The Journal of Prevention of Alzheimer's Disease 13 (2026) 100474

Contents lists available at ScienceDirect

The Journal of Prevention of Alzheimer's Disease

journal homepage: www.elsevier.com/locate/tjpad

Original Article

Cost-effectiveness analysis of blood-based biomarker testing in the diagnosis of Alzheimer's disease pathology

Yonghong Li *, Robert J. Lagier, Michael K. Racke, Yuri A. Fesko

Quest Diagnostics, San Juan Capistrano, CA 92675, USA

ARTICLE INFO

Keywords:
Alzheimer's disease
Blood-based biomarker
Cost-effectiveness analysis
Mild cognitive impairment

ABSTRACT

Objectives: We aimed to evaluate the cost-effectiveness of blood-based biomarker (BBM) testing vs amyloid positron emission tomography (PET) in patients with signs and symptoms of cognitive decline in a neurologist/specialist care setting.

Methods: We constructed a decision-tree model to compare diagnostic outcomes and costs of two testing strategies: BBM testing with confirmatory PET scan vs PET scan alone. Their cost-effectiveness was evaluated from a payer perspective with test performance taken from a clinical study and costs including testing/imaging and physician fees.

Results: When access to PET scans is unlimited, BBM triage testing would identify 98.2 % of PET+ patients with a lower average cost per diagnosis compared with PET scan alone ($8868 vs 10,345 per PET+ diagnosis). In terms of incremental cost-effectiveness, BBM triage testing would save $93,984 for each loss of PET+ diagnosis (9.1 times the average cost per PET+ diagnosis by PET scan). Under limited capacity of PET scans, more test-positive patients could be identified using BBM testing than PET scan alone. When access to PET scans is limited to 50 % of the patients, BBM testing would identify 90.6 % more test-positive patients (at 93 % sensitivity) at an incremental cost-effectiveness ratio of $3484 per gain of positive diagnosis, lower than the average cost of a PET+ diagnosis by PET scan ($10,938).

Conclusion: BBM testing, compared with PET scan alone, is more efficient in the utilization of available amyloid PET scans and is cost-effective for assessment of Alzheimer's disease pathology in patients with signs and symptoms of cognitive decline.

1. Introduction

Mild cognitive impairment (MCI) is a highly prevalent and multifactorial condition in the elderly population. In the United States, approximately 12–18 % of the individuals aged 60 and older are living with MCI, posing a considerable economic burden on the healthcare system and society [1]. This condition can stem from underlying neurological diseases and other medical conditions or lifestyle factors. Based on biomarker studies with positron emission tomography (PET) and cerebrospinal fluid (CSF) testing, about half of the MCI patients have amyloid pathology [2], which is a hallmark of Alzheimer's disease (AD), a progressive neurodegenerative disorder that causes memory loss, cognitive decline, and other changes in brain function. AD is also associated with intracellular neurofibrillary tangles (NFTs) composed of aggregated hyperphosphorylated tau protein.

Two disease-modifying, monoclonal antibody-based therapies for AD are being used in the clinic following their approvals by the US Food and Drug Administration (FDA) [3,4]. Timely and accurate diagnosis of the MCI patients with underlying AD pathology is important before they receive these therapies. To help determine if MCI is due to AD, assessment of amyloid and tau pathology would be an important part of the comprehensive evaluation of the patient. Traditionally, amyloid PET scans are performed to detect amyloid plaques and CSF testing is used to measure amyloid-beta (Aβ) burden and phosphorylated tau (p-tau) proteins [5,6]. While they are well established methods for the diagnosis of amyloid/tau pathology, PET scans are expensive and are not widely available and CSF testing is infrequently used [7,8]. Capacity and cost constraints can hinder the use of PET scans, reduce the number of patients with confirmed amyloid pathology, and lead to delays in appropriate treatment [9].

Recently, blood-based biomarker (BBM) tests have been developed to assess amyloid and tau pathologies in plasma [10–14]. A BBM test

* Corresponding author at: Quest Diagnostics, 33608 Ortega Hwy, San Juan Capistrano, CA 92675, USA.
E-mail address: yonghong.x.li2@questdiagnostics.com (Y. Li).

https://doi.org/10.1016/j.tjpad.2025.100474
Received 29 October 2025; Received in revised form 9 December 2025; Accepted 10 December 2025
Available online 14 January 2026

based on pTau217/ß-Amyloid 1–42 has recently been cleared by the FDA for adult patients aged 55 years and older presenting at a specialized care setting with signs and symptoms of cognitive decline [15]. BBM tests can be used as triage tests to identify MCI patients who are likely to have AD and thus help to prioritize further testing and evaluation [16–18]. In this application, patients with a positive result are further evaluated and considered for amyloid PET scan or CSF testing, whereas patients with a negative result are considered unlikely to have amyloid pathology. An expert panel survey found that specialists would conduct CSF or PET testing in 80 % of those with a positive test result and 10 % of those with a negative test result when BBM testing is used to triage patients [19]. BBM tests with ≥90 % sensitivity and specificity can also be used as a substitute for amyloid PET imaging for MCI patients at a specialized care setting [18].

A cost-effectiveness analysis of using BBM testing in AD diagnosis could help provide economic rationale in the adoption of the tests in clinical application [20]. However, a recent panel convened by the Alzheimer's Association "could not make a judgment about the cost-effectiveness of BBMs due to a lack of sufficient data on this topic" [18]. Here we report a cost-effectiveness analysis of using an FDA-cleared BBM test to evaluate patients with signs and symptoms of cognitive decline in a neurologist/specialist care setting.

2. Methods

Reporting of this study followed the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) guidelines [21]. The analysis was conducted from March to November 2025, using publicly available data.

2.1. Model structure, population, and setting

A decision-tree model was developed to estimate the diagnostic outcomes and costs of two diagnostic pathways (thereafter termed "diagnostic strategies") in MCI or dementia patients following Alzheimer's Association Clinical Practice Guideline [18] (Fig. 1), which states that "a BBM test should not be obtained before a comprehensive clinical evaluation by a healthcare professional, and test results should always be interpreted within the clinical context". A neurologist's comprehensive evaluation includes detailed medical and cognitive history, a neurological exam, blood tests, brain imaging, and neuropsychological testing. The modeled population includes MCI or dementia patients aged 55 years and older who have received a comprehensive clinical evaluation and are being considered for further assessment of amyloid pathology. Since the purpose of amyloid biomarker testing is to determine the eligibility for anti-amyloid therapy, patients with other treatable causes of cognitive issues or those not eligible for amyloid treatment (e.g., when brain imaging shows microhemorrhages) are not included in the model. Similarly, the model also does not consider other types of follow-up test, such as a metabolic PET scan, that may be performed for patients who test negative for amyloid biomarker.

In one strategy (PET-scan strategy), all patients receive PET scans and a follow-up consultation. Diagnostic outcomes are either PET positive (PET+) or negative (PET-). In another strategy (BBM-test strategy), all patients first receive BBM testing and a follow-up consultation. When PET scan capacity is unlimited, patients who have high- and intermediate-risk results and a small proportion of those who have low-risk results (10 % in the base-case scenario [19]) are followed up with PET scans and a second consultation after PET scan. If PET scan capacity is limited, BBM testing is used to triage patients until capacity is filled. For those who do not undergo PET scans, BBM test results are considered confirmatory: high risk as test positive, intermediate risk as indeterminate, and low risk as test negative. The diagnostic outcomes are defined by the final test/scan (Fig. 1). Although PET scans may produce equivocal results in a small percentage of patients [22], the model assumes only positive and negative results. CSF testing is not included in the model in the base-case analysis (because it is infrequently used in the clinic [7]) but is added to the model in a scenario analysis when access to PET scans is limited.

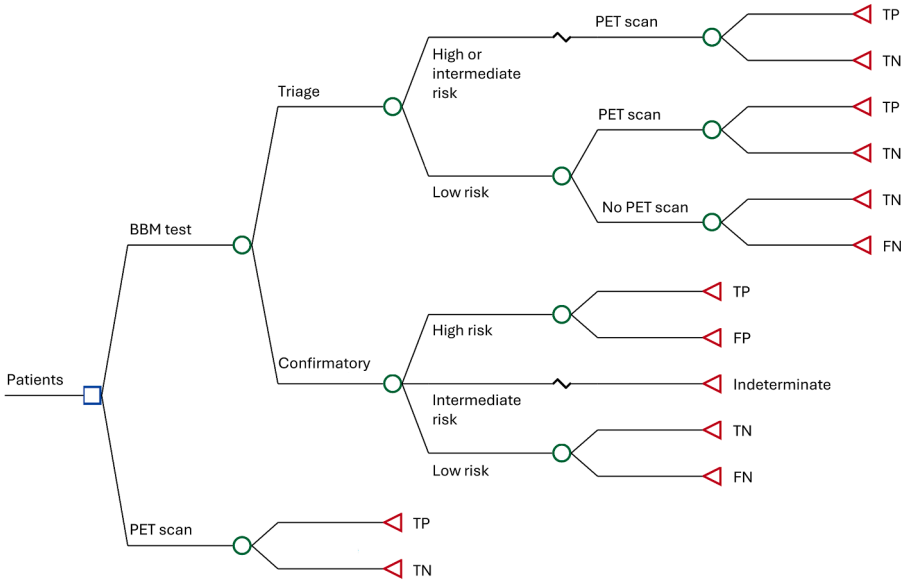

Fig. 1. Decision tree diagram. Model outputs (terminal nodes) are the possible outcomes of the final test provided in a given model pathway. Since PET scan is considered the gold standard in diagnosis of amyloid pathology, model outcomes for PET scan are defined as true positive (PET+) or true negative (PET-). BBM testing is not a perfect predictor of PET positivity (amyloid pathology); consequently, model outcomes for BBM positive test results (high risk) are defined as either true positive or false positive and BMM negative test results (low risk) are defined as either true negative or false negative. Model outcome for BBM intermediate-risk results is indeterminate if no PET scan is performed. In a scenario analysis, cerebrospinal fluid (CSF) testing is also provided in addition to PET scan. Therefore, the "PET scan" node is replaced with "PET scan/CSF testing" in that analysis. The square indicates the decision node, the circle indicates chance node, and the triangle indicates terminal node. Abbreviations: BBM, blood-based biomarker; PET, positron emission tomography. TP, true positive; TN, true negative; FP, false positive; FN, false negative.

2.2. Model parameters

Model parameters are listed in Table 1. We assumed that clinical performance of BBM testing was as those described for the validation study in the 510(k) decision summary of the Lumipulse G pTau217/ß-Amyloid 1–42 Plasma Ratio (compared with PET scan or CSF testing), a test cleared by the FDA [23]. This clinical validation study included both MCI and dementia patients with age of 55 to 93 years. Cost for physician office visit is based on the national average listed in MDSave.com [24]. This cost occurs for (1) the initial consultation on the use of BBM testing or PET scan, (2) the subsequent consultation to review BBM testing or PET scan results and (3) for those receiving both BBM testing and PET scan, the final consultation to review PET scan results. Cost for BBM testing is $500 in the base case and ranges up to $1200 in sensitivity analysis [25]. Total cost of amyloid PET scan includes costs for technical, professional, and diagnostic radiopharmaceutical components [26]. Cost of CSF testing includes costs for both lumbar puncture and testing [26]. All costs are in year 2025 dollars (costs of PET scan and CSF testing were inflated to 2025 dollars from the 2023 dollars in the publication [26] according to the consumer price index for medical care).

Table 1
Input parameters.

Variable	Base case	Lower input	Higher input	Reference #
Probability of BBM test result				
High risk	0.439	0.395	0.484	[23]
Intermediate risk	0.196	0.162	0.231	[23]
Low risk	0.365	ND	ND	[23]
Probability of PET+ in BBM test groups				
High risk	0.918	0.878	0.946	[23]
Intermediate risk	0.500	0.413	0.588	[23]
Low risk	0.027	0.012	0.061	[23]
PET referral rate for low-risk patients	0.100	0.050	0.150	[19]
Cost, $				
Neurology office visit	303	227	379	[24]
BBM test	500	375	625	[25]
PET scan	4679	3509	5849	[26]
CSF test	749	ND	ND	[26]

The lower and higher probability inputs of the BBM low-risk group are not defined (ND) but vary with changes in the intermediate- and high-risk groups because probabilities in the three risk groups must sum to 1. BBM, blood-based biomarker; CSF, cerebrospinal fluid; PET, positron emission tomography.

2.3. Perspective, time horizon, and analysis

This study was conducted from a payer perspective in the US with a time horizon of 1 year during which BBM testing and/or PET scan were expected to be completed. Given the perspective and short time horizon, only direct medical costs were considered, and no discount was applied to the cost or effectiveness. This analysis took into consideration test availability in a relatively short time horizon because of the importance of timely diagnosis—from clinical point of view, a delayed diagnosis might no longer be useful for some patients when their disease has progressed to a stage where disease-modifying treatment is no longer effective.

The primary outcome is the incremental cost per additional positive diagnosis or decremental cost per loss of PET+ diagnosis. We note that while PET scan is considered reference standard for the detection of amyloid pathology, it has false positives and negatives when compared with autopsy. Other outcomes include the number of patients with positive diagnosis, the total cost, the average cost per diagnosis, and the sensitivity and specificity of BBM test strategy.

One-way sensitivity analysis was performed to assess how the cost-effectiveness outcomes are affected by changes in a single input parameter at its lower and higher values. For the probabilities of risk classification after BBM testing and the probabilities of PET+ in each risk group, their lower and higher values are the upper and lower limits of their 95 % confidence intervals. Costs vary by ±25 % from the base-case values.

Two-way sensitivity analysis was performed to assess how the cost-effectiveness outcomes are affected by simultaneous changes in two input parameters across their lower and higher values. Specifically, the two input parameters are the costs of BBM testing and PET scan. The ranges of the cost are $500 to $1200 for BBM testing and $4000 to $8000 for PET scan.

Probabilistic sensitivity analysis was performed by the Monte-Carlo simulation to assess how the cost-effectiveness outcomes are affected by simultaneous changes in all input parameters across their lower and higher values. In each run of a simulation (n = 10,000 runs), input parameters are randomly drawn according to their probability distribution, and the model is recalculated. Beta distributions are used for probability inputs and gamma distributions are used for cost inputs.

Scenario analyses were performed to assess how the cost-effectiveness outcomes are affected by changes in model assumptions. In one scenario, clinical information is used to prioritize patients for PET scans when access to PET scans is limited. It is assumed that this prioritization improves the PET+ diagnostic rate. In the second scenario, both PET scan and CSF testing are assumed to be used when the access to PET scans is limited. In the third scenario, the proportion of BBM high-risk group is expanded to assess the impact of amyloid prevalence on the cost-effectiveness outcomes. In this scenario, the proportion of low-risk group would vary with changes in the proportion of BBM high-risk group, and proportion of intermediate-risk group remains at the base-case value (probabilities in the three risk groups always sum to 1).

All analyses were performed using TreeAge Pro Version 2023 R2.0 (TreeAge Software, Williamstown, MA).

2.4. Willingness-to-pay (WTP) and willingness-to-accept (WTA)

WTP is the maximum amount a payer is willing to pay for a gain of positive diagnosis, and WTA is the minimum amount of money a payer is willing to receive ("saved") to tolerate a loss of positive diagnosis. Since amyloid PET scan is covered by healthcare insurers including Centers for Medicare & Medicaid Services (CMS) [27], its average cost per positive diagnosis can be used as the WTP threshold. The WTA threshold is twice the WTP threshold [28]. We note, however, that payers may choose other thresholds in evaluating the cost-effectiveness of diagnostic strategies.

A testing strategy is considered cost-effective if it has an incremental cost-effectiveness ratio (ICER) (compared with another testing strategy) lower than WTP or if it has a decremental cost-effectiveness ratio (d-CER) higher than WTA. The formula for ICER (or D-CER) is

$$\frac{\textit{Cost of BBM test strategy} - \textit{Cost of PET scan strategy}}{\#\textit{Positive diagnosis by BBM test strategy} - \#\textit{Positive diagnosis by PET scan strategy}}$$

Table 2
Cost-effectiveness outcomes.

PET scan capacity, %	Test strategy	Cost, $	Positive diagnosis, n	Cost per diagnosis, $	ICER or D-CER, $
100	PET scan	5285,000	511	10,345	Comparator
	BBM triage	4451,413	502	8868	93,984
50	PET scan	2794,000	255	10,938	Comparator
	BBM triage/confirmatory	3597,000	486	7403	3484
25	PET scan	1548,500	128	12,125	Comparator
	BBM triage/confirmatory	2351,500	462	5085	2399

Outcomes are for 1000 patients, and calculations of cost per diagnosis and ICER or D-CER are based on unrounded results. ICER is presented in $ per gain of diagnosis, and D-CER in $ saved per loss of diagnosis. BBM, blood-based biomarker; D-CER, decremental cost-effectiveness ratio; ICER, incremental cost-effectiveness ratio; PET, positron emission tomography.

3. Results

3.1. Scenario with unlimited access to PET scans

We first evaluated the cost-effectiveness of BBM triage testing vs PET scan alone when access to PET scans is unlimited. For 1000 MCI or dementia patients, diagnostic outcomes are presented in **Supplementary Table 1**. Fewer patients receive PET scans following BBM triage testing than PET scan alone: 672 vs 1000 patients (a 32.8 % reduction in the use of PET scans). BBM triage testing results in slightly fewer PET+ patients than PET scan alone: 502 vs 511, corresponding to 98.2 % sensitivity. The average cost per PET+ diagnosis is lower by BBM triage testing than PET scan alone: $8868 vs $10,345 (the WTP threshold) (Table 2). The D-CER is $93,984; that is, for each loss of PET+ diagnosis by BBM triage testing (vs PET scan alone), the cost saved is $93,984 which is 4.5 times of the WTA threshold ($20,690 [twice WTP]). Therefore, compared with PET scan alone, BBM triage testing is much cheaper and almost as good.

We performed several sensitivity analyses to assess the robustness of the cost-effectiveness outcomes to parameter variations. In one-way sensitivity analysis, the D-CER is most sensitive to two factors: (1) the probability of PET+ among those who are classified low risk by BBM testing and (2) the cost of PET scan (**Supplementary Fig. 1**). The D-CER value would increase if the probability of PET+ among individuals with low risk is lower than the base-case value or the cost of PET scan is higher. All D-CER values are greater than the WTA threshold. In a Monte-Carlo simulation (n = 10,000 runs), all runs have a D-CER value ≥$30,000 and 91.4 % of the runs have a D-CER value ≥$60,000 (**Supplementary Fig. 2**). In a two-way sensitivity analysis, BBM triage testing remains mostly cost-effective, even under higher WTA thresholds, when the cost of BBM testing is in the range of $500–1200 and the cost of PET scan is in the range of $4000–8000 (**Supplementary Fig. 3**). Finally, when more patients have BBM high-risk results than in the base case (for example 65.4 % if amyloid prevalence is increased in the test population vs 51.1 %), BBM triage testing is still considered cost-effective according to a one-way sensitivity analysis (d-CER>twice WTP, **Supplementary Table 2**). These results suggest that BBM triage testing is highly likely to be cost-effective compared with PET scan alone.

3.2. Scenario with limited access to PET scans

Since the number of MCI or dementia patients far exceeds the existing capacity of amyloid PET scans, we next evaluated the cost-effectiveness outcome of the two testing strategies incorporating the availability of PET scans. In this scenario, a fraction of patients in PET-scan strategy receive PET scans until capacity is filled. All patients in BBM-test strategy first receive BBM testing, and those eligible for PET scans according to BBM test results receive PET scan until capacity is filled.

When PET scan capacity is below 98.3 %, more patients would test positive using BBM testing (triage and confirmatory) than PET scan alone (Fig. 2). For example, if 500 PET scans are available to 1000 MCI patients, PET scan alone would identify 255 PET+ patients, leaving 500 patients without assessment for amyloid pathology (Table 2 and **Supplementary Table 3**). In contrast, if all 1000 patients first receive BBM testing, 439 patients would be found to be at high risk, 196 patients at intermediate risk and 365 patients at low risk. If 500 PET scans are offered to eligible patients after BBM testing, 374 would be confirmed as PET+ (46.6 % more PET+ than PET scan alone). Including those who have a BBM high-risk result but do not undergo a follow-up PET scan, the total number of test-positive patients would be 486 (a 90.6 % increase compared with PET scan alone) (Table 2 and **Supplementary Table 3**). Among the 486 test-positive patients, 9 are false positive (therefore 93 % sensitivity [477/511]). The ICER value by BBM testing vs PET scan alone is $3484, far below the WTP threshold (the average cost of a PET+ diagnosis by PET scan or $10,938). Therefore, BBM testing is cost-effective compared with PET scan alone when access to PET scans is limited.

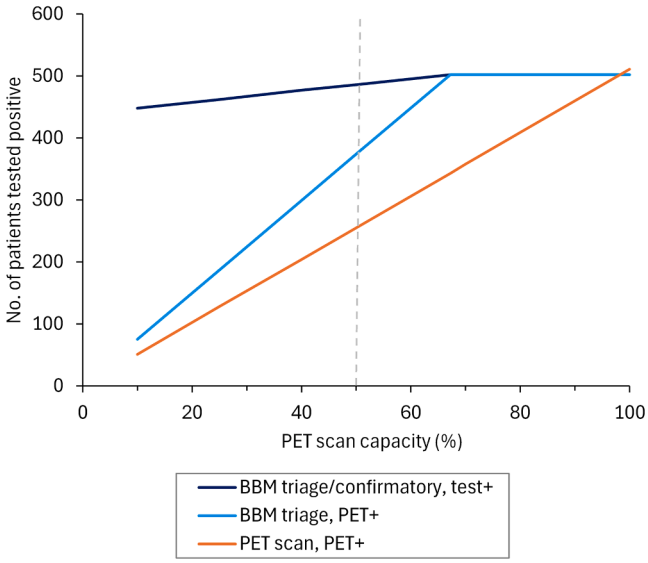

Fig. 2. Expected number of diagnostic outcomes. The number of PET+ or test positives was estimated for 1000 patients. When access to PET scans is limited, test positives in BBM-test strategy include both those who test positive by PET scan and those who have a BBM high-risk result but do not undergo PET scan. A 50 % PET scan capacity means that 500 PET scans are available for 1000 patients. Abbreviations: BBM, blood-based biomarker; PET, positron emission tomography.

In sensitivity analyses, the ICER values are minimally affected by parameter variations (**Supplementary Fig. 4**), the BBM-test strategy has a 100 % probability of being cost-effective (**Supplementary Fig. 5**), and BBM-test strategy remains cost-effective when the cost of BBM testing increases to $1200 using the WTP threshold of $10,000 per diagnosis (**Supplementary Fig. 6**).

Table 3
Cost-effectiveness outcomes when CSF testing is also available.

Strategy	Cost, $	Positive diagnosis, n	Cost per diagnosis, $	ICER, $
PET/CSF testing	2899,200	307	9459	Comparator
BBM triage/confirmatory	3702,200	495	7475	4254

Outcomes are for 1000 patients with 500 PET scans and 100 CSF testing available. Calculations of cost per diagnosis and ICER are based on unrounded results. ICER is presented in $ per gain of diagnosis. BBM, blood-based biomarker; CSF, cerebrospinal fluid; ICER, incremental cost-effectiveness ratio; PET, positron emission tomography.

We further performed two scenario analyses to evaluate the cost-effectiveness outcomes under different model assumptions. In one scenario, for PET-scan strategy, patients are prioritized for PET scans with consideration of clinical information, presumably resulting in higher diagnostic rate than if patients are randomly selected for PET scans. For example, if 500 in 1000 patients are randomly selected for PET scans, 255 would be PET+. However, if PET scans are prioritized for patients who are deemed to have risk of AD pathology based on clinical information, 357 could be PET+ (a 40 % improvement). In this scenario, BBM testing remains cost-effective (**Supplementary Table 4**). In another scenario, CSF testing is also provided when there is limited access to PET scans. If 500 PET scans and 100 CSF tests are available for 1000 patients, BBM testing would identify more test-positive patients than PET/CSF testing alone at an ICER value less than the average cost per diagnosis by PET/CSF testing (Table 3).

4. Discussion

In this decision-analytical modeling analysis, we show that compared with PET scan (when access is unlimited), BBM triage testing could identify nearly all (98.2 %) PET+ patients with a lower average cost per PET+ diagnosis ($8868 vs 10,345 per PET+ diagnosis). The ICER by BBM triage testing vs PET scan alone is $93,984 saved per loss of diagnosis, which is much larger than the WTA threshold at 2 times the average cost of PET+ diagnosis by PET scan alone. Therefore, BBM triage testing is much cheaper and almost as good compared with PET scan alone. Such decrementally cost-effective innovations offer an opportunity to improve the efficiency of healthcare resource allocation [28]. Viewed differently, if the average cost by PET scan for each of the 502 PET+ diagnosis (out of 511) were $8868 (as BBM triage testing), each of the additional 9 PET+ diagnoses by PET scan would have cost $93,984, which is much higher than the WTP threshold (average cost per PET+ diagnosis by PET scan). Therefore, BBM triage testing is an acceptable, high-value test strategy that can help maximize diagnostic outcomes while minimizing costs [29].

In addition, when access to amyloid PET scans is limited, using BBM testing (triage and confirmatory) to evaluate patients was projected to improve the utilization of existing PET capacity and identify more PET+ and test-positive patients. The ICER value by BBM testing vs PET scan alone is much lower than the WTP threshold. Therefore, BBM testing (triage/confirmatory) is a cost-effective testing strategy. Since PET scan capacity constraint is an important issue in current clinical practice as well as in foreseeable future [9], these results are particularly relevant as BBM testing is beginning to be implemented in clinical practice [15].

This study has some limitations. First, our effectiveness outcome is the number of PET+ or test-positive patients instead of quality-adjusted life years (QALY). Although QALY is often used as the effectiveness measurement in cost-effectiveness analysis, other natural units are also used, including the number of patients with a successful diagnosis in the case of alternative diagnostic strategies [30–32]. As used in other studies [33–35], diagnosis of amyloid pathology is highly relevant in patient care [36] and accurate diagnosis of amyloid pathology is associated with lower risk of institutionalization, lower mortality and lower care cost in a real-world evidence study [37]. We note that BBM testing has the possibility of false-positive and false-negative results, which could lead to inappropriate diagnosis and unnecessary or delayed treatment and consequently patient health outcomes. However, with follow-up amyloid PET scans for all or some of the patients with BBM high- and intermediate-risk results, the overall false-positive and false-negative rates are very low. We also note that the outcomes of amyloid PET scans in our model include only positive and negative results but not potentially (a small percentage [22]) equivocal results which may need additional evaluation. We have not estimated QALY, which would require the model to include amyloid-targeting treatment. Such a model has its own limitations including the uncertainty of extrapolating life-long treatment effect from short-term efficacy observed in clinical trials [38,39].

Second, the use and interpretation of BBM testing could be influenced by clinical information [18], which is not considered in modeling (although we have performed a sensitivity analysis on PET scan diagnosis). All patients with BBM high-risk results receive PET scans in the model when access to PET scans is unlimited, but fewer such patients might do so in clinical practice. An expert survey reported an 80 % rate of PET scan or CSF testing in BBM test-positive patients [19] while another study reported a 20 % rate of PET scan in BBM high-risk patients [26]. PET scans might also be prioritized for those who have BBM intermediate-risk results [40], particularly when access to PET scans is limited. Modeling with lower rates of PET scans among high-risk patients would increase cost-effectiveness of BBM-test strategy.

Third, BBM testing has various clinical applications and its utilization and clinical decision/interpretation may vary in different settings [16–18,41]. This study models the use of a BBM test specifically cleared by the FDA for the detection of amyloid pathology associated with Alzheimer's disease in a specialist care setting. Findings from this study should not be simply extrapolated to primary care or other community settings. A different BBM test has recently been cleared by the FDA for use in primary care to rule out Alzheimer's-related amyloid pathology [42]. Therefore, new methods are needed to specifically model the application of such a BBM test in the primary care setting.

Fourth, given potential differences in the costs of biomarker testing and patient care across different countries, findings from this study should not be extrapolated to locations outside the US. However, cost-effectiveness of BBM testing could be evaluated using the model framework developed in this study with country-specific input parameters.

This study also has notable strengths. We have followed the recently published Alzheimer's Association Clinical Practice Guideline for BBM testing [18]. We have conducted the cost-effectiveness analysis of an FDA-cleared test using performance parameters from a multi-center clinical study including both MCI and dementia patients [23]. Following the standard methodologies for cost-effectiveness analysis including multiple sensitivity and scenario analyses, we have shown that the cost-effectiveness outcomes are robust to variations in test parameters and assumptions. Our findings might be applicable to other BBM tests with similar clinical performance [43]. Analysis of claims data could help validate the cost-effectiveness of BBM testing in the diagnosis of AD pathology in the clinic.

5. Conclusion

When access to PET scans is unlimited, BBM triage testing, compared with PET scan alone, is much cheaper and almost as good for the evaluation of Alzheimer's pathology in MCI or dementia patients aged 55 years and older. Given PET scan capacity constraint, using BBM testing (triage and confirmatory) is more efficient in the utilization of available PET scans and leads to the diagnosis of more patients who have Alzheimer's pathology. The incremental cost for each additional diagnosis is much lower than the WTP threshold implied from the current coverage of PET scans, suggesting that BBM testing is cost-effective. These observations provide strong economic rationale for the implementation of BBM testing in the clinical care of MCI or dementia patients.

Data availability

All data supporting the findings of this study are available within the paper.

Declaration of generative AI and AI-assisted technologies in the writing process

We have not used AI in the writing process.

Funding

The authors received no specific financial support for this study other than regular employment compensation.

Note added in proof

Fujirebio, the manufacturer of the FDA cleared assay, has notified Quest Diagnostics of a quality issue in their *in vitro* diagnostic (IVD) kit for Lumipulse® pTau 217/β-Amyloid 1-42 Plasma Ratio. Fujirebio has detected a positive bias which may classify results incorrectly. The manufacturer is investigating the cause of the issue. It should be noted that this issue did not affect results analyzed in this study and this issue does not negatively impact the overall conclusions raised by this study.

CRediT authorship contribution statement

Yonghong Li: Writing – original draft, Methodology, Investigation, Formal analysis, Conceptualization. **Robert J. Lagier:** Writing – review & editing, Validation, Investigation. **Michael K. Racke:** Writing – review & editing, Investigation. **Yuri A. Fesko:** Writing – review & editing, Supervision, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: All authors are employed by Quest Diagnostics.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.tjpad.2025.100474.

References

[1] More than normal aging: Understanding mild cognitive impairment. https://www.alz.org/alzheimers-dementia/what-is-dementia/related_conditions/mild-cognitive-impairment. Accessed May 7, 2025.
[2] Jansen WJ, Ossenkoppele R, Knol DL, Tijms BM, Scheltens P, Verhey FR, et al. Prevalence of cerebral amyloid pathology in persons without dementia: a meta-analysis. JAMA 2015;313:1924–38.
[3] Sims JR, Zimmer JA, Evans CD, Lu M, Ardayfio P, Sparks J, et al. Donanemab in early symptomatic Alzheimer disease: the TRAILBLAZER-ALZ 2 randomized clinical trial. JAMA 2023;330:512–27.
[4] van Dyck CH, Swanson CJ, Aisen P, Bateman RJ, Chen C, Gee M, et al. Lecanemab in early Alzheimer's disease. N Engl J Med 2023;388:9–21.
[5] Rabinovici GD, Knopman DS, Arbizu J, Benzinger TLS, Donohoe KJ, Hansson O, et al. Updated appropriate use criteria for amyloid and tau PET: a report from the Alzheimer's Association and Society for Nuclear Medicine and Molecular Imaging Workgroup. Alzheimers Dement 2025;21:e14338.
[6] Lee JC, Kim SJ, Hong S, Kim Y. Diagnosis of Alzheimer's disease utilizing amyloid and tau as fluid biomarkers. Exp Mol Med 2019;51:1–10.
[7] Yan JT, Dillon A, Meng T, Ramesh V, Sabbagh MN, Sharma V, et al. Real-world use of diagnostic tests for mild cognitive impairment, Alzheimer's disease, and other dementias in Medicare fee-for-service beneficiaries. Alzheimers Dement (Amst) 2025;17:e70156.
[8] Roth S, Yan JT, Patru M-M, Mattke S, Ortsater G, Gustavsson A. Capacity for Alzheimer's Disease confirmatory testing in the US - current situation and simulations for future increase. Alzheimers Dement 2024;20:e085540.
[9] Mattke S, Cho SK, Bittner T, Hlavka J, Hanson M. Blood-based biomarkers for Alzheimer's pathology and the diagnostic process for a disease-modifying treatment: projecting the impact on the cost and wait times. Alzheimers Dement (Amst) 2020;12:e12081.
[10] Hu Y, Kirmess KM, Meyer MR, Rabinovici GD, Gatsonis C, Siegel BA, et al. Assessment of a plasma amyloid probability score to estimate amyloid positron emission tomography findings among adults with cognitive impairment. JAMA Netw Open 2022;5:e228392.
[11] Barthelemy NR, Salvado G, Schindler SE, He Y, Janelidze S, Collij LE, et al. Highly accurate blood test for Alzheimer's disease is similar or superior to clinical cerebrospinal fluid tests. Nat Med 2024;30:1085–95.
[12] Palmqvist S, Tideman P, Mattsson-Carlgren N, Schindler SE, Smith R, Ossenkoppele R, et al. Blood biomarkers to detect Alzheimer disease in primary care and secondary care. JAMA 2024;332:1245–57.
[13] Weber DM, Taylor SW, Lagier RJ, Kim JC, Goldman SM, Clarke NJ, et al. Clinical utility of plasma Abeta42/40 ratio by LC-MS/MS in Alzheimer's disease assessment. Front Neurol 2024;15:1364658.
[14] Meyer MR, Kirmess KM, Eastwood S, Wente-Roth TL, Irvin F, Holubasch MS, et al. Clinical validation of the PrecivityAD2 blood test: a mass spectrometry-based test with algorithm combining %p-tau217 and Abeta42/40 ratio to identify presence of brain amyloid. Alzheimers Dement 2024;20:3179–92.
[15] FDA clears first blood test used in diagnosing Alzheimer's disease. https://www.fda.gov/news-events/press-announcements/fda-clears-first-blood-test-used-diagnosing-alzheimers-disease. Accessed June 14, 2025.
[16] Mielke MM, Anderson M, Ashford JW, Jeromin A, Lin PJ, Rosen A, et al. Recommendations for clinical implementation of blood-based biomarkers for Alzheimer's disease. Alzheimers Dement 2024;20:8216–24.
[17] Schindler SE, Galasko D, Pereira AC, Rabinovici GD, Salloway S, Suarez-Calvet M, et al. Acceptable performance of blood biomarker tests of amyloid pathology - recommendations from the Global CEO Initiative on Alzheimer's Disease. Nat Rev Neurol 2024;20:426–39.
[18] Palmqvist S, Whitson HE, Allen LA, Suarez-Calvet M, Galasko D, Karikari TK, et al. Alzheimer's Association Clinical Practice Guideline on the use of blood-based biomarkers in the diagnostic workup of suspected Alzheimer's disease within specialized care settings. Alzheimers Dement 2025;21:e70535.
[19] Mattke S, Chen J, Hanson M, Johnson KG, Leahy C, Merrill DA, et al. Estimation of the value-based price of a blood test for Alzheimer's disease pathology in primary and specialty care in the U.S. J Prev Alzheimers Dis 2025:100219.
[20] Deverka PA, Lin GA, Phillips KA. Payer coverage considerations for Alzheimer disease blood-based biomarker tests. JAMA 2024;332:1877–8.
[21] Husereau D, Drummond M, Augustovski F, de Bekker-Grob E, Briggs AH, Carswell C, et al. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) statement: updated reporting guidance for health economic evaluations. Value Health 2022;25:3–9.
[22] Oh M, Seo M, Oh SY, Kim H, Choi BW, Oh JS, et al. A 4-year follow-up of subjects with visually equivocal amyloid positron emission tomography findings from the Alzheimer's Disease Neuroimaging Initiative cohort. Nucl Med Mol Imaging 2021;55:71–8.
[23] Lumipulse G pTau217 /P-Amyloid 1-42 Plasma Ratio. https://www.accessdata.fda.gov/cdrh_docs/pdf24/K242706.pdf. Accessed July 10, 2025.
[24] MDSave. https://www.mdsave.com. Accessed April 18, 2025.
[25] First Blood Test to Diagnose Alzheimer's Cleared by FDA. https://www.everydayhealth.com/neurological-disorders/first-blood-test-to-diagnose-alzheimers-cleared-by-fda, #:~:text=PET%20scans%20and%20spinal%20taps,might%20cost%20%24500%20to%20%241%2C000. Accessed July 15, 2025.
[26] Canestaro WJ, Bateman RJ, Holtzman DM, Monane M, Braunstein JB. Use of a blood biomarker test improves economic utility in the evaluation of older patients presenting with cognitive impairment. Popul Health Manag 2024;27:174–84.
[27] Beta amyloid positron emission tomography in dementia and neurodegenerative disease. https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx, ?proposed=N&NCAId=308. Accessed June 5, 2025.
[28] Nelson AL, Cohen JT, Greenberg D, Kent DM. Much cheaper, almost as good: decrementally cost-effective medical innovation. Ann Intern Med 2009;151:662–7.
[29] Sacristan JA. How to assess the value of low-value care. BMC Health V Res 2020;20:1000.
[30] Michelly Goncalves Brandao S, Brunner-La Rocca HP, Pedroso de Lima AC, Alcides Bocchi E. A review of cost-effectiveness analysis: from theory to clinical practice. Medicine 2023;102:e35614.

[31] Hull R, Hirsh J, Sackett DL, Stoddart G. Cost effectiveness of clinical diagnosis, venography, and noninvasive testing in patients with symptomatic deep-vein thrombosis. N Engl J Med 1981;304:1561–7.
[32] Robinson R. Cost-effectiveness analysis. BMJ 1993;307:793–5.
[33] Sato K, Niimi Y, Ihara R, Iwata A, Suzuki K, Iwatsubo T. Blood-based biomarker prescreening with different testing combinations and cutoffs: a simulation study examining efficacy and cost-effectiveness in Alzheimer's disease prevention studies. Alzheimers Dement 2025;11:e70065.
[34] Contador J, Vargas-Martinez AM, Sanchez-Valle R, Trapero-Bertran M, Llado A. Cost-effectiveness of Alzheimer's disease CSF biomarkers and amyloid-PET in early-onset cognitive impairment diagnosis. Eur Arch Psychiatry Clin Neurosci 2023;273:243–52.
[35] Noda K, Lim Y, Goto R, Sengoku S, Kodama K. Cost-effectiveness comparison between blood biomarkers and conventional tests in Alzheimer's disease diagnosis. Drug Discov Today 2024;29:103911.
[36] Rabinovici GD, Gatsonis C, Apgar C, Chaudhary K, Gareen I, Hanna L, et al. Association of amyloid positron emission tomography with subsequent change in clinical management among medicare beneficiaries with mild cognitive impairment or dementia. JAMA 2019;321:1286–94.
[37] van Maurik IS, Broulikova HM, Mank A, Bakker ED, de Wilde A, Bouwman FH, et al. A more precise diagnosis by means of amyloid PET contributes to delayed institutionalization, lower mortality, and reduced care costs in a tertiary memory clinic setting. Alzheimers Dement 2023;19:2006–13.
[38] Aye S, Handels R, Winblad B, Jonsson L. Optimising Alzheimer's disease diagnosis and treatment: assessing cost-utility of integrating blood biomarkers in clinical practice for disease-modifying treatment. J Prev Alzheimers Dis 2024;11:928–42.
[39] Wimo A, Handels R, Blennow K, Kirsebom BE, Selnes P, Bon J, et al. Cost-effectiveness of diagnosing and treating patients with early Alzheimer's disease with anti-amyloid treatment in a clinical setting. J Alzheimers Dis 2025;104:1167–84.
[40] Brum WS, Cullen NC, Janelidze S, Ashton NJ, Zimmer ER, Therriault J, et al. A two-step workflow based on plasma p-tau217 to screen for amyloid beta positivity with further confirmatory testing only in uncertain cases. Nat Aging 2023;3:1079–90.
[41] Hansson O, Blennow K, Zetterberg H, Dage J. Blood biomarkers for Alzheimer's disease in clinical practice and trials. Nat Aging 2023;3:506–19.
[42] Alzheimer's Association welcomes FDA clearance of first blood test for use in primary care to rule out Alzheimer's-related amyloid pathology. https://www.alz.org/news/2025/fda-clearance-blood-test-primary-care-rule-out-alzheimers-related-amyloid-pathology. Accessed November 21, 2025.
[43] Schindler SE, Petersen KK, Saef B, Tosun D, Shaw LM, Zetterberg H, et al. Head-to-head comparison of leading blood tests for Alzheimer's disease pathology. Alzheimers Dement 2024;20:8074–96.