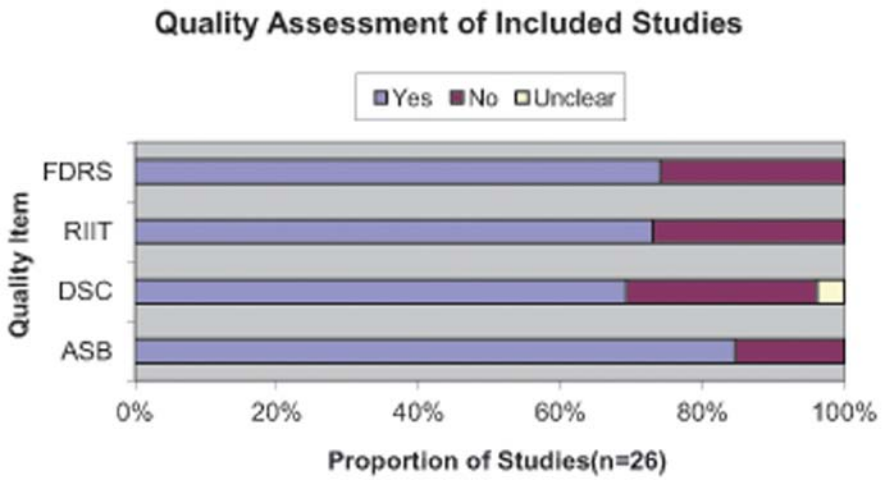

Fig. E-1

Quality assessment of included studies. FDRS = full description of reference standard, RIIT = reference standard independent of index test, DSC = description of selection criteria, and ASB = avoids spectrum bias.

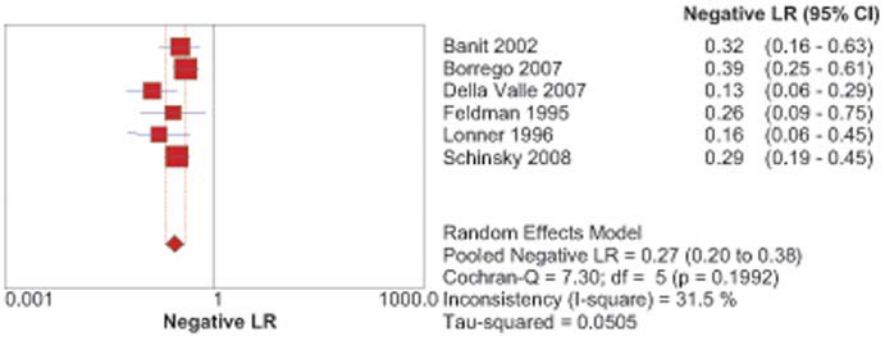

Fig. E-2

Forest plot of the likelihood ratio (LR) of a negative frozen section result using a threshold of 10 polymorphonuclear leukocytes per high-power field for the exclusion of periprosthetic joint infection. CI = confidence interval, and df = degrees of freedom.

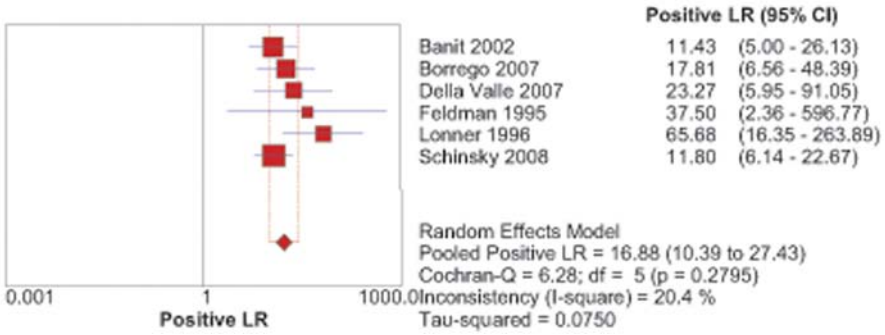

Fig. E-3

Forest plot of the likelihood ratio (LR) of a positive frozen section result using a threshold of 10 polymorphonuclear leukocytes per high-power field for the diagnosis of periprosthetic joint infection. CI = confidence interval, and df = degrees of freedom.

Appendix 4: Summary Receiver Operator Characteristic Curve of Frozen Sections compared to Microbiology Cuture in the Diagnosis of PJI

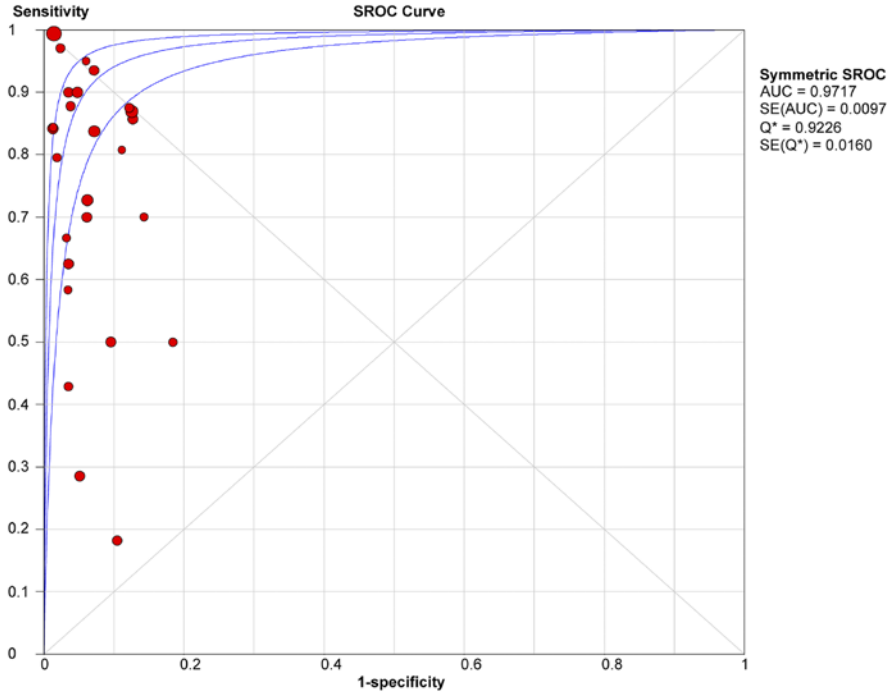

Fig. E-4

Summary receiver operating characteristic (SROC) curve of frozen sections compared with microbiologic culture for the diagnosis of periprosthetic joint infection. AUC = area under the curve, SE = standard error, and Q* = Cochran Q value.

TABLE E-1 Characteristics of the Included Studies*

Author, Year	Study Design†	No. of Patients	No. (%) of PJIs	Frozen Section Threshold Criteria			PJI Definition		Exclusion Criteria§
				PMNs	No. of Fields	Magnification	Culture	Additional Criteria‡	
Abdul-Karim, 1998	R	64	7 (11)	5	5	NS	Y	Y	Rx
Athanasou, 1995	R	106	22 (21)	1	10	400	Y	N	—
Banit, 2002	P	119	21 (18)	5	1	400	Y	N	—
Banit, 2002	P	118	20 (17)	10	1	400	Y	N	—
Borrego, 2007	C	146	32 (22)	10	1	400	Y	N	—
Bori, 2006	R	61	12 (20)	5	5	400	Y	N	OI
Della Valle, 2007	P	94	41 (44)	10	5	NS	Y	Y	ST
Fehring, 1994	R	97	11 (11)	NS	NS	600	Y	N	IA, Rx
Fehring, 1996	R	130	4 (3)	NS	NS	NS	Y	Y	IA, Rx
Feldman, 1995	R	33	9 (27)	10	5	400	Y	N	—
Feldman, 1995	R	33	9 (27)	5	5	400	Y	N	—
Fink, 2008	P	145	40 (28)	5	1	400	Y	Y	—
Kanner, 2008	R	132	14 (11)	5	5	NS	Y	N	RA
Ko, 2005	R	40	9 (23)	5	5	400	Y	N	RA, OI, ST
Lonner, 1996	P	172	19 (11)	5	1	400	Y	N	ST
Lonner, 1996	P	172	19 (11)	10	1	400	Y	N	ST
Malhotra, 2004	R	41	12 (29)	NS	NS	NS	Y	N	—
Mirra, 1982	C	35	26 (74)	5	5	250	Y	N	—
Morawietz, 2006	R	233	80 (34)	NS	NS	400	Y	N	—
Muller, 2009	P	106	92	NS	NS	NS	Y	Y	—

			(87)						
Nilsdotter-Augustinsson, 2007	P	47	21 (45)	5	NS	NS	Y	Y	−
Nuñez, 2007	R	136	49 (36)	5	NS	400	Y	N	OI, NSI
Pandey, 1999	P	602	79 (13)	1	10	400	Y	N	IA
Pandey, 1999	P	602	79 (13)	5	10	400	Y	N	IA
Pons, 1999	P	80	16 (20)	5	NS	NS	Y	Y	—
Savarino, 2009	P	31	10 (32)	1	1	600	Y	N	—
Schäfer, 2008	P	284	92 (32)	5	10	400	Y	N	—
Schinsky, 2008	C	201	55 (27)	10	5	NS	Y	Y	IA, ST
Shokeir, 1996	P	82	8 (10)	5	NS	NS	Y	N	—
Tohtz, 2009	P	52	15 (29)	2	10	400	Y	Y	—

*PJI = periprosthetic joint infection, PMN = polymorphonuclear leukocyte, and NS = none specified. †R = retrospective (historical) cohort, P = prospective cohort, and C = cross-sectional study. ‡Clinical or laboratory parameters suggestive of infection. §Rx = prior antibiotics, OI = obvious infection, ST = sinus tract, IA = inflammatory arthritis, RA = rheumatoid arthritis, and NSI = no suspicion of infection.

TABLE E-2 Search Terms Used in the Systematic Review

Search No.	Search Terms	No. of Results
Ovid MEDLINE 1950 to January Week 2 2010		
1	arthroplasty, replacement, hip/ or arthroplasty, replacement, knee/	16,683
2	arthroplasty/ and (hip joint/ or knee joint/)	1449
3	joint prosthesis/ and (hip joint/ or knee joint/)	1875
4	hip prosthesis/ or knee prosthesis/	21,095
5	prosthesis/ and (hip joint/ or knee joint/)	535
6	or/1-5	35,158
7	exp bacterial infections/co, di, ep, pa, mi or exp bacteria/pa, ip	431,698
8	6 and 7	605
9	prosthesis-related infection/co, mi, pa, di, ep	2540
10	7 and 9	1286
11	8 or 10	1633
12	6 and neutrophils/pa	12
13	11 or 12	1640
14	reoperation/ or revised.mp. or revision.mp. or intraoperative*.mp. or (intra adj operative*).mp. [mp = title, original title, abstract, name of substance word, subject heading word, unique identifier]	190,997
15	13 and 14	374
16	limit 15 to humans	370
17	frozen$.mp. and 16 [mp = title, original title, abstract, name of substance word, subject heading word, unique identifier]	14
18	16 and (histolog* or microbiolog* or histopathol*).mp. [mp = title, original title, abstract, name of substance word, subject heading word, unique identifier]	68
19	17 or 18	74
20	limit 19 to "diagnosis (optimized)"	32
21	"sensitivity and specificity"/ or exp diagnostic errors/ or predictive value of tests/ or ROC.mp. or AUC.mp. or (positive adj predictive).mp. or (negative adj predictive).mp. [mp = title, original title, abstract, name of substance word, subject heading word, unique identifier]	388,196
22	((likelihood adj ratio*) or cutoff or (cut adj "off")).mp. [mp = title, original title, abstract, name of substance word, subject heading word, unique identifier]	35,578
23	19 and (21 or 22)	28
24	19 and (prospective* or retrospective* or cross-section* or cohort*).mp. [mp = title, original title, abstract, name of substance word, subject heading word, unique identifier]	32
25	(arthroplasty, replacement, hip/ae or arthroplasty, replacement, knee/ae or (arthroplasty/ae and (hip joint/ae or knee joint/ae)) or (joint prosthesis/ae and (hip joint/ae or knee joint/ae)) or (hip prosthesis/ae or knee prosthesis/ae) or (prosthesis/ae and (hip joint/ae or knee joint/ae))) and (7 or neutrophils/pa or prosthesis-related infection/)	1019
26	25 and (frozen*.mp. or 21 or 22 or (intra adj operative*).mp. or intraoperative*.mp.) [mp = title, original title, abstract, name of substance word,	159

	subject heading word, unique identifier]	
27	26 and (di or mi or pa).fs.	107
28	19 or 23 or 24 or 27	164
29	limit 28 to humans	163
EMBASE 1988 to 2010 Week 03		
1	exp infection/	955,754
2	exp hip arthroplasty/	18,983
3	exp knee replacement/	12,782
4	(2 or 3) and 1	3907
5	frozen section/	6235
6	4 and 5	25
7	4 and frozen*.mp. [mp = title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]	49
8	(6 or 7) and ((intra adj operative) or intraoperative*).mp. [mp = title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]	22
9	prosthesis infection/ and (2 or 3) and frozen*.mp. and (intraoperative* or (intra adj operative*) or preoperative*).mp. [mp = title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]	7
10	8 or 9	23

TABLE E-3 QUADAS Tool Questionnaire*

1. Was the spectrum of patients representative of the patients who will receive the test in practice?
2. Were selection criteria clearly described?
3. Is the reference standard likely to correctly classify the target condition?
4. Is the time period between reference standard and index test short enough to be reasonably sure that the target condition did not change between the two tests?
5. Did the whole sample or a random selection of the sample, receive verification using a reference standard of diagnosis?
6. Did patients receive the same reference standard regardless of the index test result?
7. Was the reference standard independent of the index test (i.e., the index test did not form part of the reference standard)?
8. Was the execution of the index test described in sufficient detail to permit replication of the test?
9. Was the execution of the reference standard described in sufficient detail to permit its replication?
10. Were the index test results interpreted without knowledge of the results of the reference standard?
11. Were the reference standard results interpreted without knowledge of the results of the index test?
12. Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?
13. Were uninterpretable/intermediate test results reported?
14. Were withdrawals from the study explained?

*QUADAS = Quality Assessment of Diagnostic Accuracy Studies. Item 1 concerns generalizability. Items 3, 4, 5, 6, 7, 10, 11, and 12 concern validity. Items 2, 8, 9, 13, and 14 concern clarity.

TABLE E-4 Quality Assessment of the Included Studies

	QUADAS Quality Item No.*													
Author, Year	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Abdul-Karim, 1998	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Athanasou, 1995	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Banit, 2002	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Borrego, 2007	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Bori, 2006	●	○	●	●	●	●	●	●	●	●	●	●	●	●
Della Valle, 2007	●	●	●	●	●	●	○	●	●	●	●	●	●	●
Fehring, 1994	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Fehring, 1996	●	●	●	●	●	●	○	●	●	●	●	●	●	●
Feldman, 1995	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Fink, 2008	●	?	●	●	●	●	○	●	○	●	●	●	●	●
Kanner, 2008	●	●	●	●	●	●	●	●	○	●	●	●	●	●
Ko, 2005	○	●	●	●	●	●	●	●	●	●	●	●	●	●
Lonner, 1996	●	●	●	●	●	●	●	●	○	●	●	●	●	●
Malhotra, 2004	●	○	●	●	●	●	●	●	○	●	●	●	●	●
Mirra, 1982	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Morawietz, 2006	●	○	●	●	●	●	●	●	○	●	●	●	●	●
Muller, 2009	●	●	●	●	●	●	○	●	●	●	●	●	●	●
Nilsdotter-Augustinsson, 2007	○	●	●	●	●	●	●	●	●	●	●	●	●	●
Nuñez, 2007	○	●	●	●	●	●	●	●	●	●	●	●	●	●
Pandey, 1999	●	○	●	●	●	●	●	●	●	●	●	●	●	●
Pons, 1999	●	○	●	●	●	●	○	●	●	●	●	●	●	●
Savarino, 2009	●	●	●	●	●	●	●	●	○	●	●	●	●	●
Schäfer, 2008	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Schinsky, 2008	●	●	●	●	●	●	○	●	●	●	●	●	●	●
Shokeir, 1996	●	○	●	●	●	●	●	●	●	●	●	●	●	●
Tohtz, 2009	●	●	●	●	●	●	○	●	●	●	●	●	●	●

*QUADAS = Quality Assessment of Diagnostic Accuracy Studies. ● = yes, ○ = no, and ? = unclear.

TABLE E-5 Subgroup Analyses of Diagnostic Accuracy Outcomes According to Prevalence of PJI, Inclusion or Exclusion of Frozen Sections in the Reference Standard for PJI, and Study Design*

Subgroup	No. of Studies	Likelihood Ratio of a Positive Test		Likelihood Ratio of a Negative Test		Diagnostic Odds Ratio		
		Ratio (95% CI)	I^2 *(%)*	Ratio (95% CI)	I^2 *(%)*	Ratio (95% CI)	I^2 *(%)*	P Value for Interaction
Prevalence of PJI								0.92
<20	8	11.36 (4.43 to 29.10)	85.7	0.31 (0.11 to 0.90)	95.6	40.0 (8.0 to 200.77)	84.1	
20-40	14	10.86 (7.47 to 15.78)	56.5	0.24 (0.17 to 0.33)	66.4	54.4 (30.56 to 96.18)	54.2	
≥40	4	16.61 (6.76 to 40.79)	0	0.14 (0.08 to 0.24)	40	128.51 (43.65 to 378.33)	0	
Reference standard independent of index test								0.15
Yes	19	10.97 (7.10 to 16.93)	74.2	0.27 (0.16 to 0.44)	90.7	43.35 (22.29 to 84.32)	70	
No	7	14.98 (8.86 to 25.31)	26	0.16 (0.09 to 0.29)	69.0	106.7 (38.29 to 297.51)	55.1	
Study design								0.70
Historical cohort	11	7.76 (4.80 to 12.53)	53.7	0.37 (0.21 to 0.67)	90.2	23.78 (9.68 to 58.40)	70.4	
Prospective	12	17.93 (9.16 to 35.11)	80.4	0.15 (0.09 to 0.24)	59.8	140.88 (54.62 to 361.09)	65.5	
Cross-sectional	3	13.74 (8.42 to 22.43)	0	0.26 (0.17 to 0.40)	51.1	51.28 (27.04 to 97.26)	0	

*CI = confidence interval, I^2 = inconsistency index, and PJI = periprosthetic joint infection.