Bibliographic Cite	PMID Link	Literature Type	AMSTAR Appraisal	Level of Evidence	Purpose	Population	Intervention and Outcome Measures	Results/ Recommendations	Study Limitiations
Archer HA, Smailagic N, John C, et al. Regional cerebral blood flow single photon emission computed tomography for detection of Frontotemporal dementia in people with suspected dementia. Cochrane Database Syst Rev. 2015(6):Cd010896.	26102272	systematic review	well-developed study	Low level of evidence	To determine the diagnostic accuracy of rCBF SPECT for diagnosing FTD in populations with suspected dementia in secondary / tertiary healthcare settings and in the differential diagnosis of FTD from other dementia subtypes.	The authors included both case-control and cohort (delayed verification of diagnosis) studies. Where studies used a case-control design the authors included all participants who had a clinical diagnosis of FTD or other dementia subtype using standard clinical diagnostic criteria. For cohort studies, the authors included studies where all participants with suspected dementia were administered rCBF SPECT at baseline. The authors excluded studies of participants from selected populations (e.g. post-stroke) and studies of participants with a secondary cause of cognitive impairment.	Two review authors extracted information on study characteristics and data for the assessment of methodological quality and the investigation of heterogeneity. The authors assessed the methodological quality of each study using the QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies) tool. The authors produced a narrative summary describing numbers of studies that were found to have high/low/unclear risk of bias as well as concerns regarding applicability. To produce 2 x 2 tables, the authors dichotomised the rCBF SPECT results (scan positive or negative for FTD) and cross-tabulated them against the results for the reference standard. These tables were then used to calculate the sensitivity and specificity of the index test. Meta-analysis was not performed due to the considerable between-study variation in clinical and methodological characteristics.	Eleven studies (1117 participants) met the authors' inclusion criteria. These consisted of six case-control studies, two retrospective cohort studies and three prospective cohort studies. Three studies used single-headed camera SPECT while the remaining eight used multiple-headed camera SPECT. Study design and methods varied widely. Overall, participant selection was not well described and the studies were judged as having either high or unclear risk of bias. Often the threshold used to define a positive SPECT result was not predefined and the results were reported with knowledge of the reference standard. Concerns regarding applicability of the studies to the review question were generally low across all three domains (participant selection, index test and reference standard).Sensitivities and specificities for differentiating FTD from non-FTD ranged from 0.73 to 1.00 and from 0.80 to 1.00, respectively, for the three multiple-headed camera studies. Sensitivities were lower for the two single-headed camera studies; one reported a sensitivity and specificity of 0.40 (95% confidence interval (CI) 0.05 to 0.85) and 0.95 (95% CI 0.90 to 0.98), respectively, and the other a sensitivity and specificity of 0.36 (95% CI 0.24 to 0.50) and 0.92 (95% CI 0.88 to 0.95), respectively.Eight of the 11 studies which used SPECT to differentiate FTD from Alzheimer's disease used multiple-headed camera SPECT. Of these studies, five used a case-control design and reported sensitivities of between 0.52 and 1.00, and specificities of between 0.41 and 0.86. The remaining three studies used a cohort design and reported sensitivities of between 0.73 and 1.00, and specificities of between 0.94 and 1.00. The three studies that used single-headed camera SPECT reported sensitivities of between 0.40 and 0.80, and specificities of between 0.61 and 0.97. At present, the authors would not recommend the routine use of rCBF SPECT in clinical practice because there is insufficient evidence from the available literature to support this.Further research into the use of rCBF SPECT for differentiating FTD from other dementias is required. In particular, protocols should be standardised, study populations should be well described, the threshold for 'abnormal' scans predefined and clear details given on how scans are analysed. More prospective cohort studies that verify the presence or absence of FTD during a period of follow up should be undertaken.	Heterogeneity - one or more key results were highly variable with studies concluding opposite things or with I^2 statistic > 75% Risk of bias - one or more key results were based on studies with a majority having a high risk of bias A weakness of this review is the limited number and variability of the different studies available for review. As we have illustrated, a wide range of recruitment techniques, both retrospective and prospective studies, different cohort composition and sizes have been reported.
Fantoni ER, Chalkidou A, O'Brien JT, Farrar G, Hammers A. A systematic review and aggregated analysis on the impact of amyloid PET brain imaging on the diagnosis, diagnostic confidence, and management of patients being evaluated for Alzheimer's disease. J Alzheimers Dis. 2018; 63(2):783-796.	29689725	systematic review and aggregated analysis	well-developed study	Moderate level of evidence	To provide an aggregated quantitative analysis of the value added by amyloid PET (aPET) imaging in cognitively impaired subjects.	To classify for inclusion, studies had: 1. A diagnostic and clinical utility analysis of aPET imaging visually interpreted by pre-established dichotomization methods; 2. > 10 cognitively impaired patients; 3. Pre-aPET working diagnoses based on symptoms, clinical history, neuropsychological testing and/or structural imaging and without aPET; 4. Post-aPET final diagnoses based on in vivo clinical diagnostic criteria of the highest standards available at the time of study execution; 5. A unique and sequential association between aPET and post-aPET dx. Post-aPET diagnoses accompanied by FDG/CSF tests were collected separately; 6. A publication in peer reviewed scientific journals or a conference presentation with peer reviewed abstract selection.	A systematic search was carried out through MEDLINE and EMBASE using 38 terms to identify the included population and disease type, imaging modality, tracers, clinical utility terms and publication language. References within review articles were searched for any additional papers. An additional, more focused 56-term literature search was performed by a second blinded researcher for closer inspection of publications reporting utility measures. Studies selected for inclusion were reviewed by two authors. Studies with overlapping cohorts were refined only to include the largest studies. The methodological and reporting quality of the individual studies selected was assessed with the 14- question QUADAS tool adapted by two investigators to suit this review. QUADAS was then applied to each study independently by each investigator and a consensus on scoring reached.	1,531 cases over 12 studies were included (1,142 cases over seven studies in the primary analysis where aPET was the key biomarker; the remaining cases included as defined groups in the secondary analysis). For 1,142 cases with only aPET, 31.3% of diagnoses were revised, whereas 3.2% of diagnoses changed in the delayed aPET control group (p < 0.0001). Increased diagnostic confidence following aPET was found for 62.1% of 870 patients. Management changes with aPET were found in 72.2% of 740 cases and in 55.5% of 299 cases in the control group (p < 0.0001). The diagnostic value of aPET in AUC+ patients or when FDG/CSF were additionally available did not substantially differ from the value of aPET alone in the wider population. The authors conclude that amyloid PET contributed to diagnostic revision in almost a third of cases and demonstrated value in increasing diagnostic confidence and refining management plans.	While necessary to effectively analyze diagnostic changes with respect to aPET, the reclassification of patient diagnoses into standardized groups (AD, Non-AD and indeterminate) by consideration of the latest diagnostic guidelines lead to some loss of granularity. The majority of studies assessed here are also simple observational studies with the diagnosis observed before and after the aPET scan. The presence of a single study with a control cohort represents a limitation which is recognized as a known issue. The heterogeneity of patient populations across individual studies could affect the quantification of utility. Given the detail available in each paper, it is not possible to quantify at this time how different patient groups benefit from aPET, as this requires further research to avoid speculative conclusions. This is particularly the case for Non-AD aPET positives and cognitively normals.
Martinez G, Vernooij RW, Fuentes Padilla P, et al. 18F PET with florbetapir for the early diagnosis of Alzheimer's disease dementia and other dementias in people with mild cognitive impairment (MCI). Cochrane Database of Systematic Reviews. 2017;11:CD012216.	29164603	systematic review	well-developed study	Low level of evidence	To determine the DTA of the 18F-florbetapir PET scan for detecting people with MCI at time of performing the test who will clinically progress to ADD, other forms of dementia (non-ADD), or any form of dementia at follow-up.	Progression from MCI to ADD was evaluated in 448 participants. The studies reported data on 401 participants with 1.6 years of follow-up and in 47 participants with three years of follow-up.	The authors included studies that had prospectively defined cohorts with any accepted definition of MCI at time of performing the test and the use of 18F-florbetapir scan to evaluate the DTA of the progression fromMCI to ADD or other forms of dementia. In addition, we only selected studies that applied a reference standard for Alzheimer's dementia diagnosis, for example, National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) or Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) criteria.	Progression from MCI to ADD in those with a follow-up between two to less than four years had a sensitivity of 67% (95% CI 30 to 93) and a specificity of 71% (95% CI 54 to 85) by visual assessment (n = 47, 1 study).Progression from MCI to ADD in those with a follow-up between one to less than two years had a sensitivity of 89% (95% CI 78 to 95) and a specificity of 58% (95% CI 53 to 64) by visual assessment, and a sensitivity of 87% (95% CI 76 to 94) and a specificity of 51% (95% CI 45 to 56) by quantitative assessment by the standardised uptake value ratio (SUVR)(n = 401, 1 study). MCI to any form of dementia. Progression from MCI to any form of dementia in those with a follow-up between one to less than two years had a sensitivity of 67% (95% CI 9 to 99) and a specificity of 50% (95% CI 1 to 99) by visual assessment (n = 5, 1 study). MCI to any other forms of dementia (non-ADD);There was no information regarding the progression from MCI to any other form of dementia (non-ADD). Although sensitivity was good in one included study, considering the poor specificity and the limited data available in the literature, the authors cannot recommend routine use of 18F-florbetapir PET in clinical practice to predict the progression from MCI to ADD.Because of the poor sensitivity and specificity, limited number of included participants, and the limited data available in the literature, the authors cannot recommend its routine use in clinical practice to predict the progression from MCI to any form of dementia.Because of the high financial costs of 18F-florbetapir, clearly demonstrating the DTA and standardising the process of this modality are important prior to its wider use.	Risk of bias - one or more key results were based on studies with a majority having a high risk of bias Sparse data The main limitation of this review was that our findings were based on only three studies, with insufficient detail on how the people were selected, whether the information from the scan was assessed separately from the final diagnosis. The studies were considered to be at high risk of bias due to potential conflicts of interest detected. There were concerns regarding applicability in the reference standard in all three studies. Regarding the domain of flow and timing, two studies were considered at high risk of bias.

Mishima A, Nihashi T, Ando Y, et al. Biomarkers Differentiating Dementia with Lewy Bodies from Other Dementias: A Meta-Analysis. Journal of Alzheimer's Disease. 2016;50(1):161-74.	26639967	meta-analysis	Well-developed	Moderate level of evidence	To quantitatively synthesize data on test performance in differentiating dementia with Lewy bodies (DLB) from other dementias.	The eligible studies included patients at their typical age of dementia (mean or median, 65–79) with a wide range of cognitive impairment, almost normal to moderately impaired by Mini-Mental State Examination (mean, 6–25 points for DLB). Most studies adopted the consensus diagnostic criteria for DLB and other dementias including AD. The duration of dementia symptoms before the assessment of biomarkers varied substantially (mean, 1.8–6.5 years).	Two reviewers independently screened abstracts and perused full-text articles of potentially eligible citations. Studies that assessed DAT SPECT, MIBG scintigraphy, CBF SPECT, FDG-PET, or A 42, t-tau, or p-tau181 levels in the CSF were eligible for the study. The authors meta-analyzed measures of agreement between biomarker results and clinical diagnosis. Forty-five publications were eligible.	The majority of evidence was based on studies that enrolled representative disease populations. For differentiating between DLB and Alzheimer's disease (AD) or other dementias, metaiodobenzylguanidine scintigraphy and dopamine transporter (DAT) single photon emission computed tomography (SPECT) showed, respectively, excellent (summary kappa = 0.85; 95% confidence interval [95% CI], 0.74-0.96) and good (summary kappa = 0.71; 95% CI, 0.43-0.99) agreement. Metaiodobenzylguanidine scintigraphy appeared superior to fluorodeoxyglucose- positron emission tomography (summary kappa = 0.53; 95% CI, 0.36-0.69) and cerebral blood flow SPECT (summary kappa = 0.40; 95% CI, 0.33-0.47). For differentiating DLB from AD, CSF t-tau levels (summary kappa = 0.68; 95% CI, 0.55-0.82) performed comparably to metaiodobenzylguanidine scintigraphy and DAT SPECT. Sparse direct comparative evidence failed to corroborate these indirect comparisons. Metaiodobenzylguanidine scintigraphy and DAT SPECT are highly concordant with clinical diagnosis in differentiating DLB from other dementias. However, given the limitations in the study design, the applicability of these results to real-world differential diagnosis remains unclear. Prospective studies targeting patients with atypical presentations that adopt gold standard tests would reliably estimate the true test performance of these promising biomarkers.	Heterogeneity - one or more key results were highly variable with studies concluding opposite things or with I^2 statistic > 75% Risk of bias - one or more key results were based on studies with a majority having a high risk of bias However, given the limited study methodologies in primary studies, the contribution of these results to real-life differential diagnosis remains unclear. Reliable comparative evidence among different biomarkers or specific alternative diagnostic pathways is generally limited. Prospective studies with a single-gate design targeting more clinically relevant populations such as dementia with atypical presentation, adopting more accurate reference standards, ideally autopsy confirmation, for all participants, would reliably estimate the true test performance of these promising biomarkers.
Shea YF, Barker W, Greig-Gusto MT, Loewenstein DA, Duara R, DeKosky ST. Impact of amyloid PET imaging in the memory clinic: A systematic review and meta-analysis. J Alzheimers Dis. 2018; 64(1):323-335.	29889075	systematic review and meta-analysis	well-developed study	Moderate level of evidence	To perform a systematic review and meta-analysis of the impact of amyloid PET imaging (Aβ-PET) on etiological diagnosis and clinical management in the memory clinic setting.	To be included, studies had to meet the following criteria: 1) an original research paper with a prospective or retrospective design or case series; 2) involved patients seen in a specialty memory clinic setting; 3) provided sufficient information to allow the calculation of crude percentage change in either dx, management, or diagnostic confidence as study measures for the impact of Aβ-PET; and 4) published in English. Exclusion criteria were as follows: 1) articles in languages other than English; 2) review or systematic review articles; and 3) unpublished doctoral theses.	A search of literature published between 1 January 2004 and 13 February 2018 was performed using the PubMed and MEDLINE databases. The search terms were 'Pittsburgh Compound B' AND 'memory clinic', 'PiB' AND 'memory clinic', 'florbetapir' AND 'memory clinic', 'florbetaben' AND 'memory clinic', and 'flutemetamol' AND 'memory clinic'. Two investigators searched through the articles and reviewed all retrieved studies independently. If the two investigators disagreed about the eligibility of an article, it was resolved by consensus. Meta-analysis using a random effects model was performed to determine the pooled estimate of the impact of Aβ-PET in the changes of diagnoses and changes in management plan.	After rigorous review, results from 13 studies were extracted, involving 1,489 patients. Meta-analysis revealed a pooled effect of change in diagnoses of 35.2% (95% CI 24.6–47.5). Sub-analyses showed that the pooled effect in change in diagnoses if Aβ-PET was used under the appropriate use criteria (AUC) or non-AUC criteria were 47.8% (95% CI 25.9–70.5) and 29.6% (95% CI: 21.5–39.3), respectively. The pooled effect of a change of diagnosis from Alzheimer's disease (AD) to non-AD and from non-AD to AD were 22.7% (95% CI: 17.1–29.5) and 25.6% (95% CI: 17.6–35.8), respectively. The pooled effect leading to a change of management was 59.6% (95% CI 39.4–77.0). The authors concluded that Aβ-PET has a highly significant impact on both changes in diagnosis and management among patients being seen at a specialty memory clinic.	Patients involved in these studies were heterogeneous in a number of dimensions: patient diagnoses ranged from subjective cognitive impairment to dementia. For the ordering of Aβ-PET, some followed the AUC and others did not, and for the change in diagnosis, some included a category of "indeterminate," resulting in an inability to pool some of the data. Six out of 13 studies were retrospective in nature. There was a possibility of publication bias according to the authors' analyses, in that positive rather than negative findings tend to be reported in the literature. The vast majority of studies included in the meta-analysis were from academic centers and represent a very biased sample of both patients and clinicians and results are not generalizable to the whole population.
Smailagic N, Lafortune L, Kelly S, Hyde C, Brayne C. 18F-FDG PET for prediction of conversion to Alzheimer's disease dementia in people with mild cognitive impairment: An updated systematic review of test accuracy. J Alzheimers Dis. 2018; 64(4):1175-1194.	30010119	systematic review	well-developed study	moderate level of evidence	To update the evidence and reassess the accuracy of 18F-FDG-PET for detecting people with MCI at baseline who would clinicaly convert to Alzheimer's disease (AD) dementia at follow-up.	Participants with MCI recruited from any setting were eligible if studies used the Petersen criteria or any of the classifications to describe MCI syndrome. Prospective longitudinal, nested case-control cohort studies and cohorts that analysed data retrospectively were eligible if they contained sufficient data to construct two-by-two tables expressing 18FFDG- PET results by disease status. Studies were excluded if they focused on people with a secondary cause for cognitive impairment, namely: 1) current use or history of alcohol/drug abuse; 2) central nervous system trauma, tumor, or infection; 3) other neurological conditions, e.g., Parkinson's or Huntington's diseases.	Searches were conducted of electronic databases from January 2013 to July 2017 to update the original Cochrane review. No language restrictions or search filters were applied. Two review authors independently screened references and examined reference lists of any relevant studies and systematic reviews to identify additional studies, and independently extracted data. Differences were resolved by discussion. All key review steps, including quality assessment using QUADAS 2, were performed independently and blindly by two review authors. Meta-analysis could not be conducted due to heterogeneity across studies.	When all included studies were examined across all semi-quantitative and quantitative metrics, exploratory analysis for conversion of MCI to AD dementia (n = 24) showed highly variable accuracy; half the studies failed to meet four or more of the seven sets of QUADAS 2 criteria. Variable accuracy for all metrics was also found across eleven newly included studies published in the last 5 years (range: sensitivity 56–100%, specificity 24–100%). The most consistently high sensitivity and specificity values (approximately ≥80%) were reported for the sc-SPM (single case statistical parametric mapping) metric in 6 out of 8 studies. Systematic and comprehensive assessment of studies of 18FDG-PET for prediction of conversion from MCI to AD dementia revealed many studies have methodological limitations according to Cochrane diagnostic test accuracy gold standards, and shows accuracy remains highly variable, including in the most recent studies. There is some evidence, however, of higher and more consistent accuracy in studies using computer aided metrics, such as sc-SPM, in specialized clinical settings. Robust, methodologically sound prospective longitudinal cohort studies with long (≥5 years) follow-up, larger consecutive samples, and defined baseline threshold(s) are needed to test these promising results. Further evidence of the clinical validity and utility of 18F-FDG PET in people with MCI is needed.	A substantial number of included studies had limitations in methodological and reporting quality. Areas of particular bias concern were Patient Selection and Index Test domains; only one study was graded low risk of bias for all criteria of QUADAS 2 and reported high values for sensitivity (92%) and specificity (89%) using Neurostat/3D-SSP metric. However, this study has a small sample size (n = 30); therefore, the accuracy achieved might be overestimated. The authors note that there are still methodological limitations in the available evidence and a lack of well-designed studies that meet best practice criteria for diagnostic test accuracy studies.

Smailagic N, Vacante M, Hyde C, et al. (1)(8)F-FDG PET for the early diagnosis of Alzheimer's disease dementia and other dementias in people with mild cognitive impairment (MCI). Cochrane Database Syst Rev. 2015;1:Cd010632.	25629415	systematic review	well-developed study	Low level of evidence	To determine the diagnostic accuracy of the (1)(8)F-FDG PET index test for detecting people with MCI at baseline who would clinically convert to Alzheimer's disease dementia or other forms of dementia at follow-up.	Participants recruited and clinically classified as those with MCI at baseline were eligible for this review. We include studies that used the Petersen or revised Petersen criteria or the Clinical Dementia Rating or any of the 16 different classifications of MCI described as diagnostic criteria fo rMCI. The authors excluded those studies that involve people with MCI possibly caused by: i) current use or history of alcohol/drug abuse; ii) Central Nervous System trauma (e.g. subdural haematoma), tumour or infection; iii) other neurological conditions e.g. Parkinson's or Huntington's diseases.	The authors included 14 studies that evaluated the diagnostic accuracy of ^{1} F-FDG PET to determine the conversion from MCI to Alzheimer's disease dementia or to other forms of dementia, i.e. any or all of vascular dementia, dementia with Lewy bodies, and fronto-temporal dementia. Two blinded review authors independently extracted data, resolving disagreement by discussion, with the option to involve a third review author as arbiter if necessary.We extracted and summarised graphically the data for two-by-two tables.We conducted exploratory analyses by plotting estimates of sensitivity and specificity fromeach study on forest plots and in receiver operating characteristic (ROC) space. When studies had mixed thresholds, we derived estimates of sensitivity and likelihood ratios at fixed values (lower quartile, median and upper quartile) of specificity from the hierarchical summary ROC (HSROC) models.	The sensitivities for conversion from MCI to Alzheimer's disease dementia were between 25% and 100% while the specificities were between 15% and 100%. From the summary ROC curve the authors fitted the authors estimated that the sensitivity was 76% (95% confidence interval (CI): 53.8 to 89.7) at the included study median specificity of 82%. This equates to a positive likelihood ratio of 4.03 (95% CI: 2.97 to 5.47), and a negative likelihood ratio of 0.34 (95% CI: 0.15 to 0.75). Three studies recruited participants from the same Alzheimer's Disease Neuroimaging Initiative (ADNI) cohort but only the largest ADNI study (Herholz 2011) is included in the meta-analysis. In order to demonstrate whether the choice of ADNI study or discriminating brain region (Chetelat 2003) or reader assessment (Pardo 2010) make a difference to the pooled estimate, the authors performed five additional analyses. At the median specificity of 82%, the estimated sensitivity was between 74% and 76%. There was no impact on the authors' findings. In addition to evaluating Alzheimer's disease dementia, five studies evaluated the accuracy of (1)(8)F-FDG PET for all types of dementia. The sensitivities were between 46% and 95% while the specificities were between 29% and 100%; however, the authors did not conduct a meta-analysis because of too few studies, and those studies which the authors had found recruited small numbers of participants. The authors' findings are based on studies with poor reporting, and the majority of included studies had an unclear risk of bias, mainly for the reference standard and participant selection domains. According to the assessment of Index test domain, more than 50% of studies were of poor methodological quality. It is difficult to determine to what extent the findings from the meta-analysis can be applied to clinical practice. Given the considerable variability of specificity values and lack of defined thresholds for determination of test positivity in the included studies, the current evidence does not support the routine use of (1)(8)F-FDG PET scans in clinical practice in people with MCI. The (1)(8)F-FDG PET scan is a high-cost investigation, and it is therefore important to clearly demonstrate its accuracy and to standardise the process of (1)(8)F-FDG PET diagnostic modality prior to its being widely used. Future studies with more uniform approaches to thresholds, analysis and study conduct may provide a more homogeneous estimate than the one available from the included studies the authors have identified.	Heterogeneity - one or more key results were highly variable with studies concluding opposite things or with I^2 statistic > 75% Risk of bias - one or more key results were based on studies with a majority having a high risk of bias Our findings are based on studies with poor reporting, and the majority of included studies had an unclear risk of bias, mainly for the reference standard and participant selection domains. According to the assessment of Index test domain, more than 50% of studies were of poor methodological quality.
Zhang S, Smailagic N, Hyde C, et al. (11)C-PIB-PET for the early diagnosis of Alzheimer's disease dementia and other dementias in people with mild cognitive impairment (MCI). Cochrane Database Syst Rev. 2014(7):Cd010386.	25052054	systematic review and meta-analysis	Moderately well-developed study	Low level of evidence	To determine the diagnostic accuracy of the (11)C- PIB-PET scan for detecting participants with MCI at baseline who will clinically convert to Alzheimer's disease dementia or other forms of dementia over a period of time.	Eligible participants had a number of tests, for example neuropsychological tests for cognitive deficit and checklists for activities of daily living, prior to study entry. Participants in some studies were defined as amnestic single domain, amnestic multiple domain, non-amnestic single domain, non-amnestic multiple domain, or non-specified MCI participants. Studies without reference to a particular source of recruitment (participant setting) were also considered for inclusion. Excluded studies involved patients with MCI possibly caused by: i) current or a history of alcohol or drug abuse; ii) central nervous system (CNS) trauma (for example subdural haematoma), tumour, or infection; iii) other neurological conditions (for example Parkinson's or Huntington's diseases).	The authors selected nine studies that had prospectively defined cohorts with any accepted definition of MCI with baseline 11C-PIB-PET scan. In addition, they only selected studies that applied a reference standard for Alzheimer's dementia diagnosis for example NINCDS-ADRDA or Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) criteria.	Of the 274 participants included in the meta-analysis, 112 developed Alzheimer's dementia. Based on the nine included studies, the median proportion converting was 34%. The studies varied markedly in how the PIB scans were done and interpreted.The sensitivities were between 83% and 100% while the specificities were between 46% and 88%. Because of the variation in thresholds and measures of (11)C-PIB amyloid retention, the authors did not calculate summary sensitivity and specificity. Although subject to considerable uncertainty, to illustrate the potential strengths and weaknesses of (11)C-PIB-PET scans the authors estimated from the fitted summary ROC curve that the sensitivity was 96% (95% confidence interval (CI) 87 to 99) at the included study median specificity of 58%. This equated to a positive likelihood ratio of 2.3 and a negative likelihood ratio of 0.07. Assuming a typical conversion rate of MCI to Alzheimer's dementia of 34%, for every 100 PIB scans one person with a negative scan would progress and 28 with a positive scan would not actually progress to Alzheimer's dementia.There were limited data for formal investigation of heterogeneity. The authors performed two sensitivity analyses to assess the influence of type of reference standard and the use of a pre-specified threshold. There was no effect on the authors' findings. Although the good sensitivity achieved in some included studies is promising for the value of (11)C-PIB-PET, given the heterogeneity in the conduct and interpretation of the test and the lack of defined thresholds for determination of test positivity, the authors cannot recommend its routine use in clinical practice.(11)C-PIB-PET biomarker is a high cost investigation, therefore it is important to clearly demonstrate its accuracy and standardise the process of the (11)C-PIB diagnostic modality prior to it being widely used.	Risk of bias - one or more key results were based on studies with a majority having a high risk of bias Sparse data