict reported se, sp to the 1% decimal place
Panousis (2005) [87]	mixed	10	0	92	12	80	0.67	0.64	8.04	51.2	28.8	3.96	high	rounding of counts did not contradict reported se, sp to the 1% decimal place

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Yuan (2015) [107]	hips	15	0	71	25	46	0.76	0.717	19	33	13	6	high	counts as reported
Nilsdotter-Augustinsson (2007) [83]	hips	10	0	124	22	102	0.82	0.71	18.04	72.42	29.58	3.96	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Ghanem (2009) [121]	hips	10	0	479	127	352	0.911	0.766	115.697	269.632	82.368	11.303	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Ghanem (2009) [121]	hips	20.5	0	479	127	352	0.943	0.81	119.761	285.12	66.88	7.239	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Frangiamore (2016) [108]	mixed	10	0	78	24	54	0.83	0.79	19.92	42.66	11.34	4.08	high	rounding of counts contradicted reported se, sp
Pohlig (2017) [116]	hips	5	0	20	8	12	0.75	0.667	6	8.004	3.996	2	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Rothenberg (2017) [12]	mixed	10	0	338	149	189	0.85	0.78	126	147	42	23	high	counts as reported
Fernandez-Sampedro (2018) [114]	mixed	10	0	495	128	367	0.703	0.845	90	310	57	38	high	counts as reported
Berger (2017) [115]	mixed	10	0	121	34	87	0.706	0.816	24.004	70.992	16.008	9.996	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Sigmund (2017) [117]	mixed	10	0	49	13	36	0.77	0.78	10.01	28.08	7.92	2.99	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Stylianakis (2018) [119]	mixed	10	0	70	21	49	0.9048	0.8571	19	42	7	2	high	counts as reported
Fink (2018) [110]	knees	10	1	116	27	89	0.593	0.82	16	73	16	11	unclear	counts as reported
Wouthuyzen-Bakker (2018) [111]	mixed	10	0	52	15	37	0.667	0.704	10.005	26.048	10.952	4.995	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Sebastiana (2018) [112]	mixed	10	0	40	27	13	0.925	0.924	25	12	1	2	high	counts as reported
Tani (2018) [113]	mixed	10	0	114	61	53	0.541	0.547	33	29	24	28	high	counts as reported
Claassen (2016) [118]	knees	5	0	32	8	26	0.38	0.73	3	19	7	5	high	counts as reported

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Abbreviations: 0=mixed reference standard (culture and non-culture); 1=culture as reference standard; FP=false positive; FN=false negative; Ref= reference standard; se, sens=sensitivity; sp, spec=specificity; TP=true positive; TN=true negative

Table A7: Serum ESR

Study	Joint	Cutoff mm/hr	Ref	Total	N_w_inf	N_wo_inf	sens_as_report	spec_as_report	TP	TN	FP	FN	Risk of Bias	Agreement Verification
Worthington (2010) [75]	hips	30	0	46	16	30	0.81	1	13	30	0	3	high	replied by authors
Deirmengian (2010) [76]	mixed	30	1	51	14	37	0.86	0.73	12.04	27.01	9.99	1.96	unclear	rounding of counts did not contradict reported se, sp to the 1% decimal place
Buttaro (2010) [74]	hips	NR	0	69	11	58	0.72	0.86	7.92	49.88	8.12	3.08	high	rounding of counts contradicted reported se, sp
Piper (2010) [77]	knees	30	0	297	82	215	0.71	0.89	58	191	24	24	high	counts as reported
Piper (2010) [77]	knees	19	0	297	82	215	0.89	0.74	73	159	56	9	high	counts as reported
Piper (2010) [77]	hips	30	0	221	34	187	0.47	0.84	16	158	29	18	high	counts as reported
Piper (2010) [77]	hips	13	0	221	34	187	0.82	0.6	28	113	74	6	high	counts as reported
Schinsky (2008) [79]	hips	30	0	201	55	146	0.97	0.39	53.35	56.94	89.06	1.65	high	rounding of counts contradicted reported se, sp
Alijanipour (2013) [64]	hips	48.5	0	1153	58	1095	0.78	0.9	46	986	109	12	high	replied by authors
Alijanipour (2013) [64]	knees	46.5	0	759	165	594	0.87	0.87	143.55	516.78	77.22	21.45	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Alijanipour (2013) [64]	hips	30	0	1203	108	1095	0.947	0.712	102.276	779.64	315.36	5.724	high	rounding of counts contradicted reported se, sp
Alijanipour (2013) [64]	knees	30	0	759	165	594	0.941	0.683	155.265	405.702	188.298	9.735	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Kanner (2008) [80]	mixed	16-120	0	72	18	54	0.78	0.54	14	29	25	4	high	counts as reported

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Bernard (2004) [89]	mixed	30	1	171	156	15	0.87	0.47	136	7	8	20	unclear	counts as reported
Bare (2006) [86]	knees	30	0	242	75	167	0.63	0.55	47.25	91.85	75.15	27.75	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Austin (2008) [82]	knees	30	0	296	116	180	0.91	0.72	105.56	129.6	50.4	10.44	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Cipriano (2012) [72]	mixed	32	0	810	146	664	0.872	0.671	127.312	445.544	218.456	18.688	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Della Valle (2007) [120]	knees	30	0	94	41	53	0.902	0.66	36.982	34.98	18.02	4.018	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Spangehl (1999) [104]	hips	30	0	171	34	137	0.82	0.85	28	117	20	6	high	counts as reported
Bingham (2014) [91]	mixed	30	0	61	19	42	0.5	0.8	9.5	33.6	8.4	9.5	high	rounding of counts contradicted reported se, sp
Morgan (2009) [123]	knees	30	0	831	241	590	0.3	1	66	589	1	175	high	counts as reported
Wu (2014) [125]	mixed	20	0	156	37	119	0.92	0.45	34.04	53.55	65.45	2.96	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Wu (2014) [125]	mixed	30	0	156	37	119	0.75	0.69	27.75	82.11	36.89	9.25	high	rounding of counts contradicted reported se, sp
Wu (2014) [125]	mixed	40	0	156	37	119	0.58	0.78	21.46	92.82	26.18	15.54	high	rounding of counts contradicted reported se, sp
Cansü (2014) [92]	hips	30	1	31	8	23	NR	NR	8	12	11	0	high	counts as reported
Levitsky (1991) [174]	mixed	30	0	62	10	52	0.6	0.654	6	34	18	4	high	counts as reported
Liu (2014) [100]	knees	32.5	0	38	28	10	0.917	0.857	25.676	8.57	1.43	2.324	high	rounding of counts contradicted reported se, sp
Liu (2014) [100]	knees	30	0	38	28	10	0.913	0.8	25.564	8	2	2.436	high	rounding of counts contradicted reported se, sp
Elgeidi (2014) [95]	mixed	45	0	40	11	29	0.818	0.828	8.998	24.012	4.988	2.002	high	rounding of counts did not contradict reported se, sp to the 1% decimal place

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Itasaka (2001) [98]	hips	30	1	48	6	42	0.67	0.74	4	31	11	2	unclear	counts as reported
Omar (2015) [101]	hips	29	0	80	21	59	0.767	0.909	16.107	53.631	5.369	4.893	high	rounding of counts contradicted reported se, sp
Petti (2015) [102]	mixed	NR	0	67	35	32	0.9	0.79	31.5	25.28	6.72	3.5	high	rounding of counts contradicted reported se, sp
Tohtz (2010) [78]	hips	30	0	64	19	45	0.737	0.889	14.003	40.005	4.995	4.997	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Milone (2014) [61]	mixed	45	0	98	8	90	0.75	0.82	6	73.8	16.2	2	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Milone (2014) [61]	mixed	30	0	98	8	90	0.89	0.52	7.12	46.8	43.2	0.88	high	rounding of counts contradicted reported se, sp
Greidanus (2007) [84]	knees	30	1	151	45	106	0.82	0.87	36.9	92.22	13.78	8.1	unclear	rounding of counts did not contradict reported se, sp to the 1% decimal place
Greidanus (2007) [84]	knees	22.5	1	151	45	106	0.93	0.83	41.85	87.98	18.02	3.15	unclear	rounding of counts did not contradict reported se, sp to the 1% decimal place
Di Cesare (2005) [88]	mixed	30	1	58	17	41	1	0.56	17	22.96	18.04	0	unclear	rounding of counts did not contradict reported se, sp to the 1% decimal place
Schwartz (2012) [69]	knees	27	0	172	28	144	0.792	0.73	22.176	105.12	38.88	5.824	high	rounding of counts contradicted reported se, sp
Johnson (2011) [73]	knees	30	0	113	105	8	0.91	0.33	95.55	2.64	5.36	9.45	high	rounding of counts contradicted reported se, sp
Bottner (2007) [85]	mixed	32	1	78	21	57	0.81	0.89	17.01	50.73	6.27	3.99	unclear	rounding of counts did not contradict reported se, sp to the 1% decimal place
Panousis (2005) [87]	mixed	30	0	92	12	80	0.75	0.68	9	54.4	25.6	3	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Teller (2000) [122]	mixed	40	0	132	17	115	0.29	0.88	5	101	14	12	high	counts as reported
Nilsdotter-Augustinsson (2007) [83]	hips	30	0	122	22	100	0.64	0.87	14.08	87	13	7.92	high	rounding of counts did not contradict reported se, sp to the 1% decimal place

Ghanem (2009) [121]	hips	30	0	479	127	352	0.943	0.702	119.761	247.104	104.896	7.239	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Ghanem (2009) [121]	hips	31	0	479	127	352	0.945	0.722	120.015	254.144	97.856	6.985	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Frangiamore (2016) [108]	mixed	10	0	78	24	54	0.58	0.81	13.92	43.74	10.26	10.08	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Pohlig (2017) [116]	hips	30	0	20	8	12	0.75	0.875	6	10.5	1.5	2	high	rounding of counts contradicted reported se, sp
Rothenberg (2017) [12]	mixed	30	0	341	150	191	0.88	0.78	132	149	42	18	high	counts as reported
Berger (2017) [115]	mixed	30	0	79	21	58	0.476	0.828	10	48	10	11	high	back calculated using sens, spec, ppv, npv, accuracy
Stylianakis (2018) [119]	mixed	30	0	37	11	26	0.8182	0.8077	9	21	5	2	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Wouthuyzen-Bakker (2018) [111]	mixed	30	0	47	11	36	0.727	0.696	7.997	25.056	10.944	3.003	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Sebastiana (2018) [112]	mixed	30	0	40	27	13	0.962	0.924	26	12	1	1	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Tani (2018) [113]	mixed	30	0	114	61	53	0.656	0.679	40	36	17	21	high	rounding of counts did not contradict reported se, sp to the 1% decimal place

Abbreviations: 0=mixed reference standard (culture and non-culture); 1=culture as reference standard; FP=false positive; FN=false negative; Ref= reference standard; se, sens=sensitivity; sp, spec=specificity; TP=true positive; TN=true negative

Table A8: Serum IL-6

Study	Joint	Cutoff pg/mL	Ref	Total	PJI	Aseptic	sens_as_report	spec_as_report	TP	TN	FP	FN	Risk of Bias	Agreement Verification
Randau (2014) [60]	mixed	2.6	0	120	48	72	0.7949	0.5833	38.1552	41.9976	30.0024	9.8448	high	rounding of counts did not contradict reported se, sp to the 1% decimal place

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Randau (2014) [60]	mixed	6.6	0	120	48	72	0.4872	0.8833	23.3856	63.5976	8.4024	24.6144	high	rounding of counts contradicted reported se, sp
Worthington (2010) [75]	hips	9	0	46	16	30	0.81	0.77	13	23	7	3	high	replied by authors
Buttaro (2010) [74]	hips	10	0	69	11	58	0.36	0.94	3.96	54.52	3.48	7.04	high	rounding of counts contradicted reported se, sp
Gollwitzer (2013) [67]	mixed	1.89	0	35	15	20	0.467	0.95	7.005	19	1	7.995	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Elgeidi (2014) [95]	mixed	10.4	0	44	11	33	1	0.909	11	30	3	0	high	replied by authors
Ettinger (2015) [96]	mixed	5.12	0	98	41	57	0.8	0.877	32.8	49.989	7.011	8.2	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Di Cesare (2005) [88]	mixed	10	1	58	17	41	1	0.95	17	38.95	2.05	0	unclear	rounding of counts did not contradict reported se, sp to the 1% decimal place
Randau (2011) [90]	mixed	8	0	103	32	71	0.4	0.8	12.8	56.8	14.2	19.2	high	rounding of counts contradicted reported se, sp
Bottner (2007) [85]	mixed	12	1	78	21	57	0.95	0.87	19.95	49.59	7.41	1.05	unclear	rounding of counts contradicted reported se, sp
Gallo (2018) [109]	mixed	12.55	0	197	83	114	0.867	0.895	72	102	12	11	high	counts as reported

Abbreviations: 0=mixed reference standard (culture and non-culture); 1=culture as reference standard; FP=false positive; FN=false negative; Ref= reference standard; se, sens=sensitivity; sp, spec=specificity; TP=true positive; TN=true negative

Table A9: Serum Procalcitonin

Study	Joint	Cutoff ng/mL	Ref	Total	PJI	Aseptic	sens_as_report	spec_as_report	TP	TN	FP	FN	Risk of Bias	Agreement Verification
Randau (2014) [60]	mixed	46	0	120	48	72	0.129	1	6.192	72	0	41.808	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Ettinger (2015) [96]	mixed	0.025	0	98	41	57	0.9	0.278	36.9	15.85	41.15	4.1	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Glehr (2013) [65]	mixed	0.055	0	65	41	24	0.81	0.54	33	13	11	8	high	replied by authors

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Glehr (2013) [65]	mixed	0.035	0	65	41	24	0.9	0.33	37	8	16	4	high	replied by authors
Glehr (2013) [65]	mixed	0.75	0	47	27	20	0.48	1	13	20	0	14	high	replied by authors
Randau (2011) [90]	mixed	0.04	0	103	32	71	0.13	1	4.16	71	0	27.84	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Bottner (2007) [85]	mixed	0.3	1	78	21	57	0.33	0.98	6.93	55.86	1.14	14.07	unclear	rounding of counts did not contradict reported se, sp to the 1% decimal place
Yuan (2015) [107]	hips	0.5	0	71	25	46	0.8	0.739	20	34	12	5	high	counts as reported

Abbreviations: 0=mixed reference standard (culture and non-culture); 1=culture as reference standard; FP=false positive; FN=false negative; Ref= reference standard; se, sens=sensitivity; sp, spec=specificity; TP=true positive; TN=true negative

Table A10: Serum TNF-alpha

Study	Joint	Cutoff	Ref	Total	PJI	Aseptic	sens_as_report	spec_as_report	TP	TN	FP	FN	Risk of Bias	Agreement Verification
Ettinger (2015) [96]	mixed	0.0119 ng/mL	0	98	41	57	0.35	0.86	14.35	49.02	7.98	26.65	high	rounding of counts contradicted reported se, sp
Bottner (2007) [85]	mixed	40 ng/mL	1	78	21	57	0.43	0.94	9.03	53.58	3.42	11.97	unclear	rounding of counts contradicted reported se, sp

Abbreviations: 0=mixed reference standard (culture and non-culture); 1=culture as reference standard; FP=false positive; FN=false negative; Ref= reference standard; se, sens=sensitivity; sp, spec=specificity; TP=true positive; TN=true negative

Table A11: Serum WBC

Study	Joint	Cutoff cells /μL	Ref	Total	PJI	Aseptic	sens_as_report	spec_as_report	TP	TN	FP	FN	Risk of Bias	Agreement Verification
Randau (2014) [60]	mixed	10300	0	120	48	72	0.2128	0.9444	10.2144	67.9968	4.0032	37.7856	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Muller (2008) [62]	hips	12000	0	50	37	13	0.14	0.92	5.18	11.96	1.04	31.82	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Bernard (2004) [89]	mixed	6000	1	228	207	21	0.54	0.81	112	17	4	95	unclear	counts as reported

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Spangehl (1999) [104]	hips	11000	0	202	35	167	0.2	0.96	7	161	6	28	high	counts as reported
Bingham (2014) [91]	mixed	1700	0	61	19	42	0.95	0.85	18.05	35.7	6.3	0.95	high	rounding of counts contradicted reported se, sp
Morgan (2009) [123]	knees	11000	0	903	244	659	0.3	1	67	658	1	177	high	counts as reported
Elgeidi (2014) [95]	mixed	9200	0	40	11	29	0.909	0.759	9.999	22.01	6.99	1.001	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Claassen (2014) [94]	knees	10000 (Female) or 9100 (Male)	0	77	31	46	0.23	0.98	7.13	45.08	0.92	23.87	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Itasaka (2001) [98]	hips	9000	1	48	6	42	0.33	0.91	2	38	4	4	unclear	counts as reported
Tohtz (2010) [78]	hips	10000	0	64	19	45	0.21	0.91	3.99	40.95	4.05	15.01	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Milone (2014) [61]	mixed	8100	0	81	8	73	0.5	0.77	4	56.21	16.79	4	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Di Cesare (2005) [88]	mixed	11000	1	58	17	41	0.47	1	7.99	41	0	9.01	unclear	rounding of counts did not contradict reported se, sp to the 1% decimal place
Glehr (2013) [65]	mixed	6270	0	84	55	29	0.8	0.48	44	13.92	15.08	11	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Glehr (2013) [65]	mixed	5480	0	84	55	29	0.91	0.34	50.05	9.86	19.14	4.95	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Glehr (2013) [65]	mixed	7355	0	84	55	29	0.73	0.72	40.15	20.88	8.12	14.85	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Toossi (2012) [70]	mixed	7800	0	1856	751	1105	0.55	0.66	413.05	729.3	375.7	337.95	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Randau (2011) [90]	mixed	10000	0	103	32	71	0.3	0.8	9.6	56.8	14.2	22.4	high	rounding of counts contradicted reported se, sp
Bottner (2007) [85]	mixed	6200	1	78	21	57	0.7	0.6	14.7	34.2	22.8	6.3	unclear	rounding of counts contradicted reported se, sp
Yuan (2015) [107]	hips	10500	0	71	25	46	0.64	0.543	16	25	21	9	high	counts as reported

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Stylianakis (2018) [119]	mixed	10000	0	77	21	56	0.1429	0.9821	3	55	1	18	high	counts as reported
Claassen (2016) [118]	knees	10000 (Female) or 9100 (Male)	0	32	8	26	0	0.88	0	23	3	8	high	counts as reported

Abbreviations: 0=mixed reference standard (culture and non-culture); 1=culture as reference standard; FP=false positive; FN=false negative; Ref= reference standard; se, sens=sensitivity; sp, spec=specificity; TP=true positive; TN=true negative

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Synovial Tests

Table A12: Joint Aspiration Culture

Study	Joint	Cutoff	Ref	Total	PJI	Aseptic	sens_as_report	spec_as_report	TP	TN	FP	FN	Risk of Bias	Agreement Verification
Meermans (2010) [131]	mixed	positive culture: same organism grew on 2 or more specimens	1	120	110	10	0.827	1	91	10	0	19	unclear	counts as reported
Fink (2013) [68]	hips	positive culture: same organism cultured in at least 2 samples	1	100	45	55	0.64	0.96	29	53	2	16	unclear	counts as reported
Williams (2004) [133]	hips	>=2 growth; If 2 or all 3 specimens grew organisms, this was regarded as a positive culture	1	273	71	202	0.8	0.94	57	189	13	14	low	counts as reported
Taylor (1995) [202]	hips	growth	0	86	15	71	0.93	0.96	14	68	3	1	high	counts as reported
Muller (2008) [62]	hips	growth	0	50	37	13	0.57	0.5	21.09	6.5	6.5	15.91	high	rounding of counts contradicted reported se, sp
Cross (2014) [130]	hips	growth of bacteria from plated culture medium	0	110	17	93	0.59	1	10	93	0	7	high	counts as reported
Bernard (2004) [89]	mixed	growth	1	127	111	16	0.82	0.94	91	15	1	20	unclear	counts as reported
Della Valle (2007) [120]	knees	growth of organisms on the solid media	0	86	40	46	0.8	0.933	32	44	2	8	high	replied by authors
Spangehl (1999) [104]	hips	growth in any cultures	0	180	21	159	0.86	0.94	18	150	9	3	high	counts as reported
Spangehl (1999) [104]	hips	growth in any cultures	0	180	21	159	0.81	0.97	17	154	5	4	high	counts as reported
Bingham (2014) [91]	mixed	positive growth culture	0	61	19	42	0.69	0.88	13.11	36.96	5.04	5.89	high	rounding of counts contradicted reported se, sp

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Pons (1999) [129]	hips	microorganism isolated from culture	1	79	16	63	0.62	0.96	10	61	2	6	high	counts as reported
Barrack (1993) [147]	hips	positive growth culture	0	291	10	281	0.6	0.88	6	248	33	4	high	counts as reported
Johnson (1988) [171]	mixed	NR	1	24	8	16	0.12	0.81	1	13	3	7	high	counts as reported
Duff (1996) [170]	knees	growth	1	43	19	24	1	1	19	24	0	0	high	counts as reported
Levitsky (1991) [174]	mixed	single positive culture of a definite pathogen, or multiple positive cultures of same organism	0	55	9	46	0.67	0.96	6	44	2	3	high	counts as reported
Somme (2003) [176]	hips	positive growth culture/Recovered organism	0	107	53	54	0.83	1	44	54	0	9	high	counts as reported
Shen (2014) [175]	mixed	growth	0	110	50	60	0.64	0.98	32	58.8	1.2	18	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Ryu (2014) [135]	knees	any growth	0	89	61	28	0.721	0.964	44	27	1	17	high	counts as reported
Fehring (1996) [126]	hips	positive growth culture	0	164	6	158	0.5	0.88	3	140	18	3	high	counts as reported
Itasaka (2001) [98]	hips	positive culture	1	29	5	24	0.4	0.92	2	22	2	3	unclear	counts as reported
Janz (2015) [127]	knees	NR	0	109	31	78	0.67	0.97	20.77	75.66	2.34	10.23	high	rounding of counts contradicted reported se, sp
Lachiewicz (1996) [173]	hips	growth on the solid medium or if grossly purulent fluid	0	156	27	129	0.85	0.97	23	125	4	4	high	counts as reported
Kraemer (1993) [128]	hips	positive growth culture	1	45	14	31	0.57	0.97	8	30	1	6	unclear	counts as reported
Melendez (2014) [134]	knees	NR	0	103	21	82	0.86	1	18	82	0	3	high	counts as reported
Gallo (2008) [132]	mixed	signs of growth	0	94	46	48	0.435	0.938	20	45	3	26	high	counts as reported

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Tohtz (2010) [78]	hips	growth	0	64	19	45	0.158	0.978	3.002	44.01	0.99	15.998	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Malhotra (2004) [183]	hips	positive culture	0	41	9	32	0.44	0.91	4	29	3	5	high	counts as reported
Van den Bekerom (2006) [168]	knees	positive culture	0	68	45	23	0.84	0.57	32	17	6	13	high	counts as reported
Ali (2006) [169]	hips	growth on any of the cultures obtained at aspiration	1	73	17	56	0.82	0.91	14	51	5	3	high	counts as reported
Panousis (2005) [87]	mixed	positive culture	0	48	10	38	0.7	0.95	7	36.1	1.9	3	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Teller (2000) [122]	mixed	any growth	0	137	18	119	0.28	0.99	5	118	1	13	high	counts as reported
Tigges (1993) [177]	hips	positive growth	1	147	14	133	0.928	0.917	13	122	11	1	high	counts as reported
Morgenstern (2018) [136]	mixed	positive pathogen isolated in solid media culture	0	142	77	65	0.52	0.98	40	64	1	37	high	counts as reported
Pohlig (2017) [116]	hips	at least two positive culture showed growth of the same pathogen	0	20	8	12	0.5	0.917	4	11.004	0.996	4	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Rothenberg (2017) [12]	mixed	NR	0	235	131	94	0.57	1	72	94	0	59	high	counts as reported
Huang (2018) [139]	mixed	any growth	0	67	53	14	0.698	1	37	14	0	16	high	counts as reported
Randelli (2018) [178]	hips	NR	0	26	10	16	0.6	0.81	6	13	3	4	high	counts as reported
Randelli (2018) [178]	hips	NR	0	26	9	17	0.89	0.94	8	16	1	1	high	counts as reported
Fernandez-Sampedro (2018) [114]	mixed	>=2 cultures yielded the same microorganism; only a single positive	0	426	116	310	0.457	1	53	310	0	63	high	counts as reported

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		required when S. aureus or S. lugdunensis were the microorganisms isolated												
Berger (2017) [115]	mixed	NR	0	121	34	87	0.824	0.988	28.016	85.956	1.044	5.984	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Wing (2017) [140]	knees	NR	0	78	9	69	0.55	0.55	5	38	31	4	unclear	counts as reported
Melendez (2016) [148]	knees	NR	0	284	88	196	0.761	0.974	67	191	5	21	high	counts as reported
Radhakrishnan (2015) [179]	hips	NR	1	48	24	24	0.125	1	3	24	0	21	unclear	counts as reported
Bicart-See (2017) [180]	mixed	NR	0	74	46	28	0.46	0.93	21	26	2	25	high	counts as reported
Partridge (2018) [182]	mixed	NR	1	580	192	388	0.84	0.85	161.28	329.8	58.2	30.72	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Lausmann (2017) [142]	mixed	NR	0	60	34	26	NR	NR	25	26	0	9	high	counts as reported
Fink (2018) [110]	knees	same pathogen in at least two of the samples	1	116	27	89	0.74	0.966	20	86	3	7	unclear	counts as reported
Fang (2018) [184]	mixed	at least one positive culture	0	71	38	33	0.66	1	25	33	0	13	high	counts as reported
Larsen (2018) [145]	mixed	at least three positive biopsy specimens in the set of five	0	96	39	57	NR	NR	26	56	1	13	high	counts as reported
Larsen (2018) [145]	mixed	at least three positive biopsy specimens in the set of five	0	95	39	56	NR	NR	34	54	2	5	high	counts as reported

Abbreviations: 0=mixed reference standard (culture and non-culture); 1=culture as reference standard; FP=false positive; FN=false negative; Ref= reference standard; se, sens=sensitivity; sp, spec=specificity; TP=true positive; TN=true negative

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Table A13: Synovial LER Strips

Study	Joint	Cutoff	Ref	Total	PJI	Aseptic	sens_as_report	spec_as_report	TP	TN	FP	FN	Risk of Bias	Agreement Verification
Wetters (2012) [151]	mixed	1+	0	156	18	138	0.933	0.77	16.794	106.26	31.74	1.206	high	rounding of counts contradicted reported se, sp
Wetters (2012) [151]	mixed	1+	0	93	25	68	1	0.868	25	59.024	8.976	0	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Tischler (2014) [194]	mixed	1+	0	189	52	137	0.792	0.808	41.184	110.696	26.304	10.816	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Tischler (2014) [194]	mixed	2+	0	189	52	137	0.66	0.971	34.32	133.027	3.973	17.68	high	rounding of counts contradicted reported se, sp
Shafafy (2015) [155]	mixed	(1+) 70 reading	0	103	21	82	0.857	0.866	17.997	71.012	10.988	3.003	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Shafafy (2015) [155]	mixed	(2+) 125 reading	0	103	21	82	0.818	0.929	17.178	76.178	5.822	3.822	high	rounding of counts contradicted reported se, sp
Deirmengian (2015) [154]	mixed	2+	0	38	16	22	0.688	1	11	22	0	5	high	counts as reported
Colvin (2015) [153]	mixed	2+	0	52	19	33	1	0.97	19	32	1	0	high	counts as reported
Parvizi (2011) [152]	knees	2+	0	108	30	78	0.806	1	24.18	78	0	5.82	high	rounding of counts contradicted reported se, sp
Parvizi (2011) [152]	knees	1+	0	108	30	78	0.935	0.867	28.05	67.626	10.374	1.95	high	rounding of counts contradicted reported se, sp
Parvizi (2011) [152]	knees	2+	0	17	5	12	0.8	1	4	12	0	1	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Parvizi (2011) [152]	knees	1+	0	17	5	12	1	0.417	5	5.004	6.996	0	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Wang (2017) [156]	mixed	2+	0	63	35	28	0.914	0.964	32	27	1	3	high	counts as reported

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Li (2017) [138]	mixed	2+	0	93	38	55	0.921	0.964	35	53	2	3	high	counts as reported
Koh (2017) [157]	knees	2+	0	60	38	22	0.84	1	32	22	0	6	high	counts as reported
Koh (2017) [157]	knees	1+	0	60	38	22	0.9	0.73	34	16	6	4	high	counts as reported
De Vecchi (2016) [160]	mixed	1+	0	129	27	102	0.926	0.97	25	99	3	2	high	counts as reported
Li (2018) [205]	mixed	2+	0	110	43	67	0.977	0.97	42	65	2	1	high	counts as reported
Li (2018) [205]	mixed	1+	0	110	43	67	1	0.821	43	55	12	0	high	counts as reported
Ruangsomboon (2017) [149]	knees	2+	0	46	17	29	0.941	0.896	15.997	25.984	3.016	1.003	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Lausmann (2017) [142]	mixed	2+	0	59	34	25	NR	NR	34	25	0	0	high	counts as reported
Lausmann (2017) [142]	mixed	1+	0	59	34	25	NR	NR	34	24	1	0	high	counts as reported
Li (2018) [161]	mixed	2+	0	204	88	116	0.92	0.931	80.96	107.996	8.004	7.04	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Li (2018) [161]	mixed	1+	0	204	88	116	0.977	0.802	85.976	93.032	22.968	2.024	high	rounding of counts did not contradict reported se, sp to the 1% decimal place

Abbreviations: 0=mixed reference standard (culture and non-culture); 1=culture as reference standard; FP=false positive; FN=false negative; Ref= reference standard; se, sens=sensitivity; sp, spec=specificity; TP=true positive; TN=true negative

Table A14: Synovial Alpha-defensin

Study	Joint	Cutoff	Ref	Total	PJI	Aseptic	sens_as_report	spec_as_report	TP	TN	FP	FN	Risk of Bias	Agreement Verification
Bingham (2014) [91] Lab-based	mixed	7.72 mg/mL	0	61	19	42	1	0.95	19	39.9	2.1	0	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Deirmengian (2014) [164] Lab-based	mixed	4.8 mg/mL	0	95	29	66	1	1	29	66	0	0	high	counts as reported

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Deirmengian (2015) [154] Lab-based	mixed	5.2 mg/L	0	46	23	23	1	1	23	23	0	0	high	excluded (only α-defensin): re-analysis of previously published samples
Deirmengian (2014) [207] Lab-based	mixed	5.2 mg/L	0	149	37	112	0.973	0.955	36.001	106.96	5	1	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Frangiamore (2016) [108] Lab-based	mixed	5.2 mg/L	0	78	24	54	1	0.98	24	53	1	0	high	counts as reported
Bonanzinga (2017) [206] Lab-based	mixed	signal/cutoff ratio of 1.0 *	0	156	29	127	0.97	0.97	28	123	4	1	high	counts as reported
Kelly (2018) [158] Lab-based	mixed	NR	0	39	11	28	0.82	0.82	9	23	5	2	high	counts as reported
Gehrke (2018) [165] Lab-based	mixed	signal/cutoff ratio of 1.0 *	0	173	76	97	NR	NR	68	96	1	8	high	counts as reported
Kasparek (2016) [137] Lateral Flow	mixed	2 lines (C and D)	0	40	12	28	0.67	0.93	8	26	2	4	high	counts as reported
Berger (2017) [115] Lateral Flow	mixed	2 lines (C and D)	0	121	34	87	0.971	0.965	33	84	3	1	high	counts as reported
Sigmund (2017) [117] Lateral Flow	mixed	2 lines (C and D)	0	49	13	36	0.69	0.94	8.97	33.84	2.16	4.03	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Martin (2015) [150] Lateral Flow	mixed	NR	0	14	4	10	NR	NR	3	8	2	1	unclear	counts as reported
Gehrke (2018) [165] Lateral Flow	mixed	2 lines (C and a-D)	0	195	76	119	0.921	1	70	119	0	6	high	counts as reported
Suda (2017) [141] Lateral Flow	mixed	NR	0	31	14	17	76.9	82.4	10	14	3	4	high	counts as reported
De Saint Vincent (2018) [167] Lateral Flow	mixed	NR	0	41	9	32	88.9	90.6	8	29	3	1	high	counts as reported

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Balato (2018) [143] Lateral Flow	knees	NR	0	51	16	35	87.5	97.2	14	34	1	2	high	counts as reported
Renz (2018) [166] Lateral Flow	mixed	NR	0	178	65	113	52.2	100	33.93	113	0	31.07	high	rounding of counts did not contradict reported se, sp to the 1% decimal place

*: The signal/cutoff ratio of 1.0 was achieved at the optimized cutoff of 5.2 mg/L in Deirmengian et al (2014) [207]
Abbreviations: 0=mixed reference standard (culture and non-culture); 1=culture as reference standard; FP=false positive; FN=false negative; Ref= reference standard; se, sens=sensitivity; sp, spec=specificity; TP=true positive; TN=true negative

Table A15: Synovial CRP

Study	Joint	Cutoff mg/L	Ref	Total	PJI	Aseptic	sens_as_report	spec_as_report	TP	TN	FP	FN	Risk of Bias	Agreement Verification
Jacovides (2011) [162]	mixed	3.605	0	74	31	43	0.871	0.977	27.001	42.011	0.989	3.999	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Vanderstappen (2013) [199]	knees	1.8	0	44	11	33	1	0.849	11	28.017	4.983	0	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Vanderstappen (2013) [199]	knees	2.8	0	44	11	33	0.909	0.939	9.999	30.987	2.013	1.001	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Buttaro (2015) [146]	hips	9.5	0	76	22	54	0.9	0.94	20	50	4	2	high	counts as reported
Tetreault (2014) [105]	mixed	6.6	0	119	32	87	0.88	0.85	28.16	73.95	13.05	3.84	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Tetreault (2014) [105]	hips	8.5	0	59	15	44	0.87	0.86	13.05	37.84	6.16	1.95	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Tetreault (2014) [105]	knees	14.1	0	60	17	43	0.82	0.93	13.94	39.99	3.01	3.06	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Ronde-Oustau (2014) [59]	knees	2.78	0	22	11	11	1	0.818	11	9	2	0	high	replied by authors
Ronde-Oustau (2014) [59]	knees	5.365	0	22	11	11	0.9	0.909	10	10	1	1	high	replied by authors
Deirmengian (2014) [164]	mixed	12.2	0	95	29	66	0.9	0.97	26.1	64.02	1.98	2.9	high	rounding of counts did not contradict reported se, sp to the 1% decimal place

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Omar (2015) [101]	hips	2.5	0	80	21	59	0.955	0.933	20.055	55.047	3.953	0.945	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Deirmengian (2014) [207]	mixed	3	0	149	37	112	0.973	0.786	36.001	88.032	23.968	0.999	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Parvizi (2012) [124]	knees	3.7	0	59	25	34	0.84	0.971	21	33.014	0.986	4	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Parvizi (2012) [124]	knees	0.06	0	15	10	5	0.7	1	7	5	0	3	high	counts as reported
Parvizi (2012) [188]	mixed	9.5	0	63	20	43	0.85	0.952	17	40.936	2.064	3	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Sousa (2017) [195]	mixed	1.6	0	55	23	32	0.913	0.875	20.999	28	4	2.001	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Sousa (2017) [195]	mixed	6.7	0	55	23	32	0.783	0.938	18.009	30.016	1.984	4.991	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Sousa (2017) [195]	mixed	8	0	55	23	32	0.739	0.969	16.997	31.008	0.992	6.003	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
De Vecchi (2016) [160]	mixed	10	0	129	27	102	0.815	0.941	22.005	95.982	6.018	4.995	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Kawamura (2017) [197]	hips	3.2	0	51	10	41	0.9	0.86	9	35.26	5.74	1	high	rounding of counts contradicted reported se, sp
Gallo (2018) [109]	mixed	8.8	0	72	24	48	0.917	1	22	48	0	2	high	counts as reported

Abbreviations: 0=mixed reference standard (culture and non-culture); 1=culture as reference standard; FP=false positive; FN=false negative; Ref= reference standard; se, sens=sensitivity; sp, spec=specificity; TP=true positive; TN=true negative

Table A16: Synovial IL-1b

Study	Joint	Cutoff	Ref	Total	PJI	Aseptic	sens_as_report	spec_as_report	TP	TN	FP	FN	Risk of Bias	Agreement Verification
Deirmengian (2010) [76]	mixed	112 pg/mL	1	51	14	37	1	1	14	37	0	0	unclear	counts as reported
Gollwitzer (2013) [67]	mixed	27.57 pg/mL	0	35	15	20	0.667	0.95	10.005	19	1	4.995	high	rounding of counts did not contradict reported se, sp to the 1% decimal place

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Deirmengian (2014) [164]	mixed	3.1 pg/mL	0	95	29	66	0.96	0.95	27.84	62.7	3.3	1.16	high	rounding of counts contradicted reported se, sp
Nilsdotter-Augustinsson (2007) [83]	hips	60 pg/mL	0	78	17	61	0.59	0.83	10.03	50.63	10.37	6.97	high	rounding of counts contradicted reported se, sp

Abbreviations: 0=mixed reference standard (culture and non-culture); 1=culture as reference standard; FP=false positive; FN=false negative; Ref= reference standard; se, sens=sensitivity; sp, spec=specificity; TP=true positive; TN=true negative

Table A17: Synovial IL-6

Study	Joint	Cutoff pg/mL	Ref	Total	PJI	Aseptic	sens_as_report	spec_as_report	TP	TN	FP	FN	Risk of Bias	Agreement Verification
Randau (2014) [60]	mixed	2100	0	120	48	72	0.625	0.8571	30	61.711	10.289	18	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Randau (2014) [60]	mixed	9000	0	120	48	72	0.4688	0.9762	22.502	70.286	1.7136	25.498	high	rounding of counts contradicted reported se, sp
Deirmengian (2010) [76]	mixed	13350	1	51	14	37	1	1	14	37	0	0	unclear	counts as reported
Gollwitzer (2013) [67]	mixed	1896.56	0	35	15	20	0.6	0.947	9	18.94	1.06	6	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Jacovides (2011) [162]	mixed	4270	0	74	31	43	0.871	1	27.001	43	0	3.999	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Deirmengian (2014) [164]	mixed	2300	0	95	29	66	0.89	0.97	25.81	64.02	1.98	3.19	high	rounding of counts contradicted reported se, sp
Nilsdotter-Augustinsson (2007) [83]	hips	10000	0	78	17	61	0.69	0.93	11.73	56.73	4.27	5.27	high	rounding of counts contradicted reported se, sp
Gallo (2018) [109]	mixed	20988	0	72	24	48	0.833	0.979	20	47	1	4	high	counts as reported

Abbreviations: 0=mixed reference standard (culture and non-culture); 1=culture as reference standard; FP=false positive; FN=false negative; Ref= reference standard; se, sens=sensitivity; sp, spec=specificity; TP=true positive; TN=true negative

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Table A18: Synovial IL-8

Study	Joint	Cutoff	Ref	Total	PJI	Aseptic	sens_as_report	spec_as_report	TP	TN	FP	FN	Risk of Bias	Agreement Verification
Jacovides (2011) [162]	mixed	8790 pg/mL	0	74	31	43	0.903	0.977	27.993	42.011	0.989	3.007	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Deirmengian (2014) [164]	mixed	6500 pg/mL	0	95	29	66	1	0.95	29	62.7	3.3	0	high	rounding of counts did not contradict reported se, sp to the 1% decimal place

Abbreviations: 0=mixed reference standard (culture and non-culture); 1=culture as reference standard; FP=false positive; FN=false negative; Ref= reference standard; se, sens=sensitivity; sp, spec=specificity; TP=true positive; TN=true negative

Table A19: Synovial PMN%

Study	Joint	Cutoff	Ref	Total	PJI	Aseptic	sens_as_report	spec_as_report	TP	TN	FP	FN	Risk of Bias	Agreement Verification
Deirmengian (2010) [76]	mixed	65%	1	51	14	37	1	0.73	14	27.01	9.99	0	unclear	rounding of counts did not contradict reported se, sp to the 1% decimal place
Zmistowski (2012) [187]	knees	75%	0	150	73	77	0.93	0.83	68	64	13	5	high	counts as reported
Schinsky (2008) [79]	hips	80%	0	201	55	146	0.84	0.82	46.2	119.72	26.28	8.8	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Mason (2003) [191]	knees	80%	0	86	36	50	0.57	1	20.52	50	0	15.48	high	rounding of counts contradicted reported se, sp
Mason (2003) [191]	knees	60%	0	86	36	50	0.76	0.89	27.36	44.5	5.5	8.64	high	rounding of counts contradicted reported se, sp
Dinneen (2012) [186]	mixed	65%	0	75	34	41	0.897	0.866	30.498	35.506	5.494	3.502	high	rounding of counts contradicted reported se, sp

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Cipriano (2012) [72]	mixed	78%	0	810	146	664	0.955	0.873	139.43	579.672	84.328	6.57	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Della Valle (2007) [120]	knees	65%	0	94	41	53	0.976	0.849	40.016	44.997	8.003	0.984	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Spangehl (1999) [104]	hips	80%	0	181	28	153	0.89	0.85	25	130	23	3	high	counts as reported
Chalmers (2015) [192]	knees	73%	0	433	93	340	0.894	0.936	83.142	318.24	21.76	9.858	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Omar (2015) [101]	hips	72.10%	0	80	21	59	0.9	0.901	18.9	53.159	5.841	2.1	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Mihalic (2012) [193]	hips	65%	0	206	50	156	0.76	0.96	38	149	7	12	high	counts as reported
Chalmers (2014) [185]	hips	65%	0	253	52	201	0.9	0.35	46.8	70.35	130.65	5.2	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Chalmers (2014) [185]	hips	73.5%	0	253	52	201	0.9	0.76	46.8	152.76	48.24	5.2	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Ghanem (2008) [189]	knees	64%	0	429	161	268	0.95	0.947	152.95	253.796	14.204	8.05	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Schwartz (2012) [69]	knees	60%	0	91	28	63	0.909	0.938	25.452	59.094	3.906	2.548	high	rounding of counts contradicted reported se, sp
Trampuz (2004) [190]	knees	65%	0	133	34	99	0.97	0.98	32.98	97.02	1.98	1.02	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Rothenberg (2017) [12]	mixed	80%	0	144	95	49	0.91	0.86	86	42	7	9	high	counts as reported
Higuera (2017) [204]	hips	80%	0	415	76	339	0.921	0.858	69.996	290.862	48.138	6.004	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Zahar (2018) [159]	mixed	66.1%	0	337	134	203	0.806	0.833	108.004	169.099	33.901	25.996	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Berger (2017) [115]	mixed	80%	0	92	28	64	0.893	0.962	25	59	5	3	high	back calculated using sens, spec, ppv, npv, accuracy
Sousa (2017) [195]	mixed	78%	0	55	23	32	0.87	0.719	20.01	23.008	8.992	2.99	high	rounding of counts did not contradict reported se, sp to the 1% decimal place

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Sousa (2017) [195]	mixed	81%	0	55	23	32	0.783	0.75	18.009	24	8	4.991	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Kawamura (2017) [197]	hips	41%	0	51	10	41	0.75	0.56	7.5	22.96	18.04	2.5	high	rounding of counts contradicted reported se, sp
Balato (2018) [181]	knees	80%	0	167	31	136	0.839	0.949	26.009	129.064	6.936	4.991	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Deirmengian (2013) [198]	mixed	NR	0	45	23	22	0.955	0.957	21.965	21.054	0.946	1.035	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Li (2018) [161]	mixed	NR	0	204	88	116	0.943	0.879	82.984	101.964	14.036	5.016	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Balato (2018) [143]	knees	80%	0	51	16	35	0.75	0.972	12	34	1	4	high	counts as reported
Gallo (2017) [203]	mixed	74.6%	0	330	72	258	0.931	0.911	67	235	23	5	high	back calculated using sens, spec, ppv, npv

Abbreviations: 0=mixed reference standard (culture and non-culture); 1=culture as reference standard; FP=false positive; FN=false negative; Ref= reference standard; se, sens=sensitivity; sp, spec=specificity; TP=true positive; TN=true negative

Table A20: Synovial TNF-alpha

Study	Joint	Cutoff	Ref	Total	PJI	Aseptic	sens_as_report	spec_as_report	TP	TN	FP	FN	Risk of Bias	Agreement Verification
Gollwitzer (2013) [67]	mixed	4.04 pg/mL	0	35	15	20	0.867	0.7	13.005	14	6	1.995	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Nilsdotter-Augustinsson (2007) [83]	hips	60 pg/mL	0	78	17	61	0.76	0.72	12.92	43.92	17.08	4.08	high	rounding of counts did not contradict reported se, sp to the 1% decimal place

Abbreviations: 0=mixed reference standard (culture and non-culture); 1=culture as reference standard; FP=false positive; FN=false negative; Ref= reference standard; se, sens=sensitivity; sp, spec=specificity; TP=true positive; TN=true negative

Table A21: Synovial WBC

Study	Joint	Cutoff cells /μL	Ref	Total	PJI	Aseptic	sens_as_report	spec_as_report	TP	TN	FP	FN	Risk	Agreement Verification

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Deirmengian (2010) [76]	mixed	2000	1	51	14	37	0.93	0.84	13.02	31.08	5.92	0.98	unclear	rounding of counts did not contradict reported se, sp to the 1% decimal place
Zmistowski (2012) [187]	knees	3000	0	150	73	77	0.93	0.94	68	72	5	5	high	counts as reported
Schinsky (2008) [79]	hips	4.2	0	201	55	146	0.84	0.93	46.2	135.78	10.22	8.8	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Mason (2003) [191]	knees	50	0	86	36	50	0.19	1	6.84	50	0	29.16	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Mason (2003) [191]	knees	2.5	0	86	36	50	0.69	0.98	24.84	49	1	11.16	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Dinneen (2012) [186]	mixed	1590	0	75	34	41	0.895	0.913	30.43	37.433	3.567	3.57	high	rounding of counts contradicted reported se, sp
Cipriano (2012) [72]	mixed	3450	0	810	146	664	0.91	0.93	132.86	617.52	46.48	13.14	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Trampuz (2004) [190]	knees	1700	0	133	34	99	0.94	0.88	31.96	87.12	11.88	2.04	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Della Valle (2007) [120]	knees	3000	0	94	41	53	1	0.981	41	51.993	1.007	0	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Spangehl (1999) [104]	hips	50000	0	183	28	155	0.36	0.99	10	154	1	18	high	counts as reported
Chalmers (2015) [192]	knees	4450/uL	0	433	93	340	0.904	0.985	84.072	334.9	5.1	8.928	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Chalmers (2014) [185]	hips	1700	0	253	52	201	0.92	0.72	47.84	144.72	56.28	4.16	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Chalmers (2014) [185]	hips	745	0	253	52	201	0.98	0.45	50.96	90.45	110.55	1.04	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Omar (2015) [101]	hips	3089/micrometer^3	0	80	21	59	0.85	0.863	17.85	50.917	8.083	3.15	high	rounding of counts contradicted reported se, sp
Mihalic (2012) [193]	hips	1700	0	206	50	156	0.74	0.97	37	152	4	13	high	counts as reported
Ghanem (2008) [201]	knees	1760	0	128	91	37	0.956	0.73	86.996	27.01	9.99	4.004	high	rounding of counts did not contradict reported se, sp to the 1% decimal place

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Ghanem (2008) [189]	knees	1100	0	429	161	268	0.907	0.881	146.027	236.108	31.892	14.973	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Schwartz (2012) [69]	knees	6200	0	96	28	68	0.9	0.965	25.2	65.62	2.38	2.8	high	rounding of counts contradicted reported se, sp
Nilsdotter-Augustinsson (2007) [83]	hips	1700	0	85	7	78	0.86	0.92	6.02	71.76	6.24	0.98	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Rothenberg (2017) [12]	mixed	3000	0	212	119	93	0.93	0.87	111	81	12	8	high	counts as reported
Higuera (2017) [204]	hips	3966	0	453	79	374	0.895	0.912	70.705	341.088	32.912	8.295	high	rounding of counts contradicted reported se, sp
Zahar (2018) [159]	mixed	2582	0	337	134	203	0.806	0.852	108.004	172.956	30.044	25.996	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Berger (2017) [115]	mixed	3000	0	107	28	79	0.893	0.962	25	76	3	3	high	back calculated using sens, spec, ppv, npv, accuracy
Sousa (2017) [195]	mixed	1463	0	55	23	32	1	0.719	23	23.008	8.992	0	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Sousa (2017) [195]	mixed	2064	0	55	23	32	0.913	0.75	20.999	24	8	2.001	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Choi (2016) [196]	hips	2689	0	138	50	88	0.92	0.9318	46	81.9984	6.0016	4	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Kawamura (2017) [197]	hips	812	0	51	10	41	0.9	0.78	9	31.98	9.02	1	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Balato (2018) [181]	knees	3000	0	167	31	136	0.806	0.912	24.986	124.032	11.968	6.014	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Deirmengian (2013) [198]	mixed	NR	0	45	23	22	0.955	0.957	21.965	21.054	0.946	1.035	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Li (2018) [161]	mixed	NR	0	204	88	116	0.932	0.922	82.016	106.952	9.048	5.984	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Balato (2018) [143]	knees	3000	0	51	16	35	0.75	0.914	12	32	3	4	high	counts as reported
Boettner (2016) [144]	mixed	12000 WBC/mL	1	77	21	56	1	1	21	56	0	0	unclear	counts as reported

Gallo (2017) [203]	mixed	3450	0	375	75	300	0.947	0.95	71	285	15	4	high	back calculated using sens, spec, ppv, npv

Abbreviations: 0=mixed reference standard (culture and non-culture); 1=culture as reference standard; FP=false positive; FN=false negative; Ref= reference standard; se, sens=sensitivity; sp, spec=specificity; TP=true positive; TN=true negative

Tissue Tests

Table A22: Histological Analysis, > or >=5 PMNs per HPF. A mixture of criteria such as Mirra (>=5 PMNs/HPF in >=1 out of 5 HPFs), Feldman (>5 PMNs/HPF in all 5 HPFs) [219] and other similar criteria

Study	Joint	Detail	Cutoff	Ref	Total	PJI	Aseptic	sens_as_report	spec_as_report	TP	TN	FP	FN	Risk of Bias	Agreement Verification
Bori (2011) [226]	hips	Parrafin section: Interface Membrane Histology	(Mirra) >=5 PMNs/HPF in >=5 separate fields	0	69	12	57	0.83	0.98	10	56	1	2	high	counts as reported
Bori (2011) [226]	hips	Parrafin section: Pseudocapsule Histology	(Mirra) >=5 PMNs/HPF in >=5 separate fields	0	69	12	57	0.42	0.98	5	56	1	7	high	counts as reported
Ghanem (2009) [214]	hips	Frozen section	>5 PMNs /HPF	0	551	150	401	0.31	0.99	46.5	396.99	4.01	103.5	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Ghanem (2009) [214]	knees	Frozen section	>5 PMNs /HPF	0	453	171	282	0.53	0.99	90.63	279.2	2.8	80.37	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Fink (2008) [81]	knees	Frozen section	>=5 PMNs /HPF in >=1 of 10 such fields	1	145	40	105	0.9	0.952	36	100	5	4	unclear	counts as reported
Fink (2013) [68]	hips	Not reported	>=5 PMNs /HPF in >=1 of 10 such fields	1	100	45	55	0.62	1	28	55	0	17	unclear	counts as reported
Buttaro (2010) [74]	hips	Frozen section	(Mirra) >=5 PMN/ HPF	0	69	11	58	0.81	0.98	8.91	56.84	1.16	2.09	high	rounding of counts contradicts reported se, sp

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Kanner (2008) [80]	mixed	Frozen section	(Mirra) >5 PMNs/HPF in >=5 HPFs	1	132	14	118	0.29	0.95	4	112	6	10	low	counts as reported
Ko (2005) [216]	mixed	Frozen section	(Mirra) >5 PMNs/HPF	1	40	9	31	0.67	0.97	6	30	1	3	unclear	counts as reported
Bori (2006) [215]	hips	Frozen section	(Feldman) >5 PMNs/HPF in >=5 HPFs	1	51	12	49	0.5	0.81	6	40	9	6	unclear	counts as reported
Spangehl (1999) [104]	hips	Frozen section	(Mirra) >5 PMNs/HPF in any HPF	0	202	35	167	0.8	0.94	28	157	10	7	high	counts as reported
Musso (2003) [220]	mixed	Frozen section of multiple sites	>=5 PMNs /HPF in >=5 HPFs	1	45	6	39	0.5	0.95	3	37	2	3	unclear	counts as reported
Buttaro (2015) [146]	hips	Frozen section	>=5 PMNs in 10 HPFs	0	76	22	54	NR	NR	21	54	0	1	high	counts as reported
Pons (1999) [129]	hips	Frozen section	(Mirra) >5 PMN/HPF	1	80	16	64	1	0.98	16	63	1	0	high	counts as reported
Abdul-Karim (1998) [218]	mixed	Frozen section	>5 PMNs/ HPF in >=5 separate fields	1	64	7	57	0.43	0.97	3	55	2	4	unclear	counts as reported
Banit (2002) [257]	mixed	Frozen section	>5 PMNs /HPF	1	121	21	100	0.67	0.84	14.07	84	16	6.93	unclear	rounding of counts did not contradict reported se, sp to the 1% decimal place
Wu (2014) [125]	mixed	Frozen Section 3 sites, any one positive of multiplex sites	(Mirra) >=5 Average PMNs/HPF (of at least 5 fields)	0	138	35	103	0.76	0.97	26.6	99.91	3.09	8.4	high	rounding of counts contradicted reported se, sp
Wu (2014) [125]	mixed	Frozen Section 5 sites, any one positive of multiplex sites	(Mirra) >=5 Average PMNs/HPF (of at least 5 fields)	0	117	29	88	0.86	0.96	24.94	84.48	3.52	4.06	high	rounding of counts contradicted reported se, sp
Wu (2014) [125]	mixed	Frozen Section 7 sites, any one positive of multiplex sites	(Mirra) >=5 Average PMNs/HPF (of at least 5 fields)	0	46	15	31	0.86	0.92	12.9	28.52	2.48	2.1	high	rounding of counts contradicted reported se, sp

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Ramsingh (2010) [103]	mixed	Frozen section	>5 neutrophils /HPF	1	47	9	38	0.56	0.84	5.04	31.92	6.08	3.96	unclear	rounding of counts did not contradict reported se, sp to the 1% decimal place
Feldman (1995) [219]	mixed	Frozen section	(Feldman) >5 PMNs/HPF in >=5 distinct fields	0	33	9	24	1	0.96	9	23	1	0	high	counts as reported
Pace (1997) [239]	mixed	Frozen section	(Mirra) >5 PMNs/HPF on multiple areas	1	25	11	14	0.82	0.93	9	13	1	2	unclear	counts as reported
Wong (2005) [232]	mixed	Frozen section	>5 PMNs /HPF	0	40	14	26	0.93	0.77	13.02	20.02	5.98	0.98	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Nunez (2007) [229]	hips	Frozen section	(Mirra) >=5 PMNs/HPF	1	136	49	87	0.85	0.87	42	76	11	7	unclear	counts as reported
Lonner (1996) [234]	mixed	Frozen section	(Feldman) >=5 PMNs /HPF	1	175	19	156	0.84	0.96	16	149	7	3	unclear	counts as reported
Lonner (1996) [234]	mixed	Permanent section	(Feldman) >=5 PMNs /HPF	1	175	19	156	0.94	0.98	18	147	9	1	unclear	counts as reported
Panousis (2005) [87]	mixed	Frozen section	(Mirra) >=5 PMNs/HPF in any single HPF	0	92	12	80	0.92	1	11.04	80	0	0.96	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Nilsdotter-Augustinsson (2007) [83]	hips	Permanent (paraffin fixed)	(Mirra) >=5 PMNs/HPF	0	47	21	26	0.81	1	17	26	0	4	high	counts as reported
Rothenberg (2017) [12]	mixed	NR	>5 neutrophils /HPF in 5 HPF	0	120	51	69	0.71	0.97	35	67	2	16	high	counts as reported
Li (2017) [138]	mixed	Frozen section	>5 neutrophils /HPF, >=1 out of 3 tissue blocks	0	93	38	55	0.895	0.891	34	49	6	4	high	counts as reported
Li (2017) [138]	mixed	Paraffin section	>5 neutrophils /HPF, >=1 out of 3 tissue blocks	0	93	38	55	0.974	0.855	37	47	8	1	high	counts as reported

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Frangiamore (2016) [108]	mixed	Frozen section	(Feldman) >=5 PMNs in each of 5 or more HPFs	0	78	24	54	0.458	0.981	11	53	1	13	high	counts as reported
Kwiecien (2017) [262]	mixed	Frozen section	>=5 neutrophils/HPF in >=3 HPFs	0	200	38	162	0.737	0.988	28.006	160.056	1.944	9.994	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Di Benedetto (2016) [250]	mixed	Frozen section	(Feldman) >=5 PMNs /HPF	1	157	60	97	0.383	0.825	23	80	17	37	high	counts as reported
Boettner (2016) [144]	mixed	Frozen section	(Mirra) >=5 PMNs/HPF in >=1 out of 5 HPFs	1	77	21	56	0.9	0.71	18.9	39.76	16.24	2.1	unclear	rounding of counts did not contradict reported se, sp to the 1% decimal place
Boettner (2016) [144]	mixed	Frozen section	(Feldman) >5 PMNs/HPF in all 5 HPFs	1	77	21	56	0.48	0.96	10.08	53.76	2.24	10.92	unclear	rounding of counts did not contradict reported se, sp to the 1% decimal place

Abbreviations: 0=mixed reference standard (culture and non-culture); 1=culture as reference standard; FP=false positive; FN=false negative; HPF=high power field; PMN=polymorphonuclear cells; Ref= reference standard; se, sens=sensitivity; sp, spec=specificity; TP=true positive; TN=true negative

Table A23: Histological Analysis, > or >=10 PMNs per HPF. A mixture of criteria such as Banit (>10 PMNs/HPF in >=1 out of 5 HPFs) [257], Lonner (>=10 PMNs/HPF in all 5 HPFs) [234] and other similar criteria

Study	Joint	Detail	Cutoff	Ref	Total	PJI	Aseptic	sens_as_report	spec_as_report	TP	TN	FP	FN	Risk of Bias	Agreement Verification
Schinsky (2008) [79]	hips	Frozen section	average of >10 PMNs in 5 most cellular HPFs	0	201	55	146	0.73	0.94	40.15	137.24	8.76	14.85	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Miyamae (2013) [63]	mixed	Frozen section	>10 neutrophils /HPF with 5 fields counted	1	71	7	64	0.71	0.89	5	57	7	2	high	replied by authors
Miyamae (2013) [63]	mixed	Parrafin section	>10 neutrophils /HPF with 5 fields counted	1	81	10	71	0.9	0.87	9	61.77	9.23	1	high	rounding of counts did not contradict reported se, sp to the 1% decimal place

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Della Valle (2007) [120]	knees	Frozen section	(Lonner) ave. of >10 PMNs in 5 most cellular fields	0	94	41	53	0.878	0.962	35.998	50.986	2.014	5.002	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Banit (2002) [257]	mixed	Frozen section	(Banit) >10 PMNs/HPF	1	121	21	100	0.67	0.93	14	93	7	7	unclear	counts as reported
Banit (2002) [257]	hips	Frozen section	(Banit) >10 PMNs/HPF	1	63	11	52	0.45	0.92	5	48	4	6	unclear	counts as reported
Banit (2002) [257]	knees	Frozen section	(Banit) >10 PMNs/HPF	1	55	9	46	1	0.96	9	44	2	0	unclear	counts as reported
Wu (2014) [125]	mixed	Frozen Section 3 sites, any one positive of multiplex sites	(Banit) >=10 average PMNs /HPF (of at least 5 fields)	0	138	35	103	0.32	1	11.2	103	0	23.8	high	rounding of counts contradicted reported se, sp
Wu (2014) [125]	mixed	Frozen Section 5 sites, any one positive of multiplex sites	(Banit) >=10 average PMNs /HPF (of at least 5 fields)	0	117	29	88	0.35	1	10.15	88	0	18.85	high	rounding of counts contradicted reported se, sp
Wu (2014) [125]	mixed	Frozen Section 7 sites, any one positive of multiplex sites	(Banit) >=10 average PMNs /HPF (of at least 5 fields)	0	46	15	31	0.35	1	5.25	31	0	9.75	high	rounding of counts contradicted reported se, sp
Chimento (1996) [258]	mixed	NR	>10 PMNs /HPF	0	169	32	137	0.188	0.956	6.016	130.972	6.028	25.984	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Wong (2005) [232]	mixed	Frozen section	>10 PMNs /HPF	0	40	14	26	0.86	0.85	12.04	22.1	3.9	1.96	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Borrego (2007) [230]	knees	Frozen section	>10 PMN/HPF	1	63	24	39	0.667	0.897	16	35	4	8	unclear	counts as reported
Borrego (2007) [230]	hips	Frozen section	>10 PMN/HPF	1	83	8	75	0.5	1	4	75	0	4	unclear	counts as reported
Lonner (1996) [234]	mixed	Frozen section	(Lonner) >=10 PMNs/HPF	1	175	19	156	0.84	0.99	16	154	2	3	unclear	counts as reported

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Boettner (2016) [144]	mixed	Frozen section	(Lonner) >=10 PMNs/HPF in all 5 HPFs	1	77	21	56	0.38	0.98	7.98	54.88	1.12	13.02	unclear	rounding of counts did not contradict reported se, sp to the 1% decimal place
Boettner (2016) [144]	mixed	Frozen section	(Banit) >=10 PMNs/HPF in >=1 out of 5 HPFs	1	77	21	56	0.9	0.84	18.9	47.04	8.96	2.1	unclear	rounding of counts did not contradict reported se, sp to the 1% decimal place

Abbreviations: 0=mixed reference standard (culture and non-culture); 1=culture as reference standard; FP=false positive; FN=false negative; HPF=high power field; PMN=polymorphonuclear cells; Ref= reference standard; se, sens=sensitivity; sp, spec=specificity; TP=true positive

Table A24: Gram Stain

Study	Joint	Cutoff	Ref	Total	PJI	Aseptic	sens_as_report	spec_as_report	TP	TN	FP	FN	Risk of Bias	Agreement Verification
Zywiel (2011) [212]	knees	presence of bacteria	0	347	156	191	0.07	0.99	11	190	1	145	high	counts as reported
Johnson (2010) [213]	hips	presence of bacteria	0	202	82	120	0.098	1	8	120	0	74	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Ghanem (2009) [214]	hips	presence of organisms	0	551	150	401	0.31	1	46.5	401	0	103.5	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Ghanem (2009) [214]	knees	presence of organisms	0	453	171	282	0.3	1	51.3	282	0	119.7	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Atkins (1998) [260]	mixed	presence of organisms	0	297	41	256	0.12	0.988	4.92	252.928	3.072	36.08	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Spangehl (1999) [104]	hips	presence of organisms	0	202	27	175	0.19	0.98	5	172	3	22	high	counts as reported
Morgan (2009) [123]	knees	presence of organisms	0	921	247	674	0.27	0.999	67	673	1	180	high	counts as reported
Della Valle (1999) [259]	mixed	presence of bacteria	1	413	68	345	0.147	0.988	10	341	4	58	high	counts as reported
Kraemer (1993) [128]	hips	presence of organisms	1	55	13	42	0.23	1	3	42	0	10	high	counts as reported

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Abbreviations: 0=mixed reference standard (culture and non-culture); 1=culture as reference standard; FP=false positive; FN=false negative; Ref= reference standard; se, sens=sensitivity; sp, spec=specificity; TP=true positive; TN=true negative

Table A25: PCR

Study	Joint	Detail	Cutoff	Ref	Total	PJI	Aseptic	sens_as_rep	spec_as_rep	TP	TN	FP	FN	Risk of Bias	Agreement Verification
Miyamae (2013) [63]	mixed	Real-time PCR	over 1.9 cycles of ΔCt or with the detection of MRS in at least 1 sample	1	81	10	71	0.9	0.45	9	31.95	39.05	1	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Borde (2015) [236]	mixed	Broad-spectrum 16S rRNA gene real-time PCR and sequence analysis	sequence similarity of 97% or more (genus) and 99% or more (species); Two of three analyzed samples yielded same pathogen-related sequence	1	54	7	47	0.857	0.979	6	46	1	1	unclear	counts as reported
Borde (2015) [236]	mixed	Unyvero Implant and Tissue Infection cartridge application	at least one of the analytes reach threshold of positivity	1	28	7	21	0.429	0.952	3	20	1	4	unclear	counts as reported
Bemer (2014) [235]	mixed	16S rRNA gene PCR		0	250	206	44	0.733	0.955	151	42	2	55	high	counts as reported
Marin (2012) [211]	mixed	16S PCR on intraop tissue, or synovial fluid	positive PCR	0	497	176	321	0.671	0.978	119	317	4	57	high	counts as reported
Ryu (2014) [135]	knees	Tissue PCR	Presence of targeted bacteria	0	95	64	31	0.156	0.968	10	30	1	54	high	counts as reported
Lourtet-Hascoett (2015) [238]	mixed	Mutliplex PCR assay (PCR - Xpert MRSA/SA SSTI real time PCR)	Amplification of spa gene (SA) and amplification of mecA gene (Methicillin resistance)	1	72	42	30	0.36	0.98	15.12	29.4	0.6	26.88	unclear	rounding of counts contradicted reported se, sp

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Gallo (2008) [132]	mixed	PCR assay targeting the 16S rDNA gene	presence of 370-bp amplification product in addition to 477-bp product	0	101	35	66	0.714	0.97	25	64	2	10	high	counts as reported
Metso (2014) [222]	mixed	Prove-it Bone and Joint assay (which is a broad-range PCR and microarray-based assay)	bacteria detected in any of the samples	0	61	38	23	0.82	0.74	31	17	6	7	high	counts as reported
Rak (2013) [224]	mixed	Broad Range (BR) PCR	PCR reaction was considered positive if the difference between the Ct value of the specimens and negative controls was > 1	0	67	16	51	0.75	0.941	12	48	3	4	high	counts as reported
Panousis (2005) [87]	mixed	Broad range PCR	Positive PCR	0	92	12	80	0.92	0.74	11.04	59.2	20.8	0.96	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Zegaer (2014) [243]	mixed	Universal PCR 1		0	44	13	31	0.231	1	3.003	31	0	9.997	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Zegaer (2014) [243]	mixed	Universal PCR 2		0	44	13	31	0.231	0.968	3.003	30.008	0.992	9.997	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Morgenstein (2018) [136]	mixed	Mutliplex PCR assay	10^4 DNA fragments/pathogen/mL	0	142	77	65	0.6	0.89	46	58	7	31	high	counts as reported
Kawamura (2017) [245]	mixed	Universal PCR		0	151	45	106	0.91	0.88	41	93	13	4	high	counts as reported
Rak (2016) [246]	mixed	BR-PCR of periprosthetic tissue samples	presense of organism; detection of the 16S rRNA gene for positive results	0	87	29	58	0.76	0.93	22	54	4	7	high	counts as reported
Huang (2018) [139]	mixed	BR Real-time PCR of 16S rRNA gene	Ct of < 28 cycles	0	67	53	14	0.34	1	18	14	0	35	high	counts as reported

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Huang (2018) [139]	mixed	BR Real-time PCR of 16S rRNA gene	Ct of < 28 cycles	0	67	53	14	0.83	0.857	44	12	2	9	high	counts as reported
Melendez (2016) [148]	knees	Genus- and group-specific multi-assay panel real-time PCR		0	284	88	196	0.556	0.918	49	180	16	39	high	counts as reported
Janz (2018) [261]	mixed	16s rDNA PCR	optimal cut-off of 0.71 AU	0	58	22	36	0.82	0.89	18	32	4	4	high	counts as reported
Suda (2017) [141]	mixed	Mutliplex PCR		0	30	13	17	0.308	1	4	17	0	9	high	counts as reported
Lausmann (2017) [142]	mixed	Mutliplex PCR		1	60	33	27	0.788	1	26	27	0	7	high	counts as reported
Fink (2018) [110]	knees	Universal test kit - bacterial 16S rRNA and fungal and eukaryote 18S rRNA		1	116	27	89	0.556	0.82	15	73	16	12	unclear	counts as reported
Omar (2018) [253]	mixed	Swab 16S rRNA PCR		0	41	22	19	0.864	0.895	19	17	2	3	high	counts as reported
Fang (2018) [184]	mixed	DNA-based qPCR	a two-cycle difference from the sterile baseline	0	71	38	33	0.82	0.85	31	28	5	7	high	counts as reported
Fang (2018) [184]	mixed	rRNA-based qPCR	a two-cycle difference from the sterile baseline	0	71	38	33	0.74	1	28	33	0	10	high	counts as reported

Abbreviations: 0=mixed reference standard (culture and non-culture); 1=culture as reference standard; FP=false positive; FN=false negative; Ref= reference standard; se, sens=sensitivity; sp, spec=specificity; TP=true positive; TN=true negative

Table A26: Swab culture

Study	Joint	Cutoff	Ref	Total	PJI	Aseptic	sens_as_report	spec_as_report	TP	TN	FP	FN	Risk of Bias	Agreement Verification
Aggarwal (2013) [223]	mixed	>=1 plate growth	0	117	30	87	0.7	0.885	21	77	10	9	high	counts as reported
Aggarwal (2013) [223]	mixed	>=2 plate growth	0	117	30	87	0.533	0.977	15.99	84.999	2.001	14.01	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Spangehl (1999) [104]	hips	more than 1/3 of specimens grew	0	168	17	151	0.76	0.99	13	150	1	4	high	counts as reported

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Levine (2001) [209]	mixed	positive cultures	0	32	25	7	0.64	1	16	7	0	9	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Picado (2008) [228]	hips	two or more positive cultures implicating the same organism	0	152	7	145	0.857	0.966	6	140	5	1	high	counts as reported
Picado (2008) [228]	hips	two or more positive cultures implicating the same organism	0	111	6	105	1	0.952	6	100	5	0	high	counts as reported

Abbreviations: 0=mixed reference standard (culture and non-culture); 1=culture as reference standard; FP=false positive; FN=false negative; Ref= reference standard; se, sens=sensitivity; sp, spec=specificity; TP=true positive; TN=true negative

Table A27: Intraoperative tissue culture

Study	Joint	Cutoff	Ref	Total	PJI	Aseptic	sens_as_report	spec_as_report	TP	TN	FP	FN	Risk of Bias	Agreement Verification
Janz (2013) [66]	mixed	positive culture	0	59	23	35	0.75	1	18	36	0	5	high	counts as reported
Schinsky (2008) [79]	hips	organisms on solid media	0	201	55	146	0.87	0.92	47.85	134.32	11.68	7.15	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Atkins (1998) [260]	mixed	1 or more culture-positive specimens	0	297	41	256	0.83	0.81	34.03	207.36	48.64	6.97	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Atkins (1998) [260]	mixed	2 or more culture-positive specimens	0	297	41	256	0.71	0.97	29.11	248.32	7.68	11.89	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Atkins (1998) [260]	mixed	3 or more culture-positive specimens	0	297	41	256	0.66	0.996	27.06	254.976	1.024	13.94	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Muller (2008) [62]	hips	>= 1 growth if virulent organism, >=3 growth if low virulence organism	0	50	37	13	0.78	0.92	30	12	1	7	high	counts as reported

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Aggarwal (2013) [223]	mixed	>= 1 plate growth	0	117	30	87	0.933	0.977	27.99	84.999	2.001	2.01	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Aggarwal (2013) [223]	mixed	>= 2 plate growth	0	117	30	87	0.633	0.977	18.99	84.999	2.001	11.01	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Bare (2006) [86]	knees	presence of bacteria	0	295	79	216	0.53	0.94	41.87	203.04	12.96	37.13	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Spangehl (1999) [104]	hips	more than 1/3 of specimens grew	0	180	18	162	0.94	0.97	17	157	5	1	high	counts as reported
Barrack (1993) [147]	hips	positive growth culture	0	269	6	263	1	0.86	6	209	54	0	high	counts as reported
Portillo (2014) [241]	mixed	positive growth culture	0	231	69	162	0.61	1	42	162	0	27	high	counts as reported
Portillo (2015) [242]	mixed	same bacterium cultured in at least 2 samples	0	75	39	36	0.59	1	23.01	36	0	15.99	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Jordan (2014) [237]	mixed	NR	0	191	31	160	0.32	0.99	9.92	158.4	1.6	21.08	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Levine (2001) [209]	mixed	culture growth	0	20	13	7	0.77	1	10	7	0	3	high	counts as reported
Ryu (2014) [135]	knees	2 or more positive tissues with same organism	0	95	64	31	0.688	1	44	31	0	20	high	counts as reported
Fehring (1996) [126]	hips	positive growth culture	0	166	6	160	0.67	0.88	4	140	20	2	high	counts as reported
Janz (2015) [127]	knees	NR	0	109	31	78	0.65	1	20.15	78	0	10.85	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Padgett (1995) [240]	hips	positive intraoperative culture	0	129	1	128	1	0.69	1	88	40	0	high	counts as reported

http://dx.doi.org/10.2106/JBJS.18.00632

Tohtz (2010) [78]	hips	growth	0	64	19	45	0.368	0.911	6.992	40.995	4.005	12.008	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Rak (2013) [224]	mixed	>2 bacteria grow on 2+ culture plates	0	67	16	51	0.813	0.941	13	48	3	3	high	counts as reported
Panousis (2005) [87]	mixed	>1/3 positive	0	92	12	80	0.75	0.96	9	76.8	3.2	3	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Zegaer (2014) [243]	mixed	positive growth culture	0	44	13	31	1	0.774	13	24	7	0	high	counts as reported
Morgenstern (2018) [136]	mixed	>=2 specimen grew a low-virulent pathogen or >= 1 specimen grew high-virulent organisms	0	88	60	28	0.45	0.96	27	27	1	33	high	counts as reported
Renz (2017) [244]	mixed	>=2 specimen grew a low-virulent pathogen or >= 1 specimen grew high-virulent organisms	0	111	78	33	0.51	1	40	33	0	38	high	counts as reported
Rothenberg (2017) [12]	mixed	presence of organism	0	160	104	56	0.7	0.97	74	55	1	30	high	counts as reported
Hischebeth (2016) [247]	mixed	bacterial growth in culture of biopsies	0	80	46	34	0.6087	0.7647	28	26	8	18	high	counts as reported
Huang (2018) [139]	mixed	same organism isolated from >= 2 samples	0	67	53	14	0.717	1	38	14	0	15	high	counts as reported
Suren (2017) [248]	mixed	NR	0	38	27	11	0.8	0.89	21.6	9.79	1.21	5.4	high	rounding of counts contradicted reported se, sp
Fernandez-Sampedro (2018) [114]	mixed	>=2 cultures yielded the same microorganism; only a single positive required when S. aureus or S. lugdunensis were the microorganisms isolated	0	498	130	368	0.623	0.997	81	367	1	49	high	counts as reported
Sigmund (2017) [117]	mixed	>=1 positive culture	0	49	13	36	0.92	0.94	11.96	33.84	2.16	1.04	high	counts as reported
Sigmund (2017) [117]	mixed	>=2 positive culture	0	49	13	36	0.85	1	11.05	36	0	1.95	high	counts as reported

http://dx.doi.org/10.2106/JBJS.18.00632

Stylianakis (2018) [119]	mixed	>=2 positive culture	0	114	27	87	0.4074	0.9655	11	84	3	16	high	counts as reported
Sambri (2018) [251]	knees	>=1 showed the growth of a strict pathogen or when two yielded a skin commensal organism	0	232	86	146	0.79	1	68	146	0	18	high	counts as reported
Suda (2017) [141]	mixed	NR	0	30	13	17	0.846	1	11	17	0	2	high	counts as reported
Lausmann (2017) [142]	mixed	NR	0	60	34	26	NR	NR	33	26	0	1	high	counts as reported
Omar (2018) [253]	mixed	>=1 positive culture	0	41	22	19	0.682	0.895	15	17	2	7	high	counts as reported
Omar (2018) [253]	mixed	>=2 positive culture	0	41	22	19	0.636	1	14	19	0	8	high	counts as reported
Tarabichi (2018) [254]	mixed	>=1 positive culture	0	65	28	37	0.607	0.973	17	36	1	11	high	counts as reported
Yan (2018) [255]	mixed	same organism isolated from >= 2 samples, or if Staphylococcus aureus, Enterococcus species, or yeast was isolated from a single tissue specimen	0	187	86	101	0.651	0.98	56	99	2	30	high	counts as reported
Balato (2018) [143]	knees	2 positive cultures with phenotypically identical organisms	0	51	16	35	0.75	1	12	35	0	4	high	counts as reported
Sebastian (2018) [112]	mixed	same organism in >=2 tissue specimens	0	40	27	13	0.667	1	18.009	13	0	8.991	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Tani (2018) [113]	mixed	same organism isolated from >= 2 samples	0	114	61	53	0.5573	0.9434	33.995	50	3	27.005	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Larsen (2018) [145]	mixed	positive culture	0	108	42	66	NR	NR	31	66	0	11	high	counts as reported
Larsen (2018) [145]	mixed	positive culture	0	108	42	66	NR	NR	37	66	0	5	high	counts as reported

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Abbreviations: 0=mixed reference standard (culture and non-culture); 1=culture as reference standard; FP=false positive; FN=false negative; Ref= reference standard; se, sens=sensitivity; sp, spec=specificity; TP=true positive; TN=true negative

Table A28: Preoperative tissue culture

Study	Joint	Cutoff	Ref	Total	PJI	Aseptic	sens_as_report	spec_as_report	TP	TN	FP	FN	Risk of Bias	Agreement Verification
Meermans (2010) [131]	mixed	positive culture: same organism grew on 2 or more specimens	1	120	110	10	0.791	1	87	10	0	23	unclear	counts as reported
Fink (2008) [81]	knees	same bacterium cultured in at least 2 samples	1	145	40	105	0.775	0.981	31	103	2	9	unclear	counts as reported
Fink (2013) [68]	hips	positive culture: same organism cultured in at least 2 samples	1	100	45	55	0.73	0.98	33	54	1	12	unclear	counts as reported
Williams (2004) [133]	hips	>=2 growth; If 2 or all 3 specimens grew organisms, this was regarded as a positive culture	1	273	71	202	0.83	0.9	59	181	21	12	low	counts as reported
Corona (2012) [225]	mixed	growth within 14 days	0	24	17	7	0.8824	1	15	7	0	2	high	counts as reported
Cross (2014) [130]	hips	growth of bacteria from plated culture medium	0	110	17	93	0.41	1	7	93	0	10	high	counts as reported
Mikkelsen (2006) [231]	knees	1 or more identical pathogen from 3 or more biopsies	0	84	26	58	0.46	1	12	58	0	14	high	counts as reported
Sadiq (2005) [233]	mixed	NR	0	177	86	91	0.88	0.91	76	83	8	10	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Pohlig (2017) [116]	hips	>=2 cultures showed growth of the same pathogen	0	20	8	12	0.75	0.833	6	9.996	2.004	2	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Wing (2017) [140]	knees	unclear	0	12	1	11	0	0.82	0	9	2	1	unclear	counts as reported
Wing (2017) [140]	knees	unclear	0	64	10	54	0.6	0.8	6	43	11	4	unclear	counts as reported

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Wimmer (2017) [249]	hips	NR	0	30	20	10	0.85	1	17	10	0	3	high	counts as reported
Ottink (2018) [252]	hips	same organism isolated from >= 2 samples	1	16	3	13	0.33	0.85	0.99	11.05	1.95	2.01	high	rounding of counts did not contradict reported se, sp to the 1% decimal place
Claassen (2016) [118]	knees	infection in at least two of five samples	0	32	8	26	0.25	0.96	2	25	1	6	high	counts as reported

Abbreviations: 0=mixed reference standard (culture and non-culture); 1=culture as reference standard; FP=false positive; FN=false negative; Ref= reference standard; se, sens=sensitivity; sp, spec=specificity; TP=true positive; TN=true negative

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