Question: Diagnosis of Breast Cancer: Is FDG-PET Useful for discerning cancer from benign mammographic lesions?

Recommendation: The Panel **recommends against** routine FDG-PET in the diagnosis of breast cancer, but the panel suggested the use in specific clinical circumstances (e.g. high risk patients with masses > 2 cm or aggressive malignancy and serum tumor marker elevation).

Review	**Accuracy**							**Effect on patient outcomes**		**Quality of evidence**		
	Sensitivity	Specificity	DA	PPV	NPV	LR+	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
Facey et al **Differentiation of benign from malignant breast mass** 5 studies (n=14-144pts/ study) RT:HPA	>80%	>76%	NR	NR	NR	NR	NR	NR	NR	Low (Possible flaws, including the analysis of mixing patients and lesions)	Unclear	Low
Facey et al and BCBSA review **Patients with breast mass or abnormal mammogram and negative PET who had biopsy** 13 studies, n = 606 RT: HPA or cytological aspiration	Meta-analysis of 10 studies that had patient as unit of analysis: 89% [95CI (84-93%)]	Meta-analysis of 10 studies that had patient as unit of analysis: 80% [95CI% (70%-87%)]	NR	NR	88%, if prevalence is 50%	4.45	0.14	NR	NR	Moderate (Possible verification, spectrum and detection bias. Only 7 studies were prospective and therefore risk of false negative results is high)	High	Moderate
Facey et al and BCBSA review **Patients with low suspicious findings on mammography or other imaging and have been referred for 3-6**	NA	NA	NA	NA	NA	NA	NA	NA	NA	Unclear	NA	NA

months of follow-up, in order to perform early biopsy or avoid short-interval time imaging FU No studies were found												
Bruening et al **Different imaging tests for the diagnosis of breast abnormalities** 9 studies, n=20-86 pts/study regarding the use of PET RT: unclear	Mean threshold: PET was 82% compared with 93% of MRI and 86% of US	Mean threshold: 78% vs. 72% for MRI vs. 66% for US	NR	NR	From summary LR-: 92% for PET compared with 96% for MRI and 95% for US, if prevalence is 20%	3.78 (calculated)	Fixed effect meta-analysis: 0.33	NR	NR	Moderate	High	Moderate

Question: What is the Usefulness of FDG-PET for Assessing Axillary Involvement in Breast Cancer Patients?

Recommendation: The Panel **recommends against** routine administration of FDG-PET for axillary staging of breast cancer.

Review	**Accuracy**							**Effect on patient outcomes**		**Quality of evidence**		
	Sensitivity	Specificity	DA	PPV	NPV	LR+	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
BCBSA review **Staging of axillary lymph node metastasis irrespective of clinical nodal status** 15 studies, n=809 RT: HPA	Random effect meta-analysis: 82% [95CI (73-88%)]	Random effect meta-analysis: 90% [95CI (83-94%)]	NR	NR	NR	8.2	0.2	NR	NR	Moderate (possible flaws, including the analysis of mixing patients and lesions)	High	Moderate
Facey et al and BCBSA review **Detection of lymph node metastasis in patients with no palpable axillary lymph nodes** 4 studies, n = 203 RT: HPA	Random effect meta-analysis: 80% [95CI (46-95%)]	Random effect meta-analysis 89% [95CI (83-94%)]	NR	NR	92.1%, given a prevalence for node positive disease of 30% and assumed sensitivity of 81% and specificity of 95%	7.27	0.22	NR	NR	Moderate (possible flaws, including the analysis of mixing patients and lesions)	High	Moderate
BCBSA review **Staging lymph node metastasis in patients with palpable axillary lymph nodes** 4 studies, n = 269 RT: HPA	Random effect meta-analysis: 93% [95CI (81-98%)]	Random effect meta-analysis: 78% 95CI (49-93%)	NR	NR	NR	NR		NR	NR	Moderate	High	Moderate

Facey et al and BCBSA review **PET compared with axillary lymph node dissection (ALND) or ALND+sentinel node biopsy (SNB)** 8 studies, n=337 RT: ALND or ALND+SNB	If ALND as reference test: 40-93% If ALND+SNB as reference test: 20-50%	If ALND as reference test: 87-100%. If ALND+SNB as reference test: 82-100%	NR	NR	If ALND as reference test: 68-96% If ALND+SNB as reference test 57-80%	NR	NR	NR	NR	Moderate (possible flaws, including the analysis of mixing patients and lesions)	Moderate	Moderate

Question: What is the Usefulness of FDG-PET in the Detection of Metastatic or Recurrent Breast Cancer?

Recommendation: The Panel **recommends** that FDG-PET should routinely be used in addition to conventional work-up in detection of metastatic or recurrent breast cancer in those patients **clinically suspected** of metastasis/recurrence. The panel also **recommended against** routine use of PET in surveillance of patients who are **asymptomatic**

Review	**Accuracy**							**Effect on patient outcomes**		**Quality of evidence**		
	Sensitivity	Specificity	DA	PPV	NPV	LR+	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
Isasi et al **Impact of FDG-PET in the detection of metastatic disease and recurrence** 18 studies, n=unclear RT: HPA or FU	Patient as unit of analysis: 90%	Patient as unit of analysis: 87%	maximum combined sensitivity and specificity was 86%	NR	NR	6.92	0.11	NR	NR	Moderate	High	Moderate
Facey et al. **Evaluation of recurrence combining local and distant recurrence** 3 studies, n=30-75 RT: HPA	73%, 93%, 91%	96%, 79%, 96%	NR	NR	NR	NR	NR	NR	NR	Low (analysis of mixing patients and lesions)	Low	Low
Facey et al. **Restaging for detection of locoregional recurrence in symptomatic patients** 3 studies, n= 142 RT: HPA or FU	Overall NR	Overall NR	NR	NR	NR	NR	NR	NR	NR	Low (analysis of mixing patients and lesions)	Low	Low

Facey et al. **Detection of distant metastases/recurrence in patients with breast cancer who underwent staging evaluation** 10 studies, n=484, but 4 comparative studies with patient data (n=217) RT: HPA or FU	PET sens > 85% compared with CT or CWU (sens > 18-73%)	PET specificity was 90% in 2 studies (CWU or CT was 81/85%), 73% in 1 study (CT was 54%) and 50% in the last study (CWU specificity not stated).	NR	NR	NR	NR	NR	NR	NR	Low (possible verification and selection bias)	Low	Low
BCBSA review **Detection of distant metastases/ recurrence** 5 studies, n=196 RT: HPA or FU or other imaging techniques	Overall NR	Overall NR	NR	NR	NR	NR	NR	NR	NR	Low (possible verification and selection bias)	Moderate	Low

Question: What is the Usefulness of FDG-PET for the Diagnosis of Colorectal Carcinoma?

Recommendation: The Panel **recommends against** routine administration of FDG-PET for detection of primary colorectal carcinoma.

Review	**Accuracy**							**Effect on pts outcomes**		**Quality of evidence**		
	Sensitivity	Specificity	DA	PPV	NPV	LR+	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
Facey et al **Detection of malignant primary tumor** 2 Studies, n= 40 RT: HPA in 1, not stated in other	>85%	67% in one study, not reported in the other one	NR	NR	NR	NR	NR	NR	NR	Low	Unclear	low

Question: What is the Usefulness of FDG-PET in the Management of Colorectal Liver Metastasis?

Recommendation: The Panel **recommends** that FDG-PET should be used routinely in addition to conventional workup imaging in preoperative diagnostic work-up of the patient with potentially resectable hepatic metastasis of colorectal cancer

Review	**Accuracy**							**Effect on pts outcomes**		**Quality of evidence**		
	Sensitivity	Specificity	DA	PPV	NPV	LR+	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
Bipat et al **Colorectal liver metastases** 21 Studies, n= 1058 RT: HPA, intra-operatory observation or FU	**Per lesion (pooled mean):** 75.9% (61.1-86.3) Others (not a direct comparison): helical CT = 64% 1.0 T and 1.5T MRI = 66% and 64% Non-helical CT = 52%. **Per patient (pooled mean):** 94.6% (92.5-96.1) Others (not a direct comparison): helical CT = 65% 1.5T MRI = 76% Non-helical CT = 60%.	NR	NR	NR	NR	NR	NR	NR	NR	Moderate	High	Moderate
Wiering et al **Management of liver metastases** 32 studies, n=8-145 RT: HPA or FU, but in some studies was unclear.	**Per hepatic lesions:** PET= 88.0% (95 CI 88%-98%) CT = 82.7% (95 CI 64.2%-88.6%)	**Per hepatic lesions:** PET = 96.1% (95 CI 70%-100%) CT=84.1% (95 CI 68.2%-97.0%).	NR	NR	NR	22	0.12	PET resulted in change in clinical management 32% (20-58%) of time in the 13 out of 17 studies with the quality scores above the mean. In 6 papers with the highest quality score, the mean change in management was 25% (20-32).	NR	Moderate	High	Moderate

Kinkel et al **Detection of hepatic metastases from primary or recurrent CRC** 9 studies, n=423 RT: HPA, core biopsy, cytology or follow-up	90% [95%CI (82-96)] No statistical difference between the 7 studies that used PET only (pooled sensitivity of 90%) versus the 2 studies that used PET/CT (pooled sensitivity of 92%)	> 85% in 7 studies (in 4 out of the 7, the specificity was superior to 95%)	NR	NR	NR	NR	NR	NR	NR	Moderate	Low (some conclusions were based on indirect data and authors did not provide sufficient details to assess the quality of the included studies)	Moderate
BCBSA review **PET detecting hepatic lesions in initial staging after surgery** 8 studies, n=456 and 11 studies, n =680 RT: unclear	92%	98%	95%	Unweighted polled average 5 studies = 98%	93%, at prevalence of met of 46%	46	0.08	Authors found that 11 studies (n=680 patients) reported proportion of patients for whom PET affected management decisions (not exclusively assessing hepatic metastases only). The range of change in management was from 7% to 68% (the average was 20%). PET was influential in ruling out (unnecessary) surgery in 12% of patients, while it influenced initiating surgery in 8%. Thus, when PET affected management decisions, it was more often used to recommend against surgery in 60% of patients.	NR	Moderate	Moderate	Moderate

Huerbner et al **Restaging for detection of liver recurrence** 7 studies, n=393 with liver imaging information RT: unclear	**Hepatic involvement (patient as unit of analysis):** 96.3% [95%CI (93.6-99.0)] **Hepatic involvement (lesions as unit of analysis) (n=182):** Sens= 90.9% [95%CI (86.2-95.6)]	**Hepatic involvement (patient as unit of analysis):** 99.0% [95%CI (97.7-100)] **Hepatic involvement (lesions as unit of analysis) (n=182):** 97.4% [95%CI (92.5-100%)]	NR	NR	NR	Hepatic involvement (patient as unit of analysis) 98.2 Hepatic involvement (lesions as unit of analysis): 35	Hepatic involvement (patient as unit of analysis) 0.37 Hepatic involvement (lesions as unit of analysis): 0.09	See next question	NR	Unclear (Possibility of selection, verification, detection and spectrum bias - Unclear quality evidence across available outcomes, but the authors stated that 3 out of the 11 studies achieved more than 75% of the stipulated criteria by the reviewers. However, the information was not extractable in order to allow us to conduct an independent critical appraisal of the evidence	Low (information not available for proper critical appraisal)	Low
Facey et al **Detection of hepatic metastasis from primary or recurrent CRC, in most cases before surgery was planned** 8 studies, n= 24-115 pts per study RT = HPA	≥ 90% in all studies	≥ 95% in 6/7 studies, in 1 study - PET had specif of 57% compared with 80% of MRI and 14% of CT	NR	NR	NR	NR	NR	NR		Low (Analysis probably mixed lesions and patients)	Low (unclear)	Low

Question: Is FDG-PET Useful for the Detection of Extrahepatic Recurrence or Local Relapse?

Recommendation: The Panel **recommends** that PET scan routinely be obtained after conventional workup (CWU), especially if CEA levels are increased and CWU is negative. PET can also be used to differentiate between local relapse and postsurgical scars, but there is no evidence to define the timing and the sequence of the PET in relationship to other imaging techniques

Review	**Accuracy**							**Effect on patient outcomes**		**Quality of evidence**		
	Sensitivity	Specificity	DA	PPV	NPV	LR +	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
Huerbner et al **Restaging for detection of CRC recurrence** 5 out of 11 studies (n=281 patients) were analyzed for whole body PET RT: unclear	97.0% [95%CI (94.9-99.2)]	75.6% [95%CI (63.0-88.1)]	NR	NR	NR	4.04	0.04	Change-in-management outcome analyzed in 7 studies out of 11 studies (n= 349 pts). Change in management seen in 20 to 44% of cases. Pooled results: 29% [(95CI (25-34%)] For example, about 3 to 24 patients had avoided unnecessary surgery as a result of PET findings that upstaged the lesions.	NR	Low - Possibility of selection, verification, detection and spectrum bias - Unclear quality evidence across available outcomes, but the authors stated that 3 out of the 11 studies achieved more than 75% of the stipulated criteria by the reviewers. However, the information was not extractable in order to allow us to conduct an independent critical appraisal of the evidence	Low - information not available for proper critical appraisal	Low
Wiering et al **Management of liver metastases** 32 studies, n=8-145 RT: HPA or FU, but in some studies was unclear.	for extra-hepatic lesions**:** PET= 91.5% (95% CI 84.3%-96.2%) CT = 60.9% (95% CI 44.4%-68.9%)	for extra-hepatic lesions**:** PET= 95.4% (95% CI 71.4%-98.4%) CT = 91.1% (95% CI 66.0%-92.8%)	NR	NR	NR	19.9	0.09	PET resulted in change in clinical management 32% (20-58%) of time in 13 out of 17 studies with the quality scores above the mean. In 6 papers with the highest quality score, the mean change in management was 25% (20-32%).	NR	Moderate	High	Moderate

Facey et al **Evaluation of recurrence in suspected cases by clinical symptoms or elevated CEA** 13 studies, n=15-105 pts/study. RT: HPA	≥ 85% in 12/13 studies, 79% in the remaining studies Sensitivity and specificity was higher than CT in 4 studies and higher or better than MRI in 4 studies	≥ 90 % in 7 studies and in the remaining studies specificity ranged from 43-89%.								Low (Analysis probably mixed lesions and patients)	Low (unclear)	
Facey et al **PET scan in patients with suspected recurrence of CRC based on clinical features, imaging or abnormal tumor markers** 5 studies with PET, n=384 RT: HPA	**1) Detection of local recurrence** - 2 studies with higher sensitivity and specificity **2) Detect hepatic metastasis** - PET sens (90%) higher or similar to CT (74-100%) **3) Detection of extrahepatic metastasis** - PET sensitivity 90-100% vs CT sensitivity 57-74%. Specificity was calculated only in 1 study		NR	NR	NR	NR	NR	Where PET scan was superior, CWU had been equivocal, so PET results led to change in patient management	NR	Unclear	Unclear	Low
BCBSA review **Differentiation between local recurrence and post-operative scar** 6 studies, n= 198 RT: unclear	96%	98%	97%	99%	92% in the pooled prevalence of malignancy was 69%.	48	0.04	NR	NR	Moderate	High	Moderate

Question: Is FDG-PET Useful for Staging of Esophageal Cancer?

Recommendation: The Panel **recommends** that PET should routinely be obtained as an additional tool for staging esophageal cancer

Review	**Accuracy**							**Effect on patient outcomes**		**Quality of evidence**		
	Sensitivity	Specificity	DA	PPV	NPV	LR+	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
Van Westreenen et al **Diagnostic performance of PET scanning in preoperative staging of patients with esophageal cancer** 12 Studies, n=490 RT: all used PA, FU or surgery	For detection of local nodal metastases: 51% [95%CI (34-69%)]	For detection of local nodal metastases: 84% [95%CI (76-91%)]	NR	60%, at the mean prevalence of 55%	46%, at the mean prevalenc e of 55%	3.19	0.58	NR	NR	Moderate 92% of studies did not describe whether the reference test was blinded interpreted 3 studies with possible verification bias 4 studies with possible spectrum bias	High	Moderate
	For detection of distant metastases: 67% [95%CI (58-76%)]	For detection of distant metastases: 97% [95%CI (90-100%)]	NR	92% at the mean prevalence of 36%	83% at the mean prevalenc e of 36%	22.3	0.34	NR	NR			
Facey et al **Overview of all prognostic/ staging studies in esophageal cancer** 5 Studies, n= unclear RT: unclear	NR	NR	NR	NR	NR	NR	NR	5 studies reported change in management data, mainly to assess if surgery is to be avoided. No further details provided 2 studies reported survival 1) n=91- 30 months survival 30 months survival stated to be significantly better when PET predicted local disease. Local disease (survival = 60%) vs distant (survival = 20%), p=0.01 CT staging did not predict survival, p> 0.05 2) n= 48 – SUV predicting median survival SUV > 7, survival = 10 months SUV ≤ 7, survival = 35 months		Low (unclear)	Low (insufficient information)	Low

Question: What is the Usefulness of FDG-PET in Detection of Clinically Suspected Unknown Head and Neck Primary Tumors?

Recommendation: The Panel **recommends** that PET should be added to the routine imaging tests used in the attempt to identify unknown primary head and neck tumors. However, regardless if the initial PET findings are negative or positive, biopsy should be performed. PET would not be considered superfluous because when it is negative, it should be followed by multiple blinded biopsies while in case it is positive it will direct biopsy toward a PET positive lesion.

Review	Accuracy							Effect on patient outcomes		Quality of evidence		
	Sensitivity	Specificity	DA	PPV	NPV	LR+	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
Nieder et al **PET in the detection of unknown primary tumors in pts with cervical metastases** 8 Studies, n= 122 RT: unclear	Unweighted sum: 62%	Unweighted sum: 82%	Unweighted sum: 69%	Unweighted sum: 56%	Unweighted sum: 86%	3.72	0.40	In patients with negative clinical examination and conventional imaging, PET was able to detect primary tumors in less than 25% of cases	NR	Low (No clear statement about reference test, and small sample sizes)	Low	Low*
BCBSA review and Facey et al **PET in detection of unknown primary tumor**	Pooled = 69%, (range 44 to 100%),	Pooled = 69%, (range 20 to 100%),	NR	NR	NR	2.2	0.45	NR	NR	Low (Blinded interpretation was clearly stated only in 1 study,	High	Low*

8 studies, n=138 RT: HPA	Pooled TP: 32% Benefit over MRI not clear 4 studies studied PET when clinical examination and imaging had negative findings. The rate of TP was 28% 4 studies where CWU was not necessarily negative PET TP rate was 36%. PET was superior to CT, CT/MRI or endoscopy.								small sample size, and possible verification, spectrum and detection bias)		
Vermeersch, et al **PET in detection of unknown primary tumor** 7 studies, n unclear RT: unclear	PET identified primary tumor in 20-50% of cases, when conventional work-up was negative - PET may not detect some small tumors that are detectable by physical exam and panendoscopy	NR	NR	NR	NR	NR	NR	NR	Unclear (The paper does not address quality of evidence. It included studies cited in the reviews above)	Unclea r	Low*

* The quality of some primary research studies was low due to problems related to verification, detection, and spectrum biases in all SRs. However, the quality of many other individual research studies, particularly those recently published, was high. In these studies, all patients, with rare exceptions of patients in individual studies, had biopsy verification of disease and often multiple biopsy sampling procedures to exclude other sites in the head and neck. The group of patients was consistent in the papers published with all having standard clinical staging evaluations including direct panendoscopic evaluation that was either performed before or after PET in different studies.

Question: What is the Usefulness of FDG-PET in Diagnosis of Head and Neck Tumors?

Recommendation: The Panel **recommends against** routine use of PET in addition to CT/MRI in the diagnostic work-up of primary tumor head and neck malignancies.

review	**Accuracy**							**Effect on pts outcomes**		**Quality of evidence**		
	Sensitivity	Specificity	DA	PPV	NPV	LR+	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
Vermeersch, et al Facey et al **Diagnosis of primary head and neck cancer** 4 studies, n= unclear RT: unclear	PET= 85-95% CT=67-88% PET similar to CT/MRI (p=0.46),	PET= 67 – 100% CT= 44-75% PET had higher specificity than CT/MR (p=0.06).	NR	NR	NR	NR	NR	NR	NR	Unclear (no details were provided)	Low	Low

Question: What is the Usefulness of FDG-PET in Staging of Head and Neck Cancer?

Recommendation: The Panel **recommends** that the addition of PET to CT/MRI be routinely obtained in the attempt to improve nodal or distant disease staging of head and neck cancer for the particular clinical circumstance.

Review	Accuracy							Effect on patient outcomes		Quality of evidence		
	Sensitivity	Specificity	DA	PPV	NPV	LR+	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
BCBSA review **Detection of regional metastatic lymph nodes** 17 studies, n=540 RT: unclear	Per patient (8 studies, n=239): 83% PET vs CT, (patients as unit of analysis), 4 studies, = 123 Sensitivity= 81 vs 72% - PET vs MRI, (pts as unit analysis), 3 studies, n= 106 Sensitivity= 91% vs 82%	Per patient(8 studies, n=239): 87% PET vs CT, (pts as unit of analysis), 4 studies, = 123 and specif = 97 vs 89% PET vs MRI, (pts as unit analysis), 3 studies, n= 106 specif 88% vs 83%	NR	NR	NR	6.38	0.19	6 studies evaluated disagreements between PET and other imaging test. PET was usually correct among discordant findings in 60-100% of cases	NR	Moderate	High	Moderate
Vermeersch, et al **Detection of regional metastatic lymph nodes (SCC)** 17 studies, n= unclear RT: unclear	PET vs CT/MRI Sensitivity= 50-100% vs 36-95% (p=0.01)	PET vs CT/MRI Specif= 82-100% vs 25-100% (p=0.01)	NR	NR	NR	NR	NR	NR	NR	Unclear	Low	Low

HTA (ICES) **Detection of mets from newly diagnosed SCS** 7 studies, n = 30-78pts/study RT: HPA or CT/ MRI	4 studies compared PET vs CT/MRI for detection of lymph nodes metastases 72-87%	4 studies compared PET vs CT/MRI for detection of lymph nodes metastases 92-100%.	NR	NR	NR	PET PPV=90% /89% CT PPV= 40% and 74%)	PET NPV=93% and 99%), CT NPV= 72% and 95%)].	NR	NR	Moderate	Moderate	Moderate
Vermeersch, et al **Detection of distant mets and synchronous primaries in patients diagnosed with primary SCS of head and neck** 4 studies, n= 12-59pts/ study RT: unclear	NR	NR	NR	NR	NR	NR	NR	NR	low	Low	Low	
Facey et al **Lymph node involvement in patients with newly diagnosed head and neck cancer (*Predominantly SCC of the upper aerodigestive tract*)** 14 studies,	PET sensitivity similar to comparators in 3 studies (83%, 100%, 75%, respectively) In other 3 studies sensitivity for (PET=100%, 57%, 50%, respectively and	PET spec was similar or higher than comparators and only below 90% in 1 study	NR	NR	NR	NR	NR	2 studies reported change in management: 1 study reported 8/32 patients had management or 'intent of management changed' 1 study enrolling 12 patients PET	Unclear	Unclear	Low	

n=unclear RT: HPA	for comparator=78 %, 80%, 40%, respectively)							correctly indicated all cases of metastatic involvement (n unknown), but incorrectly indicated need for surgery in 5/12 pats				
Facey et al **Regional lymph node involvement in patients with cytologically or histologically proven primary head and neck cancer (*SCC and adenocarcinoma*)** 11 studies, n=8-106 pts/study. RT: HPA	81%,	79%	NR	NR	NR	By lymph node (n=3294) LR+ 17.3 (10.9-27.3) By patient (n=369) LR+ 3.9 (2.6-5.9)	By lymph node (n=3294) LR- 0.19 (0.13,0.27) By patient (n=369) LR- 0.24 (0.14-0.41)	NR	NR	Unclear	Unclear	Low

Question: What is the Usefulness of FDG-PET in Detection of Recurrence of Head and Neck Cancer?

Recommendation: The Panel **recommends** that PET be routinely obtained in addition to conventional imaging in the diagnostic work-up of the patient with potential recurrence of head and neck cancer

Review	**Accuracy**							**Effect on patients outcomes**		**Quality of evidence**		
	Sensitivity	Specificity	DA	PPV	NPV	LR+	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
Vermeersch, et al **PET versus CT/MRI for detection of residual or recurrent disease** 17 studies, n= uncleat RT: unclear	PET = 73 - 100% CT/MRI= 25 - 100% (p=0.01).	PET = 57 - 100% CT/MRI = 33 - 100% (p=0.02).	NR	NR	NR	NR	NR	NR	NR	Unclear	Low	Low
HTA (ICES) **Detection of recurrent SCS** 2 Studies, n= 74 RT: unclear	100% and 96% *See text for details*	93% and 61% *See text for details*	NR	NR	NR	NR	NR	NR	NR	Moderate	Moderate	Low
Facey et al and BCBSA review **Restaging in follow-up after primary treatment for head and neck cancer with radiation therapy or surgery** 24 studies, n= 568 RT=unclear	90% (43-100%)	76% (33-100%)	NR	NR	NR	3.75	0.13	Only one study has specifically addressed change in management due to PET findings, and was used to recommend palliative care instead of curative surgery in 9 of the 29 patients	NR	Moderate Small sample sizes Not all studies were comparative	Moderate	Moderate

Facey et al **Assessment of residual or recurrent head and neck cancer(PET versus CT/MRI)** 15 studies, n=10-66 pts/study RT: FU and sometimes HPA	Sensitivity ≥85% for PET in 14/15 studies, CT/MRI in 4/15	Specificity ≥80% for PET in 10/15 studies CT/MRI in 6/15 studies	NR	NR	NR	NR	NR	8 studies addressed change-in-management decisions, 3 notable studies 1) PET correctly indicated need for biopsy in 16/17 pts vs 11/17 pts for CT/MRI PET avoided biopsy in 14/21 cases 2) Distant metastasis identified by PET in 7/22 patients and treatment changed from surgery to palliation 3) 26/66 pts had change-in-management decisions following PET, and 23 of these cases were found to be correct	NR	Unclear	Unclear	Low
Facey et al **Restaging regional lymph nodes in patients with recurrent head and neck cancer, investigation at follow-up visit** 10 studies, n=350 RT: HPA	88%	78%	NR	NR	NR	4.0 (2.8-5.6)	0.16 (0.10-0.25)	NR	NR	Unclear	Unclear	Low

Question: What is the Usefulness of FDG-PET in the Differentiation between Benign and Malignant Lesions, including Evaluation of Solitary Pulmonary Nodules (SPN)?

Recommendation: The Panel **recommends** that PET scan should routinely be obtained in the diagnostic work-up of the patient with SPN

Review	**Accuracy**							**Effect on patient outcomes**		**Quality of evidence**		
	Sensitivity	Specificity	DA	PPV	NPV	LR+	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
Gould et al **Diagnostic accuracy of PET in evaluation of pulmonary nodules** 40 studies, n= unclear RT: HPA or 2 years follow-up for the majority of the studies	For 1474 focal pulmonary lesions of any size: Sensitivity: 83-100% Mean and median sensitivity = 96% and 97%, respectively. For 450 pulmonary nodules: mean sensitivity = 93.9% and median = 98%.	For 1474 focal pulmonary lesions of any size: Mean and median specificity = 73.5% and 77.8%, respectively. For 450 pulmonary nodules: mean specificity = 85.8% and median = 83.3%.	For lesions of any size: Summary log OR for FDG-PET was 4.68 (95% CI, 4.21-5.14), corresponding to a sensitivity and specificity of 91.2% (95% CI, 89.1%-92.9%), respectively. For pulmonary nodules: Summary log OR for FDG-PET was 4.40 (95% CI, 3.70-5.09), corresponding to a sensitivity and specificity of 90.0% (95% CI, 86.4%-92.7%), respectively. There was no difference in the accuracy of FDG-PET for pulmonary nodules compared with pulmonary lesions of any size (*P* = .43).	NR	NR	NR	NR	NR	NR	Moderate 14 studies met 70-80% of the methodological quality criteria. 18 studies satisfied 50-69% and 5 studies met less than 50% of the methodological quality criteria. Only 6 studies reported hyperglycemia as exclusion criteria. 5 studies did not require histology or follow-up to establish benign lesions. Masked reading of results was undertaken in 19 studies (51%) Masked reading of clinical and radiological data was undertaken in 9 studies (24%) In a sub-group analysis masked interpretation was the only aspect of study design that affected the accuracy of FDG-PET.	High	Moderate

Fischer et al **Diagnostic value of PET scanning in diagnosis and staging of NSCLC** 16 Studies of dedicated PET, n=800 patients in diagnostic studies RT: unclear	Mean (SE) for pooled values 0.96 (0.01)	Mean (SE) for pooled values 0.78 (0.03)	NR	Mean (SE) for poole d value s 0.91 (0.02)	Mean (SE) for pooled values 0.90 (0.02)	4.4	0.05	NR	NR	Moderate According to author's classification of methodological quality no study received grade A, 5 studies received grade B, 6 grade C, and 5 grade D, respectively. No clear statement about reference Test 65% of studies described masked interpretation of PET scan 37% of studies provided inadequate data regarding masked interpretation of results. Possibility of selection, verification, detection and spectrum bias	High	Moderate
HTA (ICES) review **Effectiveness of PET in distinguishing between malignant from benign lesions in the setting where CT guided biopsy has failed to make a final diagnosis or where the procedure was contra-indicated** 4 studies, n= 338 RT: HPA	86-100%	40-90%	NR	88-95%	55-100%	NR	NR	NR	NR	Moderate (blind reading of test, sample size from 50 – 109 patients/study, prospective studies)	Uncle ar	

Question: What is the Usefulness of FDG-PET in Staging of Non Small Cell Lung Cancer?

Recommendation: The Panel **recommends** that PET routinely be added to the conventional diagnostic work-up of non-small cell lung cancer patients.

Review	**Accuracy**							**Effect on patient outcomes**		**Quality of evidence**		
	Sensitivity	Specificity	DA	PPV	NPV	LR+	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
Gould et al **PET and CT for Mediastinal staging in NSCLC** 39 studies, 18-237 pts/ study RT: HPA or follow-up All CT studies= 1119 patients in 23 studies) All PET studies (1959 patients in 32 studies)	Patient as unit of analysis PET median = 85% CT median = 61% Lymph node as unit of analysis PET = 83%* CT= 62%*	Patient as unit of analysis PET median= 90%, CT median =79% Lymph node as unit of analysis PET=97% CT=91%	Joint sensitivity and specificity of FDGPET = 86% (CI, 83% to 88%) CT= 70 (67–73) - Lymph node as unit of analysis	NR	NR	Patient as unit of analysis PET= 8.1 CT= 2.8	Patient as unit of analysis PET= 0.2 CT=0.5	NR	NR	Moderate 28 studies reported patient as unit of analysis, and 5 reported patient and lesions combined as the unit of the analysis No study met all the methodological quality criteria stipulated by the reviewers 17 studies satisfied at least 70% and 5 less than 50% of the methodological quality criteria (22 items in the quality checklist) Blind interpretation of results was employed in less than 50% of studies. Readers of PET and CT were blinded to the final diagnosis in 56% of studies 11 studies indicated hyperglycemia as an exclusion criterion.	High	Moderate
	*Compared with studies that reported results by using the patient as a unit of analysis, these studies overestimated the diagnostic accuracy of both CT (*P* = 0.02) and FDG-PET (*P*= 0.04). 14 studies provided information about conditional test performance of CT and PET. PET was more sensitive but less specific when CT showed enlarged lymph nodes than when CT showed no lymph nodes enlargement (p< 0.002)					PET in patients with enlarged lymph nodes on CT (214 patients in 12 studies) LR+=4.1 and LR-= 0.1 PET in patients without enlarged lymph nodes on CT (479 patients in 14 studies) LR+=10.7 and LR-= 0.3						

Toloza et al **What are the sensitivities and specificities of CT scanning, MRI, EUS, and PET scanning for detecting malignant mediastinal lymph node involvement in lung cancer patients?** 18 PET studies, 1045 pts RT: HPA or follow-up	0.84 (95CI 0.78-0.89) <u>3 studies assessed PET+CT</u> Sensitivity from 0.78 to 0.93	0.89 (95CI 0.83-0.93) <u>3 studies assessed PET+CT</u> Specificity from 0.82 to 0.95	NR	0.79 (95CI 0.40-1.00) at pooled prevalence of 0.32 <u>3 studies assessed PET+CT</u> from 0.83 to 0.93	0.93 (95CI 0.75-1.00) at pooled prevalence of 0.32 <u>3 studies assessed PET+CT</u> from 0.88 to 0.95	7.64	0.18	NR	NR	Low Major flaws possibly including publication, selection, performance, attrition, and detection bias. No information regarding how many studies were prospective studies. Results are consistent regardless of the quality of original studies	Moderate	Low
	This SR also studied the impact of CT, EUS and MRI in the detection of metastases. But no direct comparison was performed between the PET scan and other diagnostic tests. A comparison of the summary of ROC curves demonstrated greater accuracy for PET scanning than for CT scanning, with a negative PET scan providing a > 90% certainty of the absence of positive mediastinal lymph node metastases.											

Cont. **Question**: What is the Usefulness of FDG-PET in Staging of Non Small Cell Lung Cancer?

Review	Accuracy							Effect on patient outcomes		Quality of evidence		
	Sensitivity	Specificity	DA	PPV	NPV	LR+	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
Birim et al **PET compared to CT scan in the detection of mediastinal metastases of NSCLC** 17 STUDIES, N=833 RT: HPA (mediastinoscopy or thoracotomy), 2 studies used imaging FU with CT	PET for detecting mediastinal lymph node metastases Sensitivity ranged from 66% to 100% Overall = 83% (95% CI, 77 to 87) CT scan for detecting mediastinal lymph node metastases Sensitivity ranged from 20% to 81% Overall sensitivity = 59% (95% CI, 50 to 67) * *No statistically significant heterogeneity in sensitivity or specificity was detected for both methods.*	PET for detecting mediastinal lymph node metastases Specificity ranged from 81% to 100% Overall specificity = 92% (95% CI, 89 to 95) CT scan for detecting mediastinal lymph node metastases Specificity of CT scan ranged from 44% to 100% Overall specificity = 78% (95% CI, 70 to 84)	detecting mediastinal lymph nodes PET ROC Q= 0.90 (95CI 0.86-0.95) CT ROC Q= 0.70 (95CI 0.65-0.75) P< 0.0001	NR	NR	PET= 10.35 CT=2.68	PET=0.18 CT=0.52	NR	NR	**Mode** 2 of the 17 studies used nodes as unit of analysis 4 studies met all the quality criteria stipulated by the reviewers Mean score was 14.1, ranged from 10 to 16 The most common and poorly described item was the description of the study population. Results are consistent regardless of the quality of original studies and subgroup analysis. Potential publication bias. Possible work up bias since mainly operable pts were included in the analysis.	High	Moderate

Cont. **Question**: What is the Usefulness of FDG-PET in Staging of Non Small Cell Lung Cancer?

Review	**Accuracy**							**Effect on patient outcomes**		**Quality of evidence**		
	Sensitivity	Specificity	DA	PPV	NPV	LR+	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
Dwamena et al **Comparison between PET and CT scan to detect mediastinal mets from NSCLC** RT: acceptable RTs (HPA in majority of cases) 14 studies compared PET and CT, n= 514 patients	PET scan mean sensitivity = 0.79 (95CI 0.62-0.97) CT sensitivity = 0.60 (0.25-0.89)	PET scan median specificity= 0.91 (95CI 0.79-0.99) CT specificity 0.77 (0.44-0.95)	PET log OR (± standard error) = 3.77 ± 0.51 - CT log OR (± standard error) = 1.79 ± 0.15 PET was significantly more accurate than CT (p<.001) PET= 92%(651/709) CT= 75 (2,935/3,935)* *Numbers in parentheses are number of positive results in patients or nodal stations/total number of patients or nodal stations.	PET= 90% (196/218) CT= 50 (614/ 1,220)** **Numbers in parentheses are number of true-positive results in patients or nodal stations/number of true-positive and false-positive results in patients or nodal stations. It was assumed that the sample data represented the true prevalence of disease.	PET= 93 (455/491) CT= 85 (2,321/2,715)*** ***Numbers in parentheses are number of true-negative results in patients or nodal stations/ number of true-negative and false-negative results in patients or nodal stations. It was assumed that the sample data represented the true prevalence of disease.	PET= 8.78 CT= 2.61	PET= 0.23 CT= 0.52	NR	NR	Moderate 5 of 14 studies used nodes as unit of analysis 71% of studies were prospective. No study met all the quality criteria stipulated by reviewers 93% of studies provided adequate description of patients All studies used adequate reference tests Small sample size, no independence of interpretation of results and poor reporting of results in many studies Potential publication bias Results are consistent regardless of the quality of original studies and subgroup analysis	High	Moderate

Cont. **Question**: What is the Usefulness of FDG-PET in Staging of Non Small Cell Lung Cancer?

Review	Accuracy							Effect on patient outcomes		Quality of evidence		
	Sensitivity	Specificity	DA	PPV	NPV	LR+	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
Fischer et al **Diagnostic value of PET scanning in staging of NSCLC** 17 Studies of dedicated PET, n=1000 patients in staging studies RT: unclear	17 studies, 9 about mediastinal staging 0.83 (0.02)	0.96 (0.01)	NR	0.87 (0.02)	0.95 (0.01)	21.3	0.17	NR	NR	Moderate According to author's classification of methodological quality no study received grade A, 5 studies were graded B, another 5 graded C, and 7 studies were graded D. No clear statement about reference test . 65% of studies described masked interpretation of PET scan 37% of studies provided inadequate data regarding the masked interpretation of results. Possibility of selection, verification, detection and spectrum bias	High	Mod

Cont. **Question**: What is the Usefulness of FDG-PET in Staging of Non Small Cell Lung Cancer?

Review	**Accuracy**							**Effect on patient outcomes**		**Quality of evidence**		
	Sensitivity	Specificity	DA	PPV	NPV	LR+	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
Van Tinteren et al (PLUS trial) **Effect of PET in the reduction of futile thoracotomies in patients with suspected NSCLC who were scheduled to surgery after conventional work-up** RCT, n=188 pts, 96 in the CWU arm and 92 in the CWU+PET arm RT: HPA or follow-up Futile thoracotomy definition: benign lesion, HPA proven mediastinal lymph node involvement (stage IIIA-N2), stage IIIB, exploratory thoracotomy for any other reason, recurrent disease or death from any cause within 1 year of randomization	NR	NR	NR	NR	NR	NR	NR	Significant number of patients with futile surgery in the CWU arm vs CWU+PET, Relative Reduction 51% 95CI (32-80)(p=0.003) in favor of PET scan. In the CWU arm 39 pts had a futile surgery and in the CWU+PET arm, 19 pts had futile surgery. Addition of PET to conventional work-up prevented unnecessary surgery in one out of 5 patients with suspected NSCLC. Cost-effectiveness showed that despite the additional cost of PET, the total cost was lower in the PET group.	Recurrence or death within 1 year of futile surgery: CWU = 19 vs. CWU+PET=10	High Possible detection bias (not clear if the readers were masked for intervention assignment in CWU arm)	NA	High

Viney et al **Impact of PET on the clinical management and surgical outcome in pts with stage I-II NSCLC. Does PET reduce the number of unnecessary thoracotomies?** RCT, 183 pts, no PET arm n= 92 and PET arm n= 91 RT: HPA	PET sensitivity detection of mediastinal disease was 73% [95CI (54-92%)] .	PET specif for detection of mediastinal disease was 90% [95CI (82-98%)].	NR	NR	NR	NR	NR	PET resulted in further investigation or other changes in the management in 12 pts (14%),(p =0.2). PET could have potential impact on management in 26% of pts.	With a minimum of 1 year survival: 80% of patients were alive in the PET arm and 77% in the no PET arm.	High No information about blind interpretation of imaging studies	NA	High
Herder et al **PET compared with CWU for staging NSCLC** RCT, 465 pts, PET arm = 232 pts and CT arm = 233 pts RT: HPA or follow-up (12 months)			Accuracy of clinical diagnosis (6 months follow-up) was similar (p=0.073) - PET = 0.78 95CI (0.72-0.84) and CWU = 0.85 95CI (0.80-0.90)	NR	NR	NR	NR	- Number of thoracotomies → PET= 96 (41%) and CWU = 88 (38%) - ≥ 1 invasive test for N staging PET = 52 (22%) and CWU 92 (39%), p = 0.0001		High	NA	High

Question: Detection of Distant Metastases in Patients with Proven or Suspected NSCLC

Recommendation: The Panel **recommends** that PET scan should be obtained in the diagnostic work-up for distant metastases of lung cancer patients.

Review	**Accuracy**							**Effect on patient outcomes**		**Quality of evidence**		
	Sensitivity	Specificity	DA	PPV	NPV	LR+	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
Facey et al **Detection of distant metastases in patients with proven or suspected NSCLC** 19 studies, n=1672 RT: HPA or follow-up	PET detected 10-20% more distant metastasis than other imaging methods	NR	NR	NR	NR	NR	NR	16 of the19 studies evaluated change-in-management outcome and showed that, in 9-64% of patients, change in management was made and, in most cases, patients were not taken to surgery.		Unclear (the panel of experts considered the quality of primary evidence as moderate) Some studies included only patients thought to be suitable for radical therapy, and others included all patients. Only sporadic information exist regarding change from non-resectable to resectable status	Unclear	Moderate

Question: What is the Usefulness of FDG-PET in the Diagnosis and Management of Small Cell Lung Cancer (SCLC)?

Recommendation: The Panel **makes no recommendation for or against routine** administration of FDG-PET in the diagnosis and management of SCLC.

Review	**Accuracy**							**Effect on patient outcomes**		**Quality of evidence**		
	Sensitivity	Specificity	DA	PPV	NPV	LR+	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
Facey et al **Diagnosis of occult SCLC in patients with suspected paraneuroplastic neurological syndrome in whom conventional imaging was negative** 1 study, n= 43 RT: HPA or FU	Identification of any cancer PET sensitivity, specificity = 90% Out of 9 (n=10) cancer patients identified by PET, only 3 were SCLC - Out of the 26 (n=29) correct negative scans, 2 of these were paraneoplastic - Only 5 patients had a condition of interest (preliminary results)		NR	NR	NR	NR	NR	NR	NR	Low	Unclear	Low
Facey et al **Staging in pts with SCLC to determine extension of the disease** 5 studies, sample size from 3-30 pts/study RT: HPA or FU in 3 studies	PET sensitivity = 89-100% and specificity = 100% In the largest study (n=30 pts), CT/MRI comparator had 65% sensitivity, and 100% specificity. In the second largest study (n=25), CT was comparator. CT Sensitivity = 93% and specificity = 90%.		NR	NR	NR	NR	NR	NR	NR	Low Few studies could calculate specificity as none of the patients were "truly" negative Some studies differentiated between "limited" and "extensive" disease, but PET was not used to identify the "stage" of disease, and merely noted that accuracy was high for PET despite stage of disease	Unclear	Low

Facey et al **Restaging after initial treatment for SCLC with chemotherapy and/or radiation, in order to detect residual disease or new site** 2 studies, n=58 RT: FU	<u>A) n=46</u> - Survival at 1 year → PET sensitivity = 96%, and specificity = 41% <u>- B) N= 12</u> Recurrence → PET sensitivity = 100% and specificity = 80%	NR	NR	NR	NR	NR	NR	NR	Low Few studies with small sample sizes	Unclear	Low

NCSCL - prognostic and therapeutic assessment

Review, year	Main results (Outcomes)	Quality of evidence	Quality of SR	Reviewers' Conclusions
Vansteenkiste et al, 2004 Last search: not clear, but last included study was from 2003 - - - - - - - - A) RT: follow-up B) RT: follow-up or CT C) RT:HPA D) RT: follow-up or CT or HPA E) RT: HPA, follow-up and CWI (1 study)	**A) Prognostic value at diagnosis** - 9 studies, 2 prospective, n= 57-163 pts/study - 5 retrospective studies suggested that SUV of the primary NCSLC at diagnosis is predictive for disease control and survival. - In 4 studies, SUV had a independent prognosis information after a multivariate analysis. - 3 studies pointed the ability of PET to improve selection of patients **B) Response to treatment** - 4 prospective studies (n = 30-73 pts/ study) indicated a possible role for PET in assessment of response with most studies indicating better response rate in tumors with higher glucose uptake. One study showed poor agreement with CT scan. **C) Preoperative restaging after induction treatment** - 4 studies, 3 prospective, n= 15-56 pts/ study - Restaging of primary tumors = PET usually detects residual disease (sensitivity of 90, 88 and 97%) with specificity ranging from 61%-100%. - Restaging of mediastinal lymph nodes = PET seems not to be as accurate as in untreated patients. **D) Prognostic value of post-treatment findings** - 7 studies, 5 prospective studies, n= 15-113 pts/ study - all data indicate that PET post-treatment findings have a role in prediction/ prognosis with positive PET correlating with worse survival that in PET negative patients. **E) Diagnostic value at recurrence** - 8 studies, 5 prospective, n = 13 – 126 pts/ study - All, but except 1 small study, concluded that PET is a valid way to differentiate between local recurrence and post-treatment changes. Sens ranged from 70% -100% and specif: 62%-100%	**A) Moderate** - lots of clinical heterogeneity between studies. - Cut-off for SUV fore interpretation of PET was variable. **B) Low** **C) Low** **D) Low** **E) Moderate**	**moderate**	- **A)** there is good evidence that PET has an independent prognostic value in newly diagnosed NSCLC. But agreements on methods of scanning and SUV cut-off values are needed. - **B)** limited evidence for application in clinical practice - **C)** Compared with CT, PET is promising and maybe more accurate. However, there is limited evidence for application in clinical practice. Larger prospective studies are needed. - **D)** PET data on prognosis of treated lung care are more limited and less structured than those in untreated patients, but all pointed the potential role of PET. More good quality evidence is needed before application in clinical practice. - **E)** Good prospective evidence showed the effectiveness of PET over CT in the correct identification of recurrence. Selective use can be recommended if active treatment is considered.

Question: What is the Usefulness of FGD-PET in Staging Patients with Lymphoma?

Recommendation: The Panel **suggests** that PET scan be routinely obtained in addition to CWU imaging in pretreatment staging of lymphoma patients.

review	**Accuracy**							**Effect on pts outcomes**		**Quality of evidence**		
	Sensitivity	Specificity	DA	PPV	NPV	LR+	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
BCBSA review **Lymphoma staging/restaging** 19 studies, n=608 (15 studies of diagnostic accuracy) RT: HPA or FU Note: Out of the 19 studies, 12 included a mix of patients with HL and NHL (no grade details were provided). 3 included only HL, while 3 included only NHL patients (no grade details were provided). Also, 7 studies included a mix of untreated patients and patients undergoing follow-up and 5 included only patients undergoing follow-up after treatment.	Sensitivity ranged from 43-100% (80% of studies had sensitivity > 80%)	Specificity ranged from 76-100%	PET had better overall diagnostic accuracy than CT in all studies	ranged from 36-100%	ranged from 70-100%	NR	NR	11 studies evaluated alterations in patient management due to PET findings and 5 of them reported change-in-management information PET resulted in change – in-management in 8-20% of patients (pooled proportion of 14%) 10 studies reported concordance between PET and other imaging modalities. PET was discordant with CWU in 11-55% of pts and PET was correct among discordances in 40-96% of cases. (no details available)	NR	Low Blinded interpretation of PET in 5 studies and unclear in 12. Mixed unit of analysis Only two studies selected consecutive patients. 8 studies were prospective.	High	Low

HTA (ICES) review **Staging of newly diagnosed lymphoma** 4 prospective studies, n = 42-56 pts/ study RT: unclear	A) One study of 50 patients (38 pts with NHL and 12 with HL) compared PET versus PET plus bone marrow to detect bone marrow involvement: PET sensitivity = 79% and specificity = 76%, PPV = 58% and NPV = 90% B) Another study of 56 patients (HL and NHL) PET had better PPV than bone scan to identify bone involvement		NR	NR	C) In one study (n = 44, only HL patients), PET findings led to 14% in change-in-management. D) One study of 42 <u>low grade</u> NHL patients found that If CT+ bone marrow biopsy (CWU) were replaced by PET plus bone marrow biopsy, 2 (5%) patients would be upstaged and 3 (7%) pts would be downstaged.	NR	Moderate (all prospective studies, all PET interpretations were "blinded")	Unclear	Mod
Hutchings et al **Staging of HL** 13 studies (see next column for details), n=varied RT: from none to HPA, FU CT	<u>*Studies on mixed population*</u> - 6 studies, 1 prospective, 1 retrospective, 4 unclear, N= 7 to 38 HL pts/ study mixed populations of 7 – 81 Hl and NHL pts. (no grade detail was provided) - Despite technical differences in PET scanning protocols, PET had higher diagnostic sensitivity than conventional staging procedures. <u>*Studies on HL populations – see table 1 next slide*</u> - 7 studies (3 prospective), n = 20-44 - 4 studies did not use any RT - PET sensitivity tends to be higher than CWU for extra nodal disease. - PET had a consistent, large influence on staging.	NR	NR	NR	<u>*Studies on mixed population*</u> - 2 studies clearly reported change-in-management = 8% for nodal disease and 16% for extra nodal disease in one study and 41% in another. <u>*Studies on HL populations – see table 1 next slide*</u> 4 studies reported change-in-management from 3-25%	NR	Low (possible flaws, including verification, timing, detection and spectrum bias)	High (authors decided to report as a narrative review) (the authors stated that they could not develop high-quality meta-analysis because of low quality data)	Low

Facey et al **Identification of more advanced, non bulky or bulky disease, in order to inform initial therapy** 18 studies RT: CWU or CT and follow-up or HPA and follow-up	7 studies, n = 11-93 pts/ study 2 studies (n = 52, 76) assessed bone with comparators of biopsy or scintigraphy. All had specificity > 90%. PET sensitivity 79% - 100% - 1 study (n=93) used gallium – 67 scan as comparator, sensitivity > 85% for PET and comparator, specificity not reported - Only 2 small studies used CT as comparator, total n = 27	NR	NR	NR	NR	11 papers indicated how PET changed staging and some indicated how this changed management - 2 well reported studies A) PET vs gallium (n=50) - Upstaged: PET 8, gallium 7 - Change-in-management = PET 10, gallium 7 B) N = 49 - Upstaged: PET 27 - Downstaged: PET 2 - All but 1 treated according to PET staging	NR	Low Overall 18 papers were found, but confirmation of results was only performed in a subset of patients, so sensitivity and specificity could not be calculated from all papers No differentiation between 2 forms of lymphoma and some analyses not patient based Use of duplicated papers. Evidence about change-in-management was typically related to few pts in each study, with few details given In most papers it was unclear whether change in staging was correct or how management was changed	Unclear	Low

Isasi et al **Staging lymphoma** 20 studies, n=854 RT: HPA or FU Note: 5 of the studies included only patients with HL, 3 studies included only patients with NHL and 12 studies included patients with both. Among the studies including NHL patients, 13 reported: 6 studies included patients with low-grade, intermediate-grade, and high-grade lymphoma; 6 studies included patients with low-grade and high-grade lymphoma; and 1 study included only patients with low-grade lymphoma.	Pooled data from the 14 studies that presented patient as the unit of analysis: Median: 90.3% (70.6-100%) pooled sensitivity was 90.9% (95% CI 88-93.4%) HL: 92.6 (88.4–95.6) NHL*: 89.4 (82.8–94.1)	Pooled data from the 14 studies that presented patient as the unit of analysis: Median: 91.1% (50-100%) pooled false-positive rate was 10.3% (95% CI, 7.4-13.8%). HL: 13.4 (8.0–20.6) NHL*: 11.4 (5.6–19.9)	The overall maximum joint sensitivity and specificity was 87.8% (95% CI, 85.0-90.7%)	NR	NR	NR	NR	Ten studies reported that the PET findings led to changes in the staging of patients. The percentage of patients who were upstaged ranged from 7.7–17.4% (median, 13.2%), and the percentage of patients who were downstaged ranged from 2.3–23.4% (median, 7.5%). Six of the 20 eligible studies reported changes in patient management as a result of PET findings.	Low (clinical heterogeneity, mix population of patients, verification bias)	High	Low	
	* No subgroup analysis according to the grade of NHL was performed.											

Table 1. Studies of PET for primary staging of Hodgkin lymphoma **- From Hutchings et al, 2004**

First author	Ref.	Year	Design	Reference standard	Number of patients	Upstaging by PET	Downsta-ging by PET	Change of treatment strategy according to PET	Major findings
Bangerter	[34]	1998	Prospective	None	44	5	1	6 (14%)	PET largely concordant with CT for nodal staging. PET superior to CT for detection of bone marrow involvement
Weidmann	[35]	1999	Retrospective	None	20	3	0	–	
Partridge	[36]	2000	Retrospective	None	44	18	3	11 (25%)	PET superior to CT for detection of organ involvement
Hueltenschmidt	[37]	2001	Retrospective	CT, follow-up and histology (seldom)	25	5	7	–	PET has higher nodal staging accuracy than conventional methods
Jerusalem	[38]	2001	Prospective	CT, follow-up and histology (seldom)	33	4	3	1 (3%)	PET has higher sensitivity for nodal staging than CT (except abdominal nodes)
Weihrauch	[39]	2002	Prospective	Clinical information and follow-up	22	4	5	4 (18%)	PET has higher sensitivity for nodal staging than CT
Menzel	[40]	2002	Not known	None	28	4	2	–	PET largely concordant with CT for nodal staging. PET more sensitive than CT for organ involvement

Question: What is the Usefulness of PET for evaluation of bone marrow infiltration in staging of Lymphoma?

Recommendation: The Panel **recommends** that PET scan may be used in addition to bone marrow biopsy for staging and restaging of lymphoma patients.

review	**Accuracy**							**Effect on pts outcomes**		**Quality of evidence**		
	Sensitivity	Specificity	DA	PPV	NPV	LR+	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
Pakos et al **Staging Bone Marrow in Lymphoma patients** 13 studies, n=589 Note: 5 studies of HL, 6 studies of NHL and 3 with mixed population of HL and NHL. Also 7 studies included patients with primary disease, and 6 included mixed populations of primary and recurrent lymphoma. No statement was made regarding the differentiation between low and high grade NHL. RT: biopsy	ranged from 0-100% pooled MA (REM effect): 51% [95%CI (38-64%)] HD: 76 (47–92) NHL: 43 (28–60)	ranged from 72 to 100% MA (REM effect): 91% [95% CI (85-95%)] HD: 92 (79–97) NHL: 88 (75–94)				5.75 [95CI (3.85-9.48)] HD: 9.02 (3.52 – 23.2) NHL: 3.53 (1.88 – 6.63)	0.67 [95 CI 0.55-0.82] HD: 0.33 (0.14–0.77) NHL: 0.68 (0.57–0.81)	NR	NR	Moderate (7 studies were prospective, blinding interpretation of test was reported in 9 studies)	High	Moderate

Question: What is the Usefulness of FDG-PET in Restaging/Detection of Relapse, Assessment of Residual Mass or Progression after Completion of the Initial Treatment in Lymphoma Patients?

Recommendation:
Hodgkin's lymphoma. The Panel **recommends** that PET routinely be obtained in patients in whom curative treatment was administered in addition to CWU imaging for re-staging or detection of recurrence in HD patients.
Non-Hodgkin's lymphoma. The Panel **recommends** that PET routinely be obtained in patients in whom treatment was used with curative intent in addition to CWU imaging for re-staging or detection of recurrence in NHL patients.

review	**Accuracy**							**Effect on pts outcomes**		**Quality of evidence**		
	Sensitivity	Specificity	DA	PPV	NPV	LR+	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
Facey et al Restaging to identify residual tumor masses, following partial or complete response to induction therapy, in order to avoid unnecessary consolidation radiotherapy if there is no active residual disease. 8 PET studies, n:unclear RT: FU (minimum of 6 month, most of 2 years)	- 8 PET studies, 6 CT studies *CT positive findings:* - 7 studies, n = 246 - PET sensitivity = 80% 95CI (59-94%) - PET specificity = 89% 95CI (74-97%) *Without CT information:* - 7 studies, n = 384 - PET sensitivity = 81% 95CI (63-92%) - PET specificity = 95% 95CI (90-99%) *CT:* - 6 studies, n = 266 - CT sensitivity = 75% 95CI (58-88%) - CT specificity = 45% 95CI (27-64%)		NR	NR	NR	NR	NR	Note: Economic model in Hodgkin's lymphoma predicts reduction of unnecessary consolidation radiotherapy from 36% using CT to 4% using PET (instead of CT), or 6% using CT and PET. Treatment based on the results of PET in all pts gives largest expected life years across all pts types.				

Hutchings et al *Evaluation of residual mass* 9 studies, n= 13-60 (? = some mix between pts and lesions) RT: from CWU to HPA	NR	NR	NR	See below	See below	NR	NR	PET had strong prognostic properties for evaluation of pts according to reviewers However, it is not clear if the prognostic value of PET in predicting progression-free survival (PFS) is independent of other prognostic factors	Low Most retrospective, referral bias, mixed lymphoma populations	High	Low
	Almost all pts with early-stage disease and negative post-treatment PET results survived without relapse. 2 studies of PET exclusively in HL patients with known residual mass: A) n=28 patients with thoracic mass > 2 cm post treatment "Median follow-up time was 28 months and all patients were followed for at least 1 year. PET was negative in 19 patients of whom 3 relapsed. PET was positive in 10 patients of whom 6 later relapsed. No patients were given additional treatment before the remission status was documented. The positive predictive value (PPV) was 60% and the negative predictive value (NPV) was 95% at 1 year of follow-up. Accordingly the PFS at 1 year was 95% for PET-negative patients and 40% for PET-positive patients" b) 37 patients, 50 scannings: "PPV and NPV were 46 and 96%, respectively, with a median follow-up time of 25.6 months (range 1.8–45.6 months). Unlike CT and erythrocyte sedimentation rate (ESR), PET showed a significant difference in PFS between groups that after completion of therapy had positive and negative findings, respectively." Other studies cited in the SR: "Spaepen et al. published their material of 60 HL patients who underwent whole-body PET after first-line treatment and were followed for at least 1 year. Fifty five had normal scanning results; only 5 of these relapsed with a median follow-up of 32 months. Five patients had abnormal findings on PET, they all had advanced-stage disease and they all relapsed. Only one of those patients had signs of treatment failure on CT, the rest showed complete remission. Two-year PFS was 91% for PET-negative patients and 0% for PET-positive patients." "Guay et al. performed 48 post-therapy scans. Eleven of the 12 PET-positive patients relapsed, 3 of the 36 PET-negative patients relapsed. All cases of disease progression were found within the first 12 months of follow-up. PFS for PET-negative patients was 89% at the time of final analysis."										

Question: What is the Usefulness of FDG-PET in Follow-up and Diagnosis of Relapse in Lymphoma Patients?

Recommendation: The Panel **recommends against r**outine administration of PET for the detection of relapse in asymptomatic HL or NHL

review	**Accuracy**							**Effect on pts outcomes**		**Quality of evidence**		
	Sensitivity	Specificity	DA	PPV	NPV	LR+	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
Hutchings et al PET in follow-up and diagnosis of a relapse after successful first line treatment in HL. 1 study, n= 36 patients	NR	NR	NR	NR	NR	NR	NR	NR	NR	Low	High	Low
	"CWU showed residual mass in 19 pts. PET showed positive findings in 10 pts, 4 were true positive results. Only 2 of 5 pts had clinical symptoms at the time of relapse identified by PET. Six patients had false positive PET scans where the findings could be confirmed neither by biopsy nor by other imaging methods. Confirmatory PET studies 4–6 weeks later were all negative."											

Question: What is the Usefulness of PET Scan in Detection of Metastases of Melanoma?

Recommendation: The Panel **recommends** that PET scan should be routinely obtained, in addition to conventional imaging, in staging and detection of recurrent melanoma.

Review	**Accuracy**							**Effect on patient outcomes**		**Quality of evidence**		
	Sensitivity	Specificity	DA	PPV	NPV	LR+	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
Prichard et al **Sensitivity and specificity in detection of metastatic disease** 10 studies, n=12-100 patients/study RT: unclear	74-100% PET compared to CT: 91% vs. 57%	67-100% PET compared to CT: 94% vs. 45%	NR	NR	NR	NR	NR	NR	NR	Low	Low	Low
	- 3 trials showed that PET was superior to CT/MRI for detecting regional and mediastinal metastases. -PET had a lower sensitivity than conventional imaging in detecting lung metastases. -PET had a lower sensitivity and specificity than nodal biopsy											
Mijnhout et al (Facey et al) **Sensitivity and specificity in detection of metastases** 11 studies, n=12-76 pts/study RT: HPA or SNB or follow-up	0.78 95CI (0.70 - 0.84) (from 6 studies) According to 1 study sensitivity of PET compared with SNB for initial regional staging was 17%.	0.88 95CI (0.82 - 0.92) (from 6 studies)	DOR 33.1 95CI (21.8 – 54.0) DOR for distant mets: 36.4 DOR for local mets: 19.5	NR	NR	6.5	0.25	Only one study measured the impact of PET on therapeutic decision-making. The selection of surgical or medical management was influenced specially by PET findings in 22 out of 100 patients and PET was used to clarify additional 12 cases in which CT scan was inconclusive.	NR	Low	High	Low

Schwimmer et al, **Use of PET in staging melanoma sensitivity/specificity) and change-in-management** 13 studies, n= 12-100pts/study RT: unclear in some studies, otherwise HPA or FU	Whole-body scan, data per patient (n=274): 77.2% [95CI (68.5-86.0%)] whole-body scan, data per lesion: 92.1 Regional LN scan, data per lesion: 55.3%	Whole-body scan, data per patient: 93.5% [95CI (90.0-97.1%)] whole-body scan, data per lesion: 89.6% Regional LN scan, data per lesion: 95.5%	NR	NR	NR	Whole-body scan, data per patient: 11.97	Whole-body scan, data per patient: 0.24	2 out of 13 studies had a pre-specified objective to determine change-in-management practices. Nevertheless, in total 5 studies reported change-in-management data. Overall change-in-management (n= 1 study) value was 22%. Subgroups: 4 studies reported % of upstage to surgery: % ranged from 7-14% 3 studies reported % of upstaged surgery to chemotherapy: From 4 to 11% 1 study reported % of down-staged from surgery: 16%	NR	Moderate	Moderate	Moderate
HTA (ICES) **Detection of silent metastases** 4 studies, n= 195 RT: CWU and CWU or HPA for staging	91.7-100% 1 prospective study with 38 stages II or III patients PET sens = 97% vs 62% with CWU PET specif = 56% vs 22% with CWU	56-97.7%	NR	NR	NR	NR	NR	NR	NR	Moderate	Moderate	Moderate

Facey et al **Patients with primary or suspected recurrent melanoma** 15 studies (5 studies published after Mijnhout), n = 12-100 pts/study RT: unclear	3 studies compared PET vs CT, n=38/50/76 pts PET= 94/100/97% CT: 55/92/62	3 studies compared PET vs CT, n=38/50/76 pts PET= 83/95/56% CT: 84/82/22%	NR	NR	NR	NR	NR	NR	NR	Unclear	Unclear	Unclear
	CT was better in detection of pulmonary mets and PET was better in detection of visceral and lymphatic mets											
BCBSA review **Staging or change in management** 15 studies RT= HPA or FU	Detection of lymph nodes (7 studies): 17-100%	Detection of lymph nodes (7 studies): 87-100%	Detection of lymph nodes (7 studies): 63-100%	Detection of lymph nodes (7 studies): 33-100%	Detection of lymph nodes (7 studies): 43-100%	NR	NR	4 studies reported alterations in patient management: PET altered patient management in 18% of cases (range 12 to 26%)	NR	Low	Moderate	Low

Question: What is the Usefulness of FDG-PET as an Added Test to CT Scan Imaging in the Diagnosis of Pancreatic Cancer?

Recommendation: The Panel **recommends** that a PET scan should be obtained, in addition to conventional imaging, in selected patients in whom conventional imaging findings are found to be inconclusive

Review	Accuracy							Effect on patient outcomes		Quality of evidence		
	Sensitivity	Specificity	DA	PPV	NPV	LR+	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
Orlando et al. **Diagnostic accuracy of PET/CT vs CT for the detection of pancreatic malignancy.** 17 studies, n= 13-122pts/study RT: biopsy or long term follow-up	PET=71-100% CT= 25-100%	PET= 53-100% CT =0-100%	SROC of PET when CT was positive = 0.94 SROC of PET when CT was negative = 0.93 SROC of CT alone = 0.82	NR	NR	NR	NR	NR	NR	Moderate	High	Moderate
BCBSA review **PET in addition to CWU help in distinguishing benign from malignant lesions** 13 studies, n= 675 RT: appropriate	pooled sensitivity = 91% (range from 82 to 96%) 9 studies directly compared PET to others modalities (CT, ERCP, US and 201-TI SPECT). All of them found that PET was better.	pooled specificity = 86% (range from 67 to-100%)		92% 66% prevalence of cancer, and 34% of benign lesions.	84%	6.5	0.10	6 studies reported alterations in patient management. Disagreements rates between PET results and conventional imaging results ranged from 13-54%. PET was correct among disagreements in 50-100% of cases.	NR	Moderate	High	Moderate

BCBSA review **PET in addition to conventional imaging in staging pancreatic cancer** 5 studies, n= 12-168 pts/ study RT: appropriate	Results from individuals studies widely differed	Results from individuals studies widely differed	Results from individuals studies widely differed.	See above	NR	Low	High	Low

Question: What is the Usefulness of FDG-PET for Diagnosis and Staging of Sarcomas?

Recommendation: The Panel made no **recommendation in favor or against** routine administration of PET for diagnosis or staging of sarcoma.

<table>
<tr><th rowspan="2">Review</th><th colspan="7">Accuracy</th><th colspan="2">Effect on patient outcomes</th><th colspan="3">Quality of evidence</th></tr>
<tr><th>Sensitivity</th><th>Specificity</th><th>DA</th><th>PPV</th><th>NPV</th><th>LR+</th><th>LR-</th><th>Change in management</th><th>Improve ment in PO</th><th>Primary study</th><th>SR</th><th>Overall</th></tr>
<tr><td rowspan="2">Bastiaannet et al

Diagnostic and staging of sarcomas

(29 studies, data pooled from 17 studies, n = 1163)

RT: HPA and/or FU</td><td>91% [95%CI (89 – 93%)]</td><td>85% [95%CI (82 – 88%)]</td><td>0.88 95CI (0.86 – 0.90)</td><td>NR</td><td>NR</td><td>6.07</td><td>0.11</td><td>NR</td><td>NR</td><td rowspan="2">Low

Only 28% of studies did not have detection and verification bias

Quality of evidence was assessed by the reviewers using a quality checklist (Mijnhout et al, 2001 and Cochrane)
The quality of evidence was considered poor by authors</td><td rowspan="2">High</td><td rowspan="2">Low</td></tr>
<tr><td colspan="9">10 studies reported only detection of sarcomas, 10 combined with grading, 4 only studied grading, 5 evaluated therapy response and 7 compared PET with another index test and most of them had HPA as the RT.
Difference on mean of SUV between sarcomas and benign tumors was statistically significant. (no cut off value described)

Difference on mean of SUV between low and high grade sarcomas was statistically significant for all studies and for mixed sarcomas, however, not for studies that analyzed only soft tissue sarcoma. no cut off value described)

There was a lack of systematic evidence on GIST.</td></tr>
</table>

Question: What is the Usefulness of FDG-PET in Detection of Recurrence of Thyroid Cancer?

Recommendation: PET r**ecommended** in patients previously treated for well differentiated (follicular or papillary) thyroid cancer when the ^{131}I whole-body scintigraphy is negative and the thyroglobulin serum marker is elevated > 10ng/ml. However, the Panel **recommends against** the use of PET scan in the surveillance of thyroid cancer patients. The use of PET scan when both ^{131}I whole-body scintigraphy and the thyroglobulin serum marker are negative is not recommended.

Review	Accuracy						Effect on patient outcomes		Quality of evidence		
	Sensitivity	Specificity	PPV	NPV	LR+	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
Hooft L et al **Diagnostic accuracy of FDG-PET (recurrence of follicular & papillary thyroid cancer)** 14 studies, N=402 RT: variable (from HPA to WBS to FU)	70-95% (data from 7 studies)	77-100% (data from 6 studies)	78 - 100% (data from 6 studies)	68 - 91%, (data from 6 studies)	NR	NR	NR	NR	Low (selection, spectrum, verification, attrition, and detection biases)	High	Low
Hooft L et al **FDG-PET in negative ^{131}I whole-body scintigraphy and elevated serum markers** 11 studies, n = 156 RT: variable (from HPA to WBS to F/U)	NR	NR	NR	NR	NR	NR	NR	NR	Low (selection, spectrum, verification, attrition, and detection biases)	High	Low

Hooft L et al **FDG-PET in negative 131I whole-body scintigraphy without elevated serum markers** 5 studies, n = 50 RT: from HPA to WBS to FU)	NR	NR	NR	NR	NR	NR	NR	NR	Low (verification and detection biases)	High	Low
Hooft L et al **FDG-PET compared with other imaging modalities** 3 studies, n = 20-54 RT: f rom HPA to WBS to FU	PET = 72% 99mTc-furifosmin imaging = 33%	PET = 100% 99mTc-furifosmin imaging = 100%	NR	NR	NR	NR	NR	NR	Moderate (2 out of three studies had a valid design)	High	Mod
Hooft L et al **PET in patients with known neoplastic foci** N = 1	NR	NR	NR	NR	NR	NR	NR	NR	Low	High	Low
Facey et al. **Detection of recurrent disease in previously treated pts who have metastatic epithelial disease suspected from elevated serum markers and negative 131I WBS** 11 studies, n = 244 RT: HP, imaging, FU	84% [95%CI (73-91%)] (pooled random effect MA)	56% [95%CI (27-82%)] pooled random effect MA	1.91	0.29			7 studies In 5 studies, 71% had treatment for recurrence In 4, 0-48% had successful treatment to cure In 3, 34% treated after positive PET had recurrence In 4 studies, 21% patients had no change in management despite positive PET.	NR	Low	Low	Low

Facey et al. **Detection of recurrent medullar thyroid cancer in previously treated pts who have metastatic disease suspected based on elevated serum markers and negative imaging** 6 studies, n=17 pts RT: HP, imaging, FU	NR	NR	NR	NR	NR	NR	NR	NR	Low	Low	Low

Question: What is the Usefulness of FDG-PET in the Detection of Unknown Primary Tumors?

Recommendation: The Panel **recommends** that PET scan routinely be obtained in addition to conventional diagnostic work-up of patients with unknown primary cancer.

Review	**Accuracy**							**Effect on patient outcomes**		**Quality of evidence**		
	Sensitivity	Specificity	DA	PPV	NPV	LR+	LR-	Change in management	Improvement in PO	Primary study	SR	Overall
Delgado-Bolton et al **Accuracy of PET scan in identification of primary tumor in patients with UPT** 15 studies , n= 298 RT: HPA or clinical follow-up	MA: 0.87 95CI (0.81-0.92)	MA: 0.71 95 CI (0.64-0.78)	NR	NR	NR	3.048 95CI (2.39-3.88)	0.174 95CI (0.11-0.27)	NR	NR	Low (Possible selection and verification bias, period of follow-up in patients with negative PET findings was considered inadequate in all, except 1 study, small sample size)	High	Low
Rusthoven et al **Detection of UPT in pts. with cervical metastasis after CWU (either panendoscopy or CT/ MRI or CRX)** 16 studies, n = 302 RT: HPA	88.3%	74.9%	78.8%	NR	NR	NR	NR	6 studies (n= 150) provided change-in-management outcomes. PET was responsible for a therapeutic change in 24.7% of patients.	NR	Unclear	Moderate (The assessment of quality for the included studies was not clearly described, and methods used for pooling of data were not appropriate)	Low

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Common abbreviations

Abbreviations	Meaning
131-I	131-Iodine
ACJJ	American Joint Committee on Cancer
ALNDs	axillary lymph node dissections
CEA	Carcino-embryonic antigen
CI	confidence interval
CRC	colorectal carcinoma
CT	computed tomography
CWU	conventional work-up
DA	diagnostic accuracy
DOR	diagnostic odds ratio
FDG	2-[F-18]Fluoro-2-Deoxy-D-Glucose
FU	follow-up
HL	Hodgkin's lymphoma
HPA	histopathology
HTA	health technology assessment
LR+	positive likelihood ratio
LR-	negative likelihood ratio
MA	meta-analysis
Mets	metastases
MRI	magnetic resonance imaging
NPV	negative predictive value
NR	not reported
NSCLC	non-small cell lung cancer

Abbreviations	Meaning
NHL	non-Hodgkin's lymphoma
OR	odds ratio
PET	positron emission tomography
PPV	positive predictive value
PO	patient outcomes
Pts	patients
RCT	randomized controlled trial
RT	reference standard test ("gold standard test")
SCS	squamous cell carcinoma
SCLC	small cell lung cancer
Sens	sensitivity
Spec	specificity
SNB	sentinel node biopsy
SPN	solitary pulmonary nodule
SR	systematic review
SROC	summary receiver operation characteristic
SUV	standardized uptake values
TN	true negative
TP	true positive
UPT	unknown primary tumor
US	ultrasonography
WBS	whole-body scintilography
yr	year