

## Appendix

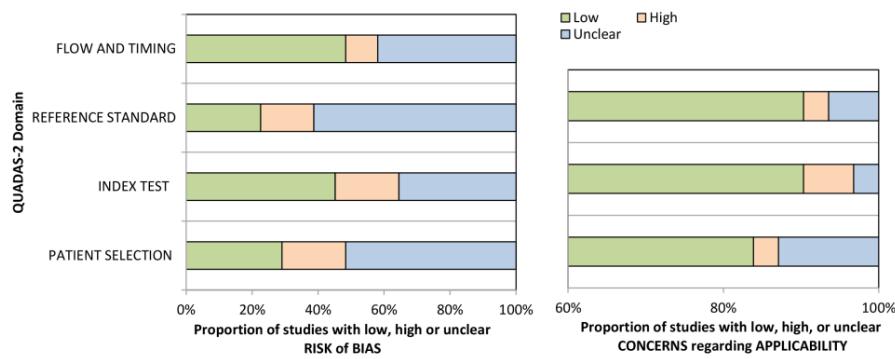


Fig. E-1

Methodological quality of the included studies with QUADAS-2.

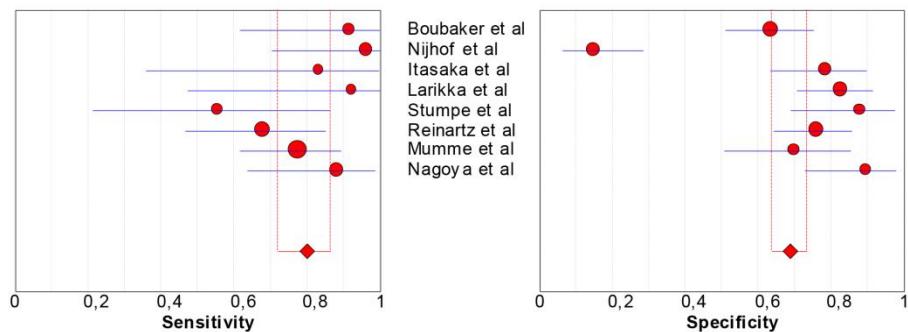


Fig. E-2

Diagnostic accuracy of bone scintigraphy for the detection of periprosthetic hip infection. The values are given as the mean with the 95% confidence interval. The diamond and vertical lines indicate the pooled estimate and the 95% confidence interval.

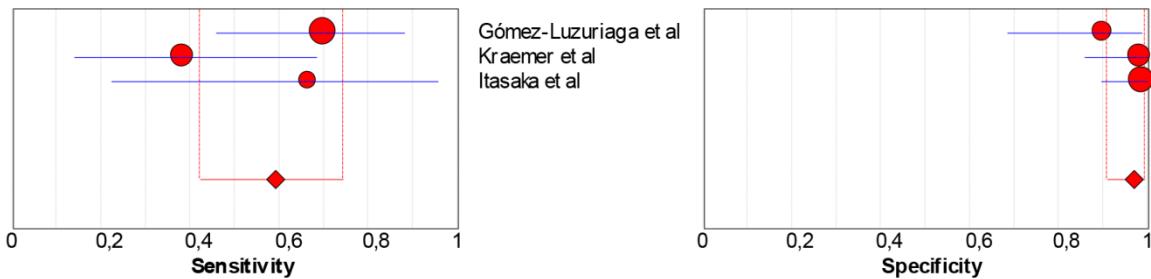


Fig. E-3

Diagnostic accuracy of combined bone and gallium scintigraphy for the detection of periprosthetic hip infection. The values are given as the mean with the 95% confidence interval. The diamond and vertical lines indicate the pooled estimate and the 95% confidence interval.

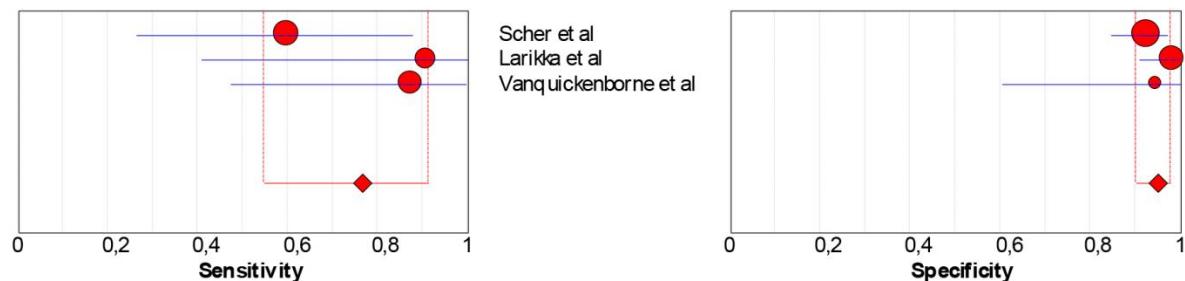


Fig. E-4

Diagnostic accuracy of combined bone and leukocyte scintigraphy for the detection of periprosthetic hip infection. The values are given as the mean with the 95% confidence interval. The diamond and vertical lines indicate the pooled estimate and the 95% confidence interval.

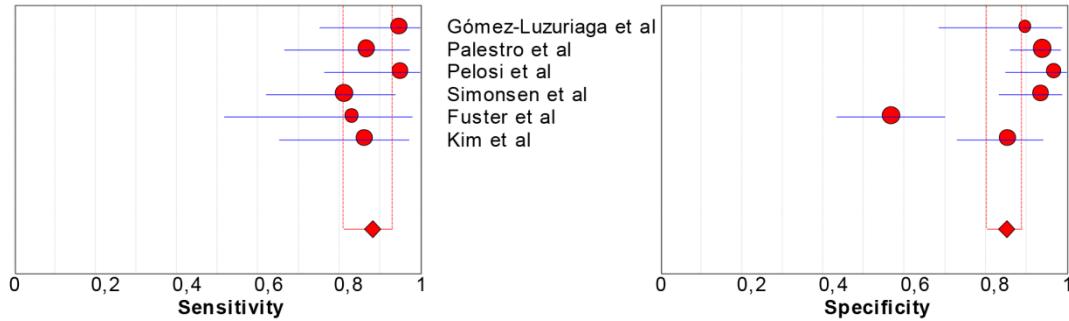


Fig. E-5  
Diagnostic accuracy of leukocyte scintigraphy for the detection of periprosthetic hip infection.  
The values are given as the mean with the 95% confidence interval. The diamond and vertical lines indicate the pooled estimate and the 95% confidence interval.

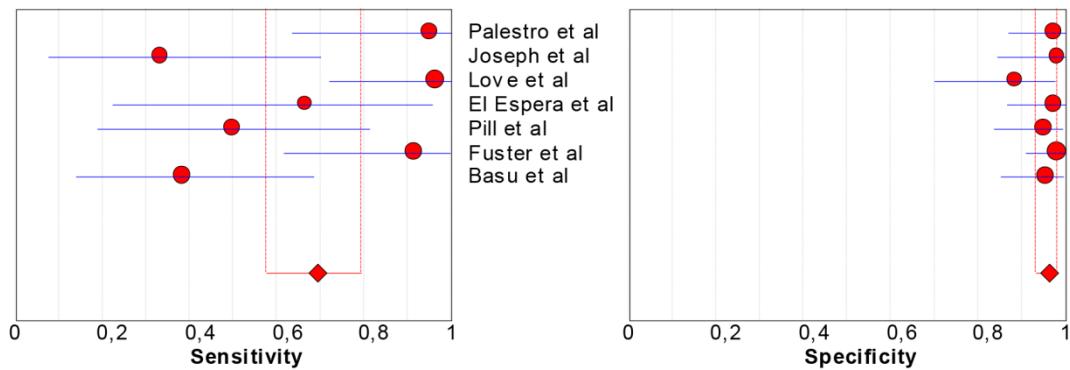


Fig. E-6  
Diagnostic accuracy of combined leukocyte and bone marrow scintigraphy for the detection of periprosthetic hip infection. The values are given as the mean with the 95% confidence interval.  
The diamond and vertical lines indicate the pooled estimate and the 95% confidence interval.

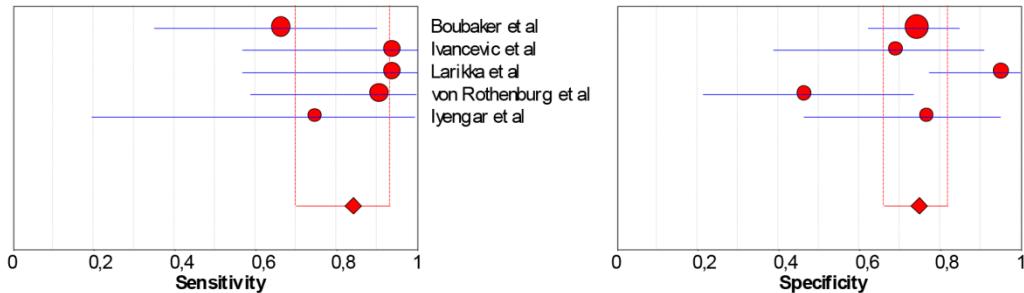


Fig. E-7

Diagnostic accuracy of antigranulocyte scintigraphy for the detection of periprosthetic hip infection. The values are given as the mean with the 95% confidence interval. The diamond and vertical lines indicate the pooled estimate and the 95% confidence interval.

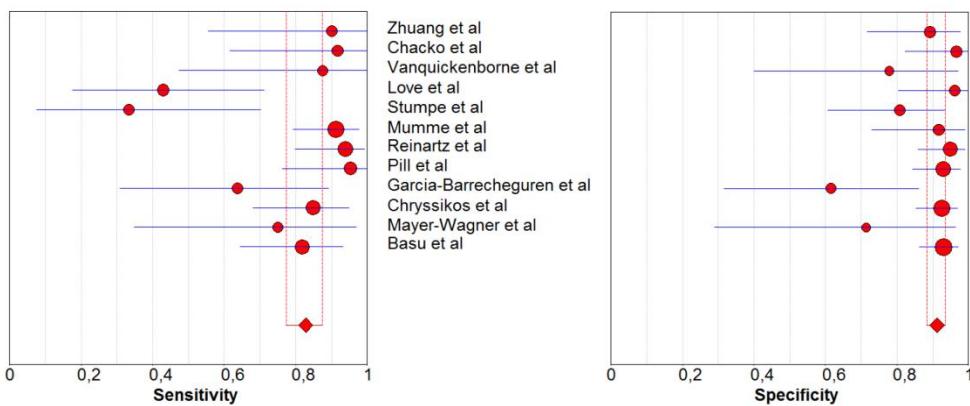


Fig. E-8

Diagnostic accuracy of FDG PET for the detection of periprosthetic hip infection. The values are given as the mean with the 95% confidence interval. The diamond and vertical lines indicate the pooled estimate and the 95% confidence interval.

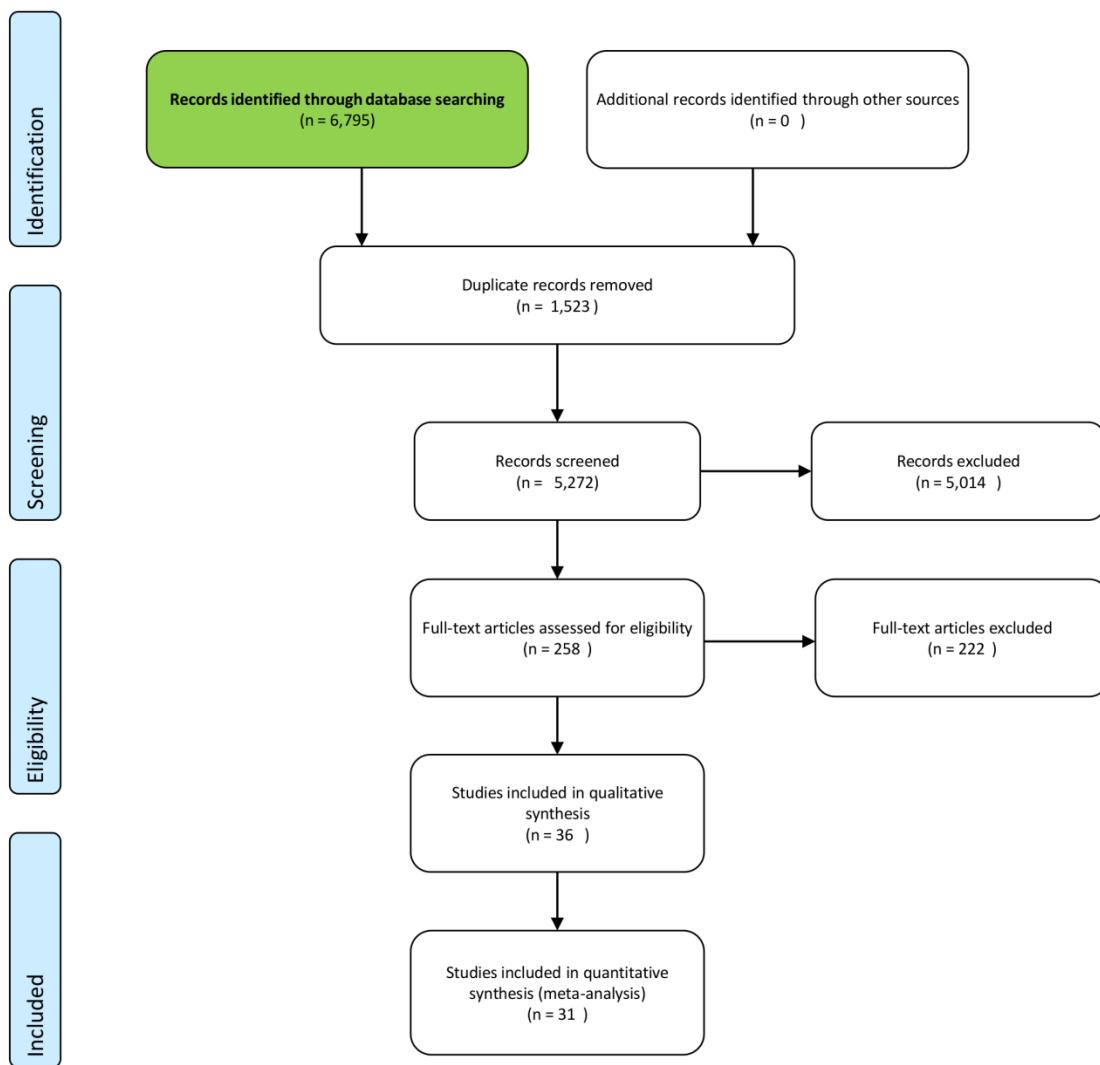


Fig. E-9  
PRISMA 2009 flow diagram.

TABLE E-1 Characteristics of the Studies Included in the Meta-Analysis\*

Study	Design†	No. of Patients	Sex (M/F)	Mean Age (Range) (yr)	No. of Prostheses	Reference Standard	Total No. of Hip Prostheses/No. Infected
Gómez-Luzuriaga et al. <sup>45</sup> (1988)	NR	40	NR	NR	40 hip	M	40/20
Palestro et al. <sup>46</sup> (1990)	Retro.	72	26/46	62.0 (20-87)	92 hip	M, IOF	92/23
Kraemer et al. <sup>54</sup> (1993)	Retro.	72	42/30	60.0 (21-82)	43 hip	M	43/13
Boubaker et al. <sup>39</sup> (1995)	Pro.	57	34/23	72.7 (29-92)	78 hip	M, IOF, CFU	78/12
Nijhof et al. <sup>40</sup> (1997)	NR	226	108/118	54.3 (5-90)	87 hip, 17 knee	M, IOF, A, CFU	87/21
Scher et al. <sup>55</sup> (2000)	NR	143	NR	61.0 (26-87)	91 hip, 40 knee	M, H, IOF	91/10
Itasaka et al. <sup>43</sup> (2001)	Retro.	46	8/38	67.5 (49-78)	48 hip	M, H	48/6
Joseph et al. <sup>52</sup> (2001)	Retro.	58	18/40	60.0 (27-82)	36 hip, 22 knee	M, H, IOF	36/9
Larikka et al. <sup>42</sup> (2001)	Pro.	64	18/46	NR	64 hip	M, IOF	64/6
Zhuang et al. <sup>38</sup> (2001)	NR	62	NR	NR (27-81)	38 hip, 36 knee	M, IOF, A, CFU	38/10
Ivančević et al. <sup>49</sup> (2002)	Retro.	30	13/17	62.0 (30-85)	21 hip, 6 knee	M, H	21/8
Larikka et al. <sup>51</sup> (2002)	NR	30	11/19	NR (25-89)	30 hip	M, IOF, A, CFU	30/8
Chacko et al. <sup>30</sup> (2002)	Retro.	32	20/12	NR (27-89)	41 hip	M, H, IOF, CFU	41/12
Vanquickenborn et al. <sup>37</sup> (2003)	Pro.	17	8/9	NR (42-77)	17 hip	M, IOF, A, CFU	17/8
El Espera et al. <sup>53</sup> (2004)	NR	60	NR	NR	45 hip, 28 knee	M, IOF, A	45/6
Love et al. <sup>17</sup> (2004)	NR	59	22/37	NR (35-89)	40 hip, 19 knee	M, H, IOF	40/14
Pelosi et al. <sup>47</sup> (2004)	Retro.	78	36/42	69.5 (30-87)	47 hip, 35 Knee	M, IOF, CFU	47/21
von Rothenburg et al. <sup>50</sup> (2004)	Retro.	38	9/29	71.0 (45-81)	26 hip, 12 knee	M, IOF, A, L	26/11
Stumpe et al. <sup>36</sup> (2004)	Pro.	35	12/23	NR (46-81)	35 hip	M, H, IOF, A, CFU	35/9
Iyengar and Vinjamuri <sup>20</sup> (2005)	Retro.	38	18/20	NR (54-89)	17 hip, 13 knee, 8 other	M, H, IOF, A, I, CFU	17/4
Mumme et al. <sup>33</sup> (2005)	NR	50	19/31	68.7 (42-89)	70 hip	M, H, CFU	70/48
Reinartz et al. <sup>35</sup> (2005)	NR	63	32/31	68.0 (43-88)	92 hip	M, H, IOF, CFU	92/8
Pill et al. <sup>34</sup> (2006)	Pro.	89	NR	NR (29-85)	92 hip	M, H, S, IOF, A, L	92/21
García-Barrecheguren et al. <sup>32</sup> (2007)	Pro.	24	12/12	67.8 (37-81)	24 hip	M, H, S, IOF	24/11

Simonsen et al. <sup>48</sup> (2007)	Retro.	66	25/41	NR (47-95)	76 hip	M, H, IOF, CFU	76/27
Chryssikos et al. <sup>31</sup> (2008)	Pro.	113	54/59	NR (31-87)	127 hip	M, H, S, IOF, A, L	127/33
Fuster et al. <sup>44</sup> (2008)	Pro.	70	28/42	68.0 (NR)	70 hip	M, CFU	70/12
Nagoya et al. <sup>41</sup> (2008)	NR	46	18/28	NR (28-81)	46 hip	M, H, IOF	46/17
Mayer-Wagner et al. <sup>21</sup> (2010)	NR	32	13/19	NR (45-90)	15 hip, 22 knee	M	15/8
Basu et al. <sup>29</sup> (2014)	Pro.	221	112/109	57.0 (18-84)	134 hip, 87 knee	M, H, IOF	134/33
Kim et al. <sup>19</sup> (2014)	Retro.	164	53/111	65.0 (17-82)	71 hip, 93 knee	M, H, IOF, CFU, A	71/26
Total		2,195					1,753/475

\*Retro. = retrospective, pro. = prospective, M = microbiology, H = histology, IOF = intraoperative findings, A = aspiration, L = laboratory (erythrocyte sedimentation rate and C-reactive protein), S = sinus tract, I = imaging, CFU = clinical follow-up of at least 6 months, and NR = not recorded. †Explicit notation in study.

TABLE E-2 Characteristics of the Reference Test(s) and Implants\*

Study	Hip Prostheses	Fixation (C, U, H)	Total Hip / Hybrid Hip Prosthesis	Mean Age of Hip Prostheses (Range)	Imaging: Minimal Time Postop.	Minimal Duration of Follow-up (mo)
Gómez-Luzuriaga et al. <sup>45</sup>	NR	NR	40/0	4.3 y (1-11 y)	>12 mo	NR
Palestro et al. <sup>46</sup>	P68, R24	C92, U0, H0	92/0	4.6 y (1 wk-17 y)	>1 wk	>6
Kraemer et al. <sup>54</sup>	NR	NR	NR	4.5 y (8 mo-13 y)	>8 mo	NR
Boubaker et al. <sup>39</sup>	NR	C59, U19, H0	NR	6.3 y (7-17 y)	>7 mo	>8
Nijhof et al. <sup>40</sup>	NR	NR	87/0	NR	NR	>12
Scher et al. <sup>55</sup>	NR	NR	91/0	47 mo	NR	NR
Itasaka et al. <sup>43</sup>	NR	C48, U0, H0	48/0	10.9 y (2-18 y)	>2 y	>24
Joseph et al. <sup>52</sup>	NR	NR	36/0	NR	NR	NR
Larikka et al. <sup>42</sup>	NR	NR	64/0	6.6 y† (2 mo-22 y)	>2 mo	>12
Zhuang et al. <sup>38</sup>	NR	NR	NR	NR (3 mo-8 y)	>3 mo	>12
Ivančević et al. <sup>49</sup>	NR	NR	21/0	NR	NR	>6
Larikka et al. <sup>51</sup>	NR	NR	30/0	12 mo (1 wk-12 y)	>1 wk	>12
Chacko et al. <sup>30</sup>	NR	NR	NR	NR	>12 mo	>9
Vanquickenborne et al. <sup>37</sup>	P10, R7	NR	17/0	NR (0-14 y)	>0 mo	>6
El Espera et al. <sup>53</sup>	NR	NR	NR	5.4 y (-)	NR	NR
Love et al. <sup>17</sup>	P30, R10	C14, U10, H16	37/3	NR (1 mo-20 y)	>1 mo	NR
Pelosi et al. <sup>47</sup>	NR	NR	47/0	NR	NR	>12
von Rothenburg et al. <sup>50</sup>	NR	C3, U23, H0	NR	NR(2 mo-10 y)	>2 mo	NR
Stumpe et al. <sup>36</sup>	P26, R9	C18, U17, H0	NR	71 mo (12-260 mo )	>1 y	>6
Iyengar and Vinjamuri <sup>20</sup>	NR	NR	NR	NR	NR	>12
Mumme et al. <sup>33</sup>	NR	C51, U17, H2	NR	9.2 y, SD 5.7	>12 mo	>9
Reinartz et al. <sup>35</sup>	NR	C60, U32, H0	NR	NR (1-31 mo)	>6 mo (FDG-PET)	>9
Pill et al. <sup>34</sup>	NR	NR	NR	NR	NR	NR
García-Barrecheguren et al. <sup>32</sup>	NR	NR	NR	NR	>6 mo	NR
Simonsen et al. <sup>48</sup>	P68, R8	C35, U19, H22	62/14	NR	1.5-2 y (0.07-14 y)	>12
Chryssikos et al. <sup>31</sup>	NR	NR	NR	NR	>12 mo	NR
Fuster et al. <sup>44</sup>	NR	NR	70/0	46 mo	>3 mo	>12
Nagoya et al. <sup>41</sup>	NR	NR	30/16	8.5 y (1 mo-28 y)	>1 mo	NR
Mayer-Wagner et al. <sup>21</sup>	NR	NR	NR	NR	NR	NR
Basu et al. <sup>29</sup>	NR	NR	NR	5.8 y (FDG PET) and 6.4 y (LS)	NR	>6
Kim et al. <sup>19</sup>	NR	NR	NR	3.0 y† (2 wk-32 y)	>2 wk	>12

\*P = primary implant, R = revision, NR = not recorded, C = cemented hip prostheses, U = uncemented hip prostheses, H = hybrid hip prostheses, SD = standard deviation, FDG PET = fluorodeoxyglucose positron emission tomography, and LS = leukocyte scintigraphy. †The value is given as the median.

TABLE E-3 Diagnostic Accuracy of Bone Scintigraphy for Detection of Periprosthetic Hip Infection\*

Study	Disease		Sensitivity (95% CI)	Specificity (95% CI)	Tracer	Dose (MBq)	Criteria for Infection
	Pos.	Neg.					
Boubaker et al. <sup>39</sup> (1995)	12	66	0.92 (0.62 - 1.00)	0.64 (0.51 - 0.75)	99mTc-DPD	740	Uptake in both the early and delayed phases
Nijhof et al. <sup>40</sup> (1997)	13	47	0.96 (0.70 - 1.00)	0.15 (0.06 - 0.28)	99mTc-MDP	600	Uptake in both the blood pool and late phases
Itasaka et al. <sup>43</sup> (2001)	6	42	0.83 (0.36 - 1.00)	0.79 (0.63 - 0.90)	99mTc-MDP	NR	Diffuse increased uptake femoral and/or acetabular (no early phase)
Larikka et al. <sup>42</sup> (2001)	6	58	0.92 (0.47 - 1.00)	0.83 (0.71 - 0.91)	99mTc-HDP	550	Uptake in arterial and soft phases
Stumpe et al. <sup>36</sup> (2004)	9	25	0.56 (0.21 - 0.86)	0.88 (0.69 - 0.97)	99mTc-DPD	700	Increased uptake in all 3 phases
Reinartz et al. <sup>35</sup> 2005)	25	67	0.68 (0.46 - 0.85)	0.76 (0.64 - 0.86)	99mTc-HDP	733	Wilson criteria: uptake in both the blood pool and late phases
Mumme et al. <sup>33</sup> (2005)	40	30	0.78 (0.62 - 0.89)	0.70 (0.51 - 0.85)	99mTc-HDP	750	Wilson Criteria: uptake in both the blood pool and late phases
Nagoya et al. <sup>41</sup> (2008)	17	29	0.88 (0.64 - 0.99)	0.90 (0.73 - 0.98)	99mTc-MDP	740	Increased uptake in all 3 phases
Total	128	364					
Pooled estimate			0.80 (0.72 - 0.86)	0.69 (0.64 - 0.73)			

\*Diagnostic odds ratio = 11,006; heterogeneity chi-squared = 6.66 (degrees of freedom = 7); p = 0.465. Inconsistency ( $I^2$ ) = 0.0%. Pos. = positive, neg. = negative, 95% CI = 95% confidence interval, 99mTc = 99m-technetium, MDP = methylene diphosphonate, HDP = hydroxymethylene diphosphonate, and DPD = dicarboxy diphosphonate.

TABLE E-4 Diagnostic Accuracy of Combined Bone and Gallium Scintigraphy for Detection of Periprosthetic Hip Infection\*

Study	Disease		Sensitivity (95% CI)	Specificity (95% CI)	Tracer	Dose	Criteria for Infection
	Pos.	Neg.					
Gómez-Luzuriaga et al. <sup>45</sup> (1988)	20	20	0.70 (0.46-0.88)	0.90 (0.68-0.99)	Tc99m/Ga67	NR	When Ga67 image was spatially incongruent with that of Tc99m, or, if spatially congruent, of greater intensity
Kraemer et al. <sup>54</sup> (1993)	13	30	0.38 (0.14-0.68)	0.98 (0.86-1.00)	Tc99m/Ga67	NR	When the gallium uptake was spatially incongruent or spatially congruent but greater than the Tc99m uptake
Itasaka et al. <sup>43</sup> (2001)	6	42	0.67 (0.22 -0.96)	0.99 (0.90-1.00)	Tc99m/Ga67	NR	When Ga67 image showed increased activity of a different distribution (incongruity) or of a relatively greater activity than the focus of the Tc99m scans
Total	49	72					
Pooled estimate			0.59 (0.42-0.74)	0.97 (0.91-0.99)			

\*Diagnostic odds ratio = 34,173; heterogeneity chi-squared = 1.23 (degrees of freedom = 2); p = 0.542. Inconsistency ( $I^2$ ) = 0.0%. Pos. = positive, neg. = negative, Tc99m = 99m-technetium, Ga67 = gallium-67, and NR = not recorded.

TABLE E-5 Diagnostic Accuracy of Combined Bone and Leukocyte Scintigraphy for Detection of Periprosthetic Hip Infection\*

Study	Disease		Sensitivity (95% CI)	Specificity (95% CI)	Tracer	Dose (MBq)	Criteria for Infection
	Pos.	Neg.					
Scher et al. <sup>55</sup> (2000)	10	81	0.60 (0.26 - 0.88)	0.93 (0.85 - 0.97)	<sup>99m</sup> Tc-HDP/ <sup>111</sup> In-Oxine	925 (25 mCi)/14.8- 18.5 (400-500 µCi)	When indium scan showed hyperactivity in a different distribution (incongruity) or a relatively greater intensity than the activity on the Tc99 scan
Larikka et al. <sup>42</sup> (2001)	5	59	0.91 (0.41 - 1.00)	0.98 (0.91 - 1.00)	<sup>99m</sup> Tc-HDP/ <sup>99m</sup> Tc-HMPAO	550/370	When periprosthetic leukocyte uptake intensity was higher than that of the bone metabolic image in at least 1 zone, or if uptake was incongruent
Vanquickenborne et al. <sup>37</sup> (2003)	8	9	0.88 (0.47 - 1.00)	0.95 (0.60 - 1.00)	<sup>99m</sup> Tc-MDP/ <sup>99m</sup> Tc-HMPAO	740/185	Moderately or substantial uptake around the hip prosthesis that was higher uptake than that of the contralateral hip region, but only when the lesions were congruous on both scans
Total	23	149					
Pooled estimate			0.77 (0.55 - 0.91)	0.95 (0.90 - 0.98)			

\*Diagnostic odds ratio = 67.336; heterogeneity chi-squared = 3.62 (degrees of freedom = 2); p = 0.164. Inconsistency ( $I^2$ ) = 44.7%. Tc99m = <sup>99m</sup>-technetium, HDP = hydroxymethylene diphosphonate, and <sup>99m</sup>Tc-HMPAO = hexamethylpropyleneamine oxime.

TABLE E-6 Diagnostic Accuracy of Leukocyte Scintigraphy for Detection of Periprosthetic Hip Infection\*

Study	Disease		Sensitivity (95% CI)	Specificity (95% CI)	Tracer	Dose	Criteria for Infection
	Pos.	Neg.					
Gómez-Luzuriaga et al. <sup>45</sup> (1988)	20	20	0.95 (0.75 - 1.00)	0.90 (0.68 - 0.99)	111In-Oxine	NR	More intense uptake than that of the contiguous bone and negative otherwise
Palestro et al. <sup>46</sup> (1990)	23	69	0.87 (0.66 - 0.97)	0.94 (0.86 - 0.98)	111In-Oxine	18.5 MBq (500 µCi)	Activity in the headzone, regardless of activity in any other zone
Pelosi et al. <sup>47</sup> (2004)	21	34	0.95 (0.76 - 1.00)	0.97 (0.85 - 1.00)	99Tc-HMPAO	430-600 MBq	SQ: K <sub>late</sub> > K <sub>early</sub> by at least 10%
Simonsen et al. <sup>48</sup> (2007)	27	49	0.81 (0.62 - 0.94)	0.94 (0.83 - 0.99)	111In-Oxine or 99Tc-HMPAO	36 MBq/628 MBq†	When periprosthetic uptake was greater than the activity in surrounding bone tissue and in the contralateral site
Fuster et al. <sup>44</sup> (2008)	12	58	0.83 (0.52 - 0.98)	0.57 (0.43 - 0.70)	99Tc-HMPAO	185 MBq	Any extramedullary periprosthetic focal uptake
Kim et al. <sup>19</sup> (2014)	22	49	0.86 (0.65 - 0.97)	0.86 (0.73 - 0.94)	99Tc-HMPAO	740-1100 MBq	Increased uptake in the periprosthetic area or if the foci in nearby soft tissue had greater activity than the background soft tissue activity
Total	125	279					
Pooled estimate			0.88 (0.81 - 0.93)	0.85 (0.80 - 0.89)			

\*Diagnostic odds ratio = 60,329; heterogeneity chi-squared = 11.57 (degrees of freedom = 5); p = 0.041. Inconsistency ( $I^2$ ) = 56.8%. Pos. = positive, neg. = negative, NR = not recorded, SQ = semiquantitative, K = suspected region of infection/reference region (bone marrow), and HMPAO = hexamethylpropylene amine oxime. †Mean dose.

TABLE E-7 Diagnostic Accuracy of Combined Leukocyte and Bone Marrow Scintigraphy for Detection of Periprosthetic Hip Infection\*

Study	Disease		Sensitivity (95% CI)	Specificity (95% CI)	Tracer	Dose	Criteria for Infection
	Pos.	Neg.					
Palestro et al. <sup>46</sup> (1990)	10	40	0.95 (0.63 - 1.00)	0.98 (0.87 - 1.00)	<sup>111</sup> In-Oxine/ <sup>99m</sup> Tc-SC	18.5 MBq (500 µCi)/370 MBq (10 mCi)	Incongruent labeled leukocyte and sulfur colloid images
Joseph et al. <sup>52</sup> (2001)	9	27	0.33 (0.07 - 0.70)	0.98 (0.84 - 1.00)	<sup>111</sup> In-Oxine/ <sup>99m</sup> Tc-SC	500 µCi /10 µCi	Pattern of activity on the indium image that was not matched on the colloid images
Love et al. <sup>17</sup> (2004)	14	26	0.97 (0.72 - 1.00)	0.88 (0.70 - 0.98)	<sup>111</sup> In-Oxine/ <sup>99m</sup> Tc-SC	18.5 MBq (500 µCi)/370 MBq (10 mCi)	Periprosthetic activity on the indium image without corresponding activity on the marrow scan, regardless of intensity or location
El Espera et al. <sup>53</sup> (2004)	6	39	0.67 (0.22 - 0.96)	0.97 (0.87 - 1.00)	<sup>111</sup> In-Oxine/ <sup>99m</sup> Tc-SC	30 MBq/185 MBq	When increased activity was observed on the leukocyte image, without corresponding uptake on the bone marrow images (incongruent patterns)
Pill et al. <sup>34</sup> (2006)	10	41	0.50 (0.19 - 0.81)	0.95 (0.83 - 0.99)	<sup>111</sup> In-Oxine/ <sup>99m</sup> Tc-SC	500 µCi/15 mCi	When activity on the leukocyte image was observed, without corresponding activity on the bone marrow scans
Fuster et al. <sup>44</sup> (2008)	12	58	0.92 (0.62 - 1.00)	0.98 (0.91 - 1.00)	<sup>99</sup> Tc-HMPAO/ <sup>99m</sup> Tc-SC	185 MBq / 370 MBq	All uptake of leukocytes inconsistent with the bone marrow images
Basu et al. <sup>29</sup> (2014)	13	46	0.38 (0.14 - 0.68)	0.96 (0.85 - 0.99)	<sup>111</sup> In-Oxine/ <sup>99m</sup> Tc-SC	500 µCi/555 MBq	When activity in the periprosthetic region on the leukocyte image was observed, without corresponding activity on the bone marrow images
Total	74	277					
Pooled estimate			0.69 (0.58 - 0.79)	0.96 (0.93 - 0.98)			

\*Diagnostic odds ratio = 65,303; heterogeneity chi-squared = 9.54 (degrees of freedom = 6); p = 0.145. Inconsistency ( $I^2$ ) = 37.1%. Pos. = positive, neg. = negative, <sup>99m</sup>Tc-SC = <sup>99m</sup>Tc-sulfur colloid, and HMPAO = hexamethylpropyleneamine oxime.

TABLE E-8 Diagnostic Accuracy of Antigranulocyte Scintigraphy for Detection of Periprosthetic Hip Infection\*

Study	Disease		Sensitivity (95% CI)	Specificity (95% CI)	Antibody Type	99mTc Dose	Criteria for Infection
	Pos.	Neg.					
Boubaker et al. <sup>39</sup> (1995)	12	63	0.67 (0.35 - 0.90)	0.75 (0.62 - 0.85)	Besilesomab†	750 MBq	When there was accumulation of the antibody in the ROI that increased with time (SQ)
Ivanćević et al. <sup>49</sup> (2002)	8	13	0.94 (0.57 - 1.00)	0.69 (0.39 - 0.91)	Sulesomab‡	<1.1 GBq	Uptake higher than that in the bone marrow of the contralateral iliac crest (SQ)
Larikka et al. <sup>51</sup> (2002)	8	22	0.94 (0.57 - 1.00)	0.95 (0.77 - 1.00)	Sulesomab‡	370 MBq	When there was distinct and constant uptake (Q)
von Rothenburg et al. <sup>50</sup> (2004)	11	15	0.91 (0.59 - 1.00)	0.47 (0.21 - 0.73)	Sulesomab‡	15-25 mCi	When there was abnormal uptake greater than could be expected from a blood pool effect (Q)
Iyengar and Vinjamuri <sup>20</sup> (2005)	4	13	0.75 (0.19 - 0.99)	0.77 (0.46 - 0.95)	Sulesomab‡	650 MBq	Abnormal image that showed increased uptake in the region of the pathological process (Q)
Total	43	126					
Pooled estimate			0.84 (0.70 - 0.93)	0.75 (0.66 - 0.82)			

\*Diagnostic odds ratio = 13,147; heterogeneity chi-squared = 5.24 (degrees of freedom = 4); p = 0.263. Inconsistency ( $I^2$ ) = 23.7%. Pos. = positive, neg. = negative, SQ = semiquantitative, Q = qualitative, and ROI = region of interest. †A mouse monoclonal antibody labeled with 99mTc-anti-NCA 95. ‡A mouse monoclonal antibody labeled with 99mTc-anti-NCA90.

TABLE E-9 Diagnostic Accuracy of FDG PET for Detection of Periprosthetic Hip Infection

Study	Disease		Sensitivity(95% CI)	Specificity (95% CI)	Tracer	Dose	Criteria for Infection
	Pos.	Neg.					
Zhuang et al. <sup>38</sup> (2001)	10	28	0.90 (0.55 - 1.00)	0.89 (0.72 - 0.98)	18F-FDG	4.22 - 4.56 MBq/kg	Increased uptake in the BPI compared with PST, not if uptake was limited to only femoral head or neck
Chacko et al. <sup>30</sup> (2002)	12	29	0.92 (0.62 - 1.00)	0.97 (0.82 - 1.00)	18F-FDG	2.52 MBq/kg	Uptake in the BPI
Vanquickenborne et al. <sup>37</sup> (2003)	8	9	0.88 (0.47 - 1.00)	0.78 (0.40 - 0.97)	18F-FDG	370 MBq	Moderately or substantially higher uptake than contralateral distal femur
Love et al. <sup>17</sup> (2004)	14	26	0.43 (0.18 - 0.71)	0.96 (0.80 - 1.00)	18F-FDG	150 - 20 MBq	Semiquantitative analysis of BPI activity in femur with T/B ratio
Stumpe et al. <sup>36</sup> (2004)	9	26	0.33 (0.07 - 0.70)	0.81 (0.61 - 0.93)	18F-FDG	300 - 400 MBq	Diffusely increased uptake in BPI, less than or comparable with bladder uptake
Mumme et al. <sup>33</sup> (2005)	46	24	0.91 (0.79 - 0.98)	0.92 (0.73 - 0.99)	18F-FDG	200-250 MBq	Increased uptake in the BPI and PST
Reinartz et al. <sup>35</sup> (2005)	33	59	0.94 (0.80 - 0.99)	0.95 (0.86 - 0.99)	18F-FDG	283 ± 38 MBq	Uptake in the PST
Pill et al. <sup>34</sup> (2006)	21	71	0.95 (0.76 - 1.00)	0.93 (0.84 - 0.98)	18F-FDG	140 µCi/kg	Uptake in BPI, not if uptake was limited to only PST or neck of prosthesis
García-Barrecheguren et al. <sup>32</sup> (2007)	11	13	0.64 (0.31 - 0.89)	0.62 (0.32 - 0.86)	18F-FDG	10 - 15 mCi	Uptake in BPI, more than PST, fistulous or synovial uptake
Chryssikos et al. <sup>31</sup> (2008)	33	94	0.85 (0.68 - 0.95)	0.93 (0.85 - 0.97)	18F-FDG	140 µCi/kg	Uptake in BPI, not if uptake was limited to only PST or neck of prosthesis
Mayer-Wagner et al. <sup>21</sup> (2010)	8	7	0.75 (0.35 - 0.97)	0.71 (0.29 - 0.96)	18F-FDG	180 MBq	Uptake in BPI, not if uptake was limited to tip of stem or neck
Basu et al. <sup>29</sup> (2014)	33	101	0.82 (0.65 - 0.93)	0.93 (0.86 - 0.97)	18F-FDG	0.14 mCi/kg	Uptake in BPI in middle portion of stem, not if uptake was limited to only PST, neck, or synovial uptake
Total	238	487					
Pooled estimate			0.83 (0.77 - 0.87)	0.91 (0.89 - 0.94)			

\*Diagnostic odds ratio = 38,189; heterogeneity chi-squared = 36.28 (degrees of freedom = 11); p < 0.0001. Inconsistency ( $I^2$ ) = 69.7%. 18F-FDG = fluorodeoxyglucose, BPI = bone-prosthesis interface, T/B = target-to-background, and PST = periprosthetic soft tissue.

TABLE E-10 Search String Used for Identifying Studies on Diagnostic Imaging in Diagnosing Periprosthetic Hip Infection

**MEDLINE:**

(((((("Hip"[Mesh] OR "Hip Joint"[Mesh]) OR "Femur"[Mesh]) OR "Acetabulum"[Mesh]) OR (hip[tiab])) OR (hips[tiab])) OR (femur\*[tiab]) OR (femoral[tiab]) OR (coxa\*[tiab]) OR (Trochanter\*[tiab]) OR (acetabul\*[tiab]) OR (Cotyloid Cavit\*[tiab]) OR (cups[tiab]) OR (cup[tiab]) OR (stem[tiab]) OR (stems[tiab]) OR (socket\*[tiab]))) AND (((((((("Prostheses and Implants"[Mesh:noexp]) OR "Joint Prosthesis"[Mesh:noexp]) OR "Hip Prosthesis"[Mesh]) OR "Metal-on-Metal Joint Prostheses"[Mesh]) OR "Prosthesis Implantation"[Mesh:noexp])) OR "Arthroplasty, Replacement"[Mesh:noexp])) OR prosthe\*[tiab]) OR implant\*[tiab]) OR arthroplast\*[tiab]) OR replac\*[tiab])) AND (((((((("Infection"[Mesh]) OR "Biofilms"[Mesh]) OR "Bacterial Adhesion"[Mesh]) OR "Adhesins, Bacterial"[Mesh]) OR "Bacterial Infections"[Mesh])) OR infect\*[tiab]) OR sepsi\*[tiab]) OR septi\*[tiab]) OR bacterie\*[tiab]) OR bacteria\*[tiab]) OR biofilm\*[tiab]) OR (bacterem\*[tiab] OR bacteraem\*[tiab])) OR inflammat\*[tiab])) AND (((((((("Magnetic Resonance Imaging"[Mesh] OR ("magnetic resonance"[tiab] AND (image[tiab] OR images[tiab] OR imaging[tiab]))) OR zeugmatograph\*[tiab] OR MRI\*[tiab] OR NMR\*[tiab] OR Magnetization\*[tiab] OR Magnetisation\*[tiab] OR fMRI\*[tiab] OR MR imag\*[tiab])) OR (Magnetic Resonance Spectroscopy[Mesh] AND (chemical shift[tiab] AND imag\*[tiab]))) OR (((("ultrasonography"[Subheading] OR "Ultrasonography"[Mesh])) OR ultraso\*[tiab]) OR echograph\*[tiab]) OR sonograph\*[tiab]) OR echotomograph\*[tiab])) OR (((((("Radionuclide Imaging"[Mesh]) OR "radionuclide imaging"[Subheading]) OR "Radiopharmaceuticals"[Pharmacological Action])) OR (scintigraph\*[tiab] OR scintiphograph\*[tiab])) OR (radionuclid\*[tiab] OR radioisotop\*[tiab])) OR Gamma Camera Imag\*[tiab]) OR (indium[tiab] OR in-111[tiab] OR 111in\*[tiab])) OR (99mtc[tiab] OR 99m[tiab]) OR scintiscan\*[tiab])) OR (((((((("Positron-Emission Tomography"[Mesh]) OR "Tomography, Emission-Computed"[Mesh])) OR "Tomography"[Mesh:noexp])) OR PET[tiab]) OR tomograph\*[tiab]) OR (((("Fluorodeoxyglucose F18"[Mesh]) OR "Deoxyglucose"[Mesh])) OR (deoxyglucose[tiab] OR deoxy-glucose[tiab] OR 2deoxyglucose[tiab])) OR (fluorin\*[tiab] OR fluoro[tiab] OR fluorodeoxyglucose[tiab] OR 18F[tiab] OR 18FDG[tiab] OR F-18DG[tiab])) OR (((("Tomography, X-Ray Computed"[Mesh]) OR (compute\*[tiab] AND tomograph\*[tiab])) OR (CT[tiab] OR CTs[tiab] OR CT's[tiab])) OR electron beam[tiab]) OR Tomodensitometr\*[tiab])) OR (((((((("Radiography"[Mesh]) OR "radiography"[Subheading])) OR radiograph\*[tiab]) OR x-ray\*[tiab]) OR x-radiograph\*[tiab]) OR xray\*[tiab]) OR Zonograph\*[tiab]) OR fluoroscop\*[tiab]) OR arthrograph\*[tiab]) OR roentgen\*[tiab]) OR rontgen\*[tiab])) OR image subtraction\*[tiab]))

**EMBASE:**

((radiography'/exp OR ('fluoroscopy'/exp OR 'xray'/exp OR 'image subtraction'/exp) OR (xradiograph\*:ab,ti OR xray\*:ab,ti OR zonograph\*:ab,ti OR fluoroscop\*:ab,ti OR arthrograph\*:ab,ti OR roentgen\*:ab,ti OR rontgen\*:ab,ti) OR (image NEAR/1 (subtraction OR subtractions)):ab,ti) OR ('computer assisted tomography'/exp OR (compute\*:ab,ti AND tomograph\*:ab,ti) OR (ct\*:ab,ti OR (electron AND beam:ab,ti) OR tomodensitometr\*:ab,ti)) OR ((('emission tomography'/exp OR 'tomography'/de OR 'fluorodeoxyglucose f 18'/exp OR 'deoxyglucose'/exp) OR

(pet:ab,ti OR tomograph\*:ab,ti OR deoxyglucose:ab,ti OR 2deoxyglucose:ab,ti OR fluorin\*:ab,ti OR fluoro:ab,ti OR fluorodeoxyglucose:ab,ti OR 18f:ab,ti OR 18fdg:ab,ti OR f18dg:ab,ti)) OR ((radioisotope diagnosis'/exp OR 'radiopharmaceutical agent'/exp OR 'radioisotope'/exp) OR (scintigraph\*:ab,ti OR scintiphograph\*:ab,ti OR radionuclid\*:ab,ti OR radioisotop\*:ab,ti OR indium:ab,ti OR in111:ab,ti OR 111in\*:ab,ti OR 99mtc:ab,ti OR 99m:ab,ti) OR ('gamma camera image':ab,ti OR 'gamma camera images':ab,ti OR 'gamma camera imaging':ab,ti)) OR ('echography'/exp OR (ultraso\*:ab,ti OR echograph\*:ab,ti OR sonograph\*:ab,ti OR echotomograph\*:ab,ti)) OR ('nuclear magnetic resonance imaging'/exp OR (magnetic AND resonance:ab,ti AND (image:ab,ti OR images:ab,ti OR imaging:ab,ti) OR zeugmatograph\*:ab,ti OR mri\*:ab,ti OR nmr\*:ab,ti OR magnetization\*:ab,ti OR magnetisation\*:ab,ti OR fmri\*:ab,ti OR mr AND imag\*:ab,ti))) AND (('hip prosthesis'/exp OR 'joint prosthesis'/de OR 'metal on metal joint prosthesis'/exp OR 'prosthesis'/de OR 'implantation'/de OR 'metal implantation'/exp OR 'hip arthroplasty'/exp) OR (prosthe\*:ab,ti OR implant\*:ab,ti OR arthroplast\*:ab,ti OR replac\*:ab,ti OR 'metal on metal':ab,ti)) AND (('acetabulum'/exp OR 'hip'/exp OR 'femur'/exp) OR (hip:ab,ti OR hips:ab,ti OR femur\*:ab,ti OR femoral:ab,ti OR coxa\*:ab,ti OR trochanter\*:ab,ti OR acetabul\*:ab,ti OR cups:ab,ti OR cup:ab,ti OR stem:ab,ti OR stems:ab,ti OR socket\*:ab,ti) OR (cotyloid:ab,ti AND cavit\*:ab,ti)) AND (('infection'/exp OR 'biofilm'/exp OR 'bacterium adherence'/exp OR 'adhesin'/exp) OR (infect\*:ab,ti OR sepsi\*:ab,ti OR septi\*:ab,ti OR bacterie\*:ab,ti OR bacteria\*:ab,ti OR biofilm\*:ab,ti OR baterem\*:ab,ti AND orbacteraem\*:ab,ti OR inflamat\*:ab,ti))

TABLE E-11 Results of Search for Studies on Diagnostic Imaging in Diagnosing Periprosthetic Hip Infection

No.	Search String	MEDLINE* (no. of studies)	Embase* (no. of studies)
1	Hip prostheses	74,103	91,982
2	Infected hip prostheses	11,341	16,476
3	Radiography or MRI or CT or scintigraphy or ultrasonography	2,305,863	3,834,824
4	No. 1 and no. 2 and no. 3	3,451	3,344

\*Search conducted on April 1, 2015.

TABLE E-12 Analysis of the Interpretation Criteria Used in the Included Studies of FDG PET for Diagnosing Periprosthetic Hip Infection Using the Z-Test\*

Criteria for Positivity for Index Test	Sensitivity (95% CI)	Comparison ( <i>p</i> value)	Specificity (95% CI)	Comparison ( <i>p</i> value)
1. BPI without limitation of location of uptake	0.87 (0.79 - 0.92)		0.91 (0.85 - 0.95)	
2. BPI with limitation of location of uptake	0.79 (0.71 - 0.86)		0.91 (0.88 - 0.94)	
1 versus 2		0.2973		1.0000
3. BPI uptake compared with uptake in bladder	0.33 (0.07 - 0.70)		0.81 (0.63 - 0.93)	
4. BPI uptake not compared with uptake in bladder	0.85 (0.79 - 0.89)		0.92 (0.89 - 0.94)	
3 versus 4		0.0064		0.0714
5. Only uptake in PST	0.94 (0.80 - 0.99)		0.95 (0.86 - 0.99)	
6. Uptake not only in PST	0.81 (0.75 - 0.86)		0.91 (0.88 - 0.93)	
7. BPI uptake > uptake PST	0.76 (0.53 - 0.92)		0.81 (0.65 - 0.91)	
8. BPI without comparison uptake PST	0.83 (0.78 - 0.88)		0.92 (0.89 - 0.95)	
5 versus 6		0.1207		0.3843
5 versus 7		0.1135		0.0588
5 versus 8		0.1648		0.4985
6 versus 7		0.6315		0.0594
7 versus 8		0.4855		0.0403
9. BPI uptake only in femoral component	0.81 (0.65 - 0.91)		0.92 (0.85 - 0.96)	
10. BPI uptake not limited to uptake in femoral component	0.83 (0.77 - 0.88)		0.91 (0.88 - 0.94)	
9 versus 10		0.7759		0.7570

\*FDG PET = fluorodeoxyglucose positron emission tomography, BPI = bone-prosthesis interface, and PST = periprosthetic soft tissue.

TABLE E-13 Comparison of Imaging Techniques in Diagnosing Periprosthetic Hip Infection with the Z-Test

Imaging Techniques Compared*		Sensitivity			Specificity		
Technique 1	Technique 2	Technique 1	Technique 2	Comparison ( <i>p</i> value)	Technique 1	Technique 2	Comparison ( <i>p</i> value)
BS	BS-GA	0.80	0.59	0.013	0.69	0.97	<0.0001
BS	BS-LS	0.80	0.77	0.760	0.69	0.95	<0.0001
BS-GA	BS-LS	0.59	0.77	0.189	0.97	0.95	0.463
LS	BS	0.88	0.80	0.097	0.92	0.69	<0.0001
LS	LS-BMS	0.88	0.69	<0.0001	0.92	0.96	0.102
LS	BS-LS	0.88	0.77	0.200	0.92	0.95	0.341
LS	BS-GA	0.88	0.59	<0.0001	0.92	0.97	0.115
LS-BMS	BS	0.69	0.80	0.083	0.96	0.69	0.000
LS-BMS	BS-GA	0.69	0.59	0.314	0.96	0.97	0.657
LS-BMS	BS-LS	0.69	0.77	0.494	0.96	0.95	0.669
AGS	BS	0.84	0.80	0.584	0.75	0.69	0.218
AGS	BS-GA	0.84	0.59	0.022	0.75	0.97	<0.0001
AGS	BS-LS	0.84	0.77	0.519	0.75	0.95	<0.0001
AGS	LS	0.84	0.88	0.528	0.75	0.92	<0.0001
AGS	LS-BMS	0.84	0.69	0.094	0.75	0.96	<0.0001
FDG-PET	BS	0.86	0.80	0.157	0.93	0.69	<0.0001
FDG-PET	BS-GA	0.86	0.59	<0.0001	0.93	0.97	0.146
FDG-PET	BS-LS	0.86	0.77	0.293	0.93	0.95	0.449
FDG-PET	LS	0.86	0.88	0.650	0.93	0.92	0.640
FDG-PET	LS-BMS	0.86	0.69	0.002	0.93	0.96	0.123
FDG-PET	AGS	0.86	0.84	0.748	0.93	0.75	<0.0001

\*BS = bone scintigraphy, BS-GA = combined bone and gallium scintigraphy, LS = leukocyte scintigraphy, LS-BMS = combined leukocyte and bone marrow scintigraphy, AGS = antigranulocyte scintigraphy, and FDG PET = fluorodeoxyglucose positron emission tomography.

TABLE E-14 QUADAS-2 Evaluation

Study	Risk of Bias*				Applicability Concerns*		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Gómez-Luzuruaga et al. <sup>45</sup>	2	2	0	2	0	2	1
Palestro et al. <sup>46</sup>	0	1	1	0	0	1	1
Kraemer et al. <sup>54</sup>	0	0	0	0	1	1	1
Boubaker et al. <sup>39</sup>	0	2	0	0	1	1	1
Nijhof et al. <sup>40</sup>	0	2	0	1	2	1	1
Scher et al. <sup>55</sup>	1	0	0	1	1	1	1
Itasaka et al. <sup>43</sup>	0	0	1	0	1	1	1
Joseph et al. <sup>52</sup>	1	1	2	1	1	1	1
Larikka et al. <sup>42</sup>	1	0	2	1	1	1	1
Zhuang et al. <sup>382</sup>	1	1	1	0	1	1	1
Ivanćević et al. <sup>49</sup>	1	1	1	1	1	1	1
Larikka et al. <sup>51</sup>	0	2	0	1	1	1	1
Chacko et al. <sup>30</sup>	0	1	0	0	1	1	1
Vanquickenborne et al. <sup>37</sup>	2	2	2	2	1	1	0
El Espera et al. <sup>53</sup>	0	1	1	1	1	1	1
Love et al. <sup>17</sup>	2	1	0	0	0	1	1
Pelosi et al. <sup>47</sup>	2	1	0	0	1	1	1
von Rothenburg et al. <sup>50</sup>	0	0	0	0	1	1	1
Stumpe et al. <sup>36</sup>	1	1	0	1	1	1	1
Iyengar and Vinjamuri <sup>20</sup>	0	0	2	2	0	1	1
Mumme et al. <sup>33</sup>	0	1	0	1	1	1	1
Reinartz et al. <sup>35</sup>	1	1	0	1	1	1	1
Pill et al. <sup>34</sup>	0	0	2	0	1	2	2
García-Barrecheguren et al. <sup>32</sup>	2	0	0	1	1	1	1

Simonsen et al. <sup>48</sup>	0	0	0	0	1	0	1
Chryssikos et al. <sup>31</sup>	0	2	0	0	1	1	1
Fuster et al. <sup>44</sup>	0	0	1	1	1	1	1
Nagoya et al. <sup>41</sup>	1	0	0	1	1	1	1
Mayer-Wagner et al. <sup>21</sup>	2	1	0	1	1	1	1
Basu et al. <sup>29</sup>	1	1	0	1	1	1	0
Kim et al. <sup>19</sup>	0	1	1	0	1	1	1

\*0 indicates unclear risk, 1 indicates low risk, and 2 indicates high risk.