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Original Article

A Protocol of Korean JOint RegistrY for ALZheimer's Treatment and Diagnostics (JOY-ALZ)

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ABSTRACT

Background and Purpose: To assess the long-term effectiveness, safety, and economic viability of recently approved Alzheimer's disease (AD) therapies, as well as to evaluate the real-world application of novel diagnostics among AD patients with diverse comorbidities, comprehensive real-world data (RWD) analysis is essential. The Korean JOint RegistrY for ALZheimer's Treatment and Diagnostics (JOY-ALZ) endeavors to create a registry of RWD derived from clinical practice on new diagnostic methods and therapeutic agents for AD introduced in Korea since 2021.

Methods: Participants must fulfill all the following: 1) be at least 19 years old; 2) be actively receiving, scheduled to initiate, or undergoing evaluation for any AD disease-modifying treatment; 3) have completed amyloid positron emission tomography or cerebrospinal fluid AD immunoassay (a positive result is not essential for participation); 4) have a

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Conflict of Interest
Sung Hoon Kang has served as the editorial board member of the *Dementia and Neurocognitive Disorders*. However, Sung Hoon Kang has not been involved in the peer reviewer process or decision-making for this article. No other potential conflict of interest relevant to this article was reported.

clinical classification of cognitively unimpaired, mild cognitive impairment, or probable AD dementia. Data generated during routine care is segmented into a minimum dataset, extended dataset, and research-only dataset requiring extra consent. Assessments encompass clinical, cognitive, functional, neurobehavioral, neuroimaging, and biomarker evaluations, in addition to systematic monitoring of new AD treatments and their safety. Data are collected and monitored at baseline, at semiannual intervals during the initial 2 years, and then annually up to 2034. To date, 46 medical centers will participate in JOY-ALZ.
Conclusions: JOY-ALZ is expected to promote understanding of the long-term clinical outcomes, safety, and cost-effectiveness of recently introduced diagnostics and treatments for AD, thereby supporting the progress of precision medicine in AD care and diagnosis.

Trial Registration: ClinicalTrials.gov Identifier: NCT06889818

Keywords: Alzheimer Disease; Treatment; Monoclonal Antibody; Diagnosis; Biomarkers; Dataset

INTRODUCTION

Alzheimer's disease (AD), the leading cause of dementia and cognitive impairment in late adulthood, is a progressive neurodegenerative disorder marked by the accumulation of abnormal amyloid-β (Aβ) and tau proteins within the brain.[1,2] Longitudinal biomarker studies reveal that cortical Aβ deposition may precede clinical memory decline by approximately 2 decades, indicating a prolonged preclinical phase that advances from cognitively unimpaired (CU) status to subjective cognitive decline (SCD), mild cognitive impairment (MCI), and ultimately dementia.[3] The landscape of AD treatment has evolved substantially with the advent of disease-modifying therapies (DMTs), notably monoclonal antibodies directed at Aβ such as lecanemab and donanemab.[4,5] In parallel with therapeutic progress, diagnostic tools have also made considerable advancements. Recently developed approaches, including fluid biomarkers (e.g., cerebrospinal fluid [CSF] Aβ42/40 ratio and plasma phosphorylated-tau [p-tau] 217),[6,7] advanced positron emission tomography (PET) imaging quantification,[8,9] and digital cognitive testing[10,11] are transforming the strategies for early detection, diagnosis, and disease monitoring throughout the AD continuum. The Korean Ministry of Food and Drug Safety (MFDS) has approved the Elecsys CSF AD immunoassay (Aβ42, p-tau181, and total-tau) and lecanemab for early AD, reflecting a notable transition toward biomarker-guided management in standard clinical practice.[12]

However, randomized controlled trials (RCTs) evaluating these therapies have primarily been performed in highly selective populations within strictly controlled environments, raising concerns regarding their applicability to real-world clinical practice. Notably, Asian populations have been underrepresented in pivotal phase 3 trials, thereby limiting our understanding of region-specific safety, efficacy, and clinical relevance. For example, subgroup analyses from the phase 3 CLARITY-AD trial of lecanemab indicated regional differences in the prevalence of amyloid-related imaging abnormalities (ARIA) between East Asian and Western groups, which may reflect the impact of genetic and environmental factors on safety and therapeutic outcomes.[4,13] These findings underscore the urgent need for Korean-specific real-world data (RWD) that adequately capture the full spectrum of clinical manifestations, therapeutic responses, and safety outcomes. Furthermore, as the follow-up duration in phase 3 clinical trials is relatively limited, ongoing research using RWD is

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essential to assess long-term efficacy, safety, and cost-effectiveness. In South Korea, the clinical integration of DMTs such as lecanemab has already begun, with a growing number of patients initiating treatment. To facilitate safe and effective utilization, it is necessary to establish a nationwide infrastructure for the systematic collection and analysis of multimodal RWD from routine clinical practice, enabling continuous monitoring of treatment effectiveness, detection of adverse events (AEs), and evidence-based policy development using population-level data. Moreover, the clinical utility of emerging diagnostic techniques for AD should be evaluated in real-world scenarios, particularly in patients presenting with diverse comorbidities.

To address this complex challenge, the Korean JOint RegistrY for ALZheimer's Treatment and Diagnostics (JOY-ALZ) was initiated in 2024. JOY-ALZ aims to establish a comprehensive registry to collect RWD generated in clinical settings concerning novel diagnostic methods and therapeutic agents for AD that have been approved by the MFDS since 2021. JOY-ALZ represents the first nationwide, prospective RWD platform in Korea specifically designed to assess the real-world adoption of newly approved and emerging DMTs and diagnostic technologies. The registry operates under the guidance of the DREAM framework, which encompasses 5 primary goals: develop a collaborative national infrastructure for data integration; record real-world diagnostic, therapeutic, and outcome information from diverse clinical environments; enhance standardization and quality across sites through unified data collection protocols; assess longitudinal safety, effectiveness, and health outcomes; and maximize data sharing and global interoperability. The distinct aims and key components of the DREAM framework are described in **Table 1**. By systematically capturing multimodal data—including clinical, imaging, biomarker, and genomic information—from a nationwide network of 46 memory clinics, JOY-ALZ aims to address significant gaps in evidence, advance precision medicine, and produce high-quality, representative RWD from Korea to inform clinical decision-making and strengthen global AD research.

METHODS

Study design

JOY-ALZ is a prospective, nationwide, multicenter registry intended to collect RWD from individuals across the AD continuum in Korea. Participating sites are required to prescribe lecanemab or other newly approved AD diagnostics by MFDS since 2021 and enlist study personnel dedicated to registry entry and data management. Thus far, 46 memory clinics affiliated with academic and general hospitals are participating in or planning to participate in the registry. **Fig. 1** illustrates the geographical distribution of participating centers. Participation by 46 sites nationwide will facilitate comprehensive geographic representation, as well as demographic diversity such as economic status and environmental exposures, thereby supporting health equity in the registry population. After enrollment, data are obtained from participants every 6 months for the first 24 months, and annually thereafter until 31 December 2034, permitting up to 10 years of follow-up for early enrollees. Scheduled assessments include data captured during routine clinical practice, with supplemental data from protocol-specific procedures as needed, maintaining the real-world relevance of the dataset. All data are collected according to harmonized protocols to uphold data quality and ensure comparability across sites. The JOY-ALZ protocol has been registered at ClinicalTrials.gov (NCT06889818). The current protocol version is 1.3.2.

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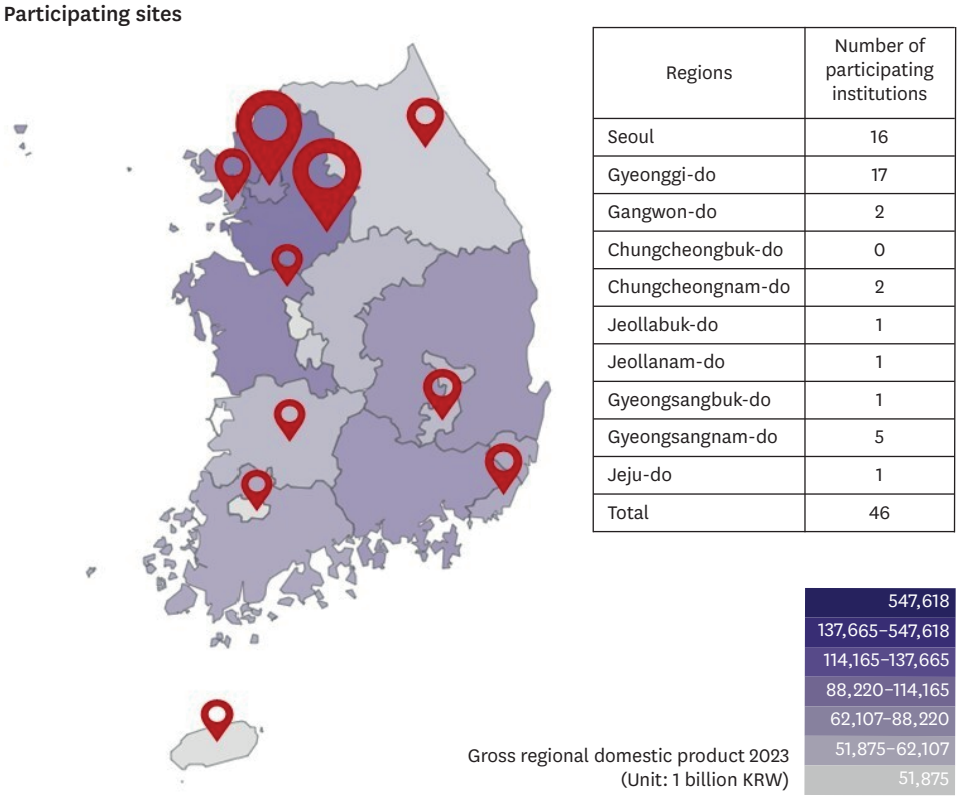
Table 1. Objectives of JOint RegistrY for ALZheimer's Treatment and Diagnostics within the DREAM framework

Aim 1 D: Develop a nationwide collaborative infrastructure	· Construct a registry network comprising memory clinics, general hospitals, and academic centers across Korea. · Develop a centralized digital system to collect longitudinal clinical, neuroimaging, and biomarker datasets. · Establish governance protocols to ensure data integrity, ethical standards, and regulated research access.
Aim 2 R: Record real-world data on treatment and diagnostics	· Collect comprehensive clinical data from patients utilizing recently approved DMTs. · Record application of advanced diagnostic techniques, such as amyloid and tau PET imaging, plasma-based biomarkers, and genetic assays. · Monitor clinical decision-making trends, treatment intervals, and adverse event occurrences in standard clinical practice.
Aim 3 E: Enhance data acquisition and standardization	· Adopt standardized case report forms and data dictionaries for site-wide data consistency. · Incorporate modules for neuroimaging and biosample acquisition to facilitate biomarker-driven investigations.
Aim 4 A: Assess outcomes and effectiveness	· Monitor longitudinal changes in cognition, function, and safety among patients treated with DMTs. · Analyze outcomes across various patient subgroups and therapeutic regimens. · Develop real-world evidence to aid clinical decision-making and support healthcare policy formulation.
Aim 5 M: Maximize data sharing and global contribution	· Implement robust protocols to ensure secure de-identification and controlled sharing of clinical, imaging, and biospecimen data. · Facilitate collaborative research initiatives with national and international consortia to expedite scientific advancements. · Provide comprehensive, Korea-specific data to enhance the global Alzheimer's disease research landscape.

DMT: disease-modifying therapy, PET: positron emission tomography.



Regions	Number of participating institutions
Seoul	16
Gyeonggi-do	17
Gangwon-do	2
Chungcheongbuk-do	0
Chungcheongnam-do	2
Jeollabuk-do	1
Jeollanam-do	1
Gyeongsangbuk-do	1
Gyeongsangnam-do	5
Jeju-do	1
Total	46

Fig. 1. Geographic distribution of JOY-ALZ participating sites.

Participants

Inclusion and exclusion criteria are presented in **Table 2**. Participants are eligible for enrollment if they meet all of the following inclusion criteria: 1) age ≥19 years; 2) currently receiving, scheduled to begin, or under evaluation for any AD disease-modifying therapy; 3) have undergone amyloid PET or CSF study to evaluate AD pathology (a positive result is not

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Table 2. Participant eligibility criteria

Inclusion criteria
I-1 Age ≥19 years at the time of informed-consent signing.
I-2 Receiving, scheduled to begin, or under evaluation for any AD disease-modifying therapy, plus comparator group (non-treatment-eligible, such as cognitively unimpaired).
I-3 Amyloid testing performed by amyloid PET or CSF, regardless of the result.
I-4 Clinical diagnosis within the AD spectrum.
· Alzheimer's disease dementia
: Fulfills the criteria for probable AD dementia as defined by the NIA-AA working groups.
: Loss of functional independence due to cognitive deterioration.
· Mild cognitive impairment due to AD
: Satisfies the NIA-AA diagnostic standards for MCI.
: Cognitive decline is reported either subjectively or by an informant.
: Delayed verbal memory recall falls below −1.0 SD relative to age- and education-adjusted reference values, or at least one cognitive domain (executive function, language, visuospatial ability, or attention) scores below −1.5 SD against age- and education-adjusted norms.
: CDR score equals 0.5.
: Maintains independent ability to perform daily activities.
: Does not fulfill the diagnostic criteria for dementia.
· Cognitively unimpaired
: Delayed verbal memory recall remains above −1.0 SD, with scores in executive function, language, visuospatial ability, and attention all above −1.5 SD when compared to age- and education-adjusted reference values.
: Independent performance in daily activities remains preserved.
: Participants who report cognitive decline themselves are categorized as having SCD.
I-5 Ambulatory status (use of walking aid allowed).
I-6 Written informed consent provided by the participant; if dementia is present, supplementary consent from a legal representative is required.
Exclusion criteria
E-1 The presence of major psychiatric disorders, such as intellectual disability, schizophrenia, major depressive disorder, bipolar disorder, or delirium.
E-2 A history of treatment for substance abuse or alcohol dependence within the past 5 years. Eligibility may still be considered if a clinician confirms stable recovery with low relapse risk, even during this period.
E-3 A history of cancer in the past 5 years without documented complete remission (however, a clinician's assessment of low recurrence risk can permit eligibility). Exceptions include cases such as localized prostate cancer, carcinoma in situ of the cervix, and non-metastatic basal cell or squamous cell carcinoma of the skin.
E-4 The presence of severe or unstable physical illness (e.g., dialysis-dependent renal failure, advanced liver disease).
E-5 Presence of significant visual or hearing impairments that would compromise accurate cognitive assessment.
E-6 Contraindications to MRI, such as metallic implants or devices that are incompatible with scanning.
E-7 Simultaneous enrollment in a drug clinical trial.
E-8 Ongoing pregnancy or breastfeeding status.

AD: Alzheimer's disease, PET: positron emission tomography, CSF: cerebrospinal fluid, NIA-AA: National Institute on Aging–Alzheimer's Association, MCI: mild cognitive impairment, SD: standard deviation, CDR: clinical dementia rating, SCD: subjective cognitive decline, MRI: magnetic resonance imaging.

required for inclusion); 4) have a clinical diagnosis of CU, MCI, or probable AD dementia. CU is defined as normal cognitive function with a delayed recall score of verbal memory greater than −1.0 standard deviation (SD) from the age- and education-adjusted normative mean, and scores in executive function, language, visuospatial construction, and attention all above −1.5 SD.[14,15] Additionally, participants must maintain independent performance in activities of daily living. Participants who report SCD but fulfill the criteria for CU are classified as having SCD.[16] MCI is defined as a delayed recall score below −1.0 SD from the age- and education-adjusted normative mean, or impairment in at least one other cognitive domain (executive function, language, visuospatial construction, or attention) with scores below −1.5 SD.[14] Participants with MCI must have a Clinical Dementia Rating (CDR) of 0.5, preserved independence in activities of daily living, absence of a clinical dementia diagnosis, and documented cognitive decline reported by the individual or an informant.[17] Probable AD dementia is diagnosed based on the 2011 National Institute on Aging–Alzheimer's Association criteria[18]; 5) ambulatory status (use of a walking aid is acceptable); 6) provision of written informed consent. For participants with dementia, consent is additionally obtained from their legal representatives.

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Participants are excluded if they meet any of the following criteria: 1) current or previous diagnosis of major psychiatric illness, including intellectual disability, schizophrenia, major depressive disorder, bipolar disorder, or delirium; 2) history of treatment for drug abuse or alcohol dependence within the previous 5 years (however, eligibility may still be considered if a clinician confirms stable recovery with low relapse risk, even during this period); 3) active cancer diagnosis within the past 5 years without documented complete remission (however, a clinician's assessment of low recurrence risk can permit eligibility), except for localized prostate cancer, cervical carcinoma in situ, non-metastatic basal-/squamous-cell skin cancer, or other cancers classified as low-risk by the investigator; 4) presence of severe or unstable medical conditions (e.g., requirement for dialysis, advanced liver disease); 5) unresolved visual or hearing impairment that could interfere with reliable cognitive assessment; 6) contraindications to magnetic resonance imaging (MRI) due to metallic implants or other medical issues; 7) current enrollment in an interventional drug trial; or 8) pregnancy or breastfeeding at screening.

Enrollment and assessment procedures

Study assessments are scheduled to coincide with routine clinical visits whenever feasible, reducing participant burden and enhancing the alignment with real-world clinical practice. All assessments adhere to a standardized schedule outlined in the study protocol, which includes a screening visit (up to 8 weeks before baseline), a baseline visit (Week 0), semiannual visits during the first 2 years (Weeks 26, 52, 78), and annual visits thereafter (Week 104 and every 12 months). At each visit, data are collected on clinical, cognitive, functional, neuropsychiatric, imaging, and biomarker measures, utilizing evaluations from routine clinical care and supplemented as needed by protocol-specified assessments. Trained study personnel enter data into a centralized, secure electronic data capture (EDC) system with integrated real-time validation functions.

Collected information and data

JOY-ALZ requires sites to submit follow-up clinical visit data in the EDC at defined post-baseline intervals: 6 months, 12 months, 18 months, 24 months, and annually thereafter until a study endpoint is reached. **Table 3** provides an overview of the dataset's structure, and **Table 4** outlines the specific minimum and extended data elements collected at each follow-up visit.

Collected data are divided into the minimum dataset (MDS) and the extended dataset (EDS) (**Table 3**). The MDS contains essential data elements routinely gathered in clinical practice, such as patient profile and demographics, lifestyle, comorbid conditions, concurrent medications, clinical diagnoses and symptoms, cognitive and functional measures, brain MRI, amyloid PET or CSF AD biomarkers, information on new AD treatments, and safety assessments. The EDS consists of optional elements gathered if available, either as part of standard clinical care or for research objectives. EDS from clinical care includes extended cognitive and functional measures, additional imaging and biomarker results, apolipoprotein E (APOE) genotype, and Aβ42 oligomerization tendency in blood.[19] Research-specific EDS comprises additional blood samples collected for plasma, serum, and DNA biobanking, contingent upon separate informed consent.

Demographic and clinical variables

MDS

Demographic and clinical data are collected at baseline and updated as appropriate throughout the study period. Variables include age, sex, years of education, marital status,

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Table 3. Minimum and extended dataset

Minimum dataset		
Patient profile	Consent; year and month of birth; sex; education level; care partner information; family history of dementia	
Demographics	Blood pressure; heart rate; weight; height	
Lifestyle	Assessment of alcohol consumption and smoking history; levels of physical activity; nutrition patterns	
Comorbidities/Concomitant medication	Diagnosis and disease onset date; therapeutic agent used, dosage, and administration date	
Clinical diagnosis	CU; MCI; AD dementia (early/ moderate/severe stage); logopenic primary progressive aphasia; posterior cortical atrophy; normal pressure hydrocephalus; dementia with Lewy body; Parkinson's disease dementia; vascular dementia; behavioral variant frontotemporal dementia; semantic variant primary progressive aphasia; non-fluent variant primary progressive aphasia	
Clinical manifestations	Initial cognitive symptoms; age at onset of cognitive symptoms; age at AD diagnosis; clinical signs indicating potential co-pathologies	
Cognitive, functional, and neurobehavioral evaluations	K-MMSE-2; K-MoCA; CDR; FAQ; AD8; EQ-5D; CGA-NPI	
Brain MRI	Baseline imaging findings; presence of microbleeds; evidence of intracranial hemorrhages; superficial siderosis; brain edema; lacunes; strokes in major vascular territories; Fazekas score; amyloid beta-related angiitis, CAA-ri, or other significant intracranial abnormalities potentially causing cognitive impairment; raw imaging data	
AD diagnostic work-up (Amyloid PET or CSF)	Amyloid PET	Radioligand used; result of positivity or negativity based on visual interpretation; raw imaging data
	CSF	Aβ42; p-tau181
Exposure to new AD treatments	Therapeutic agent administered; dosage; administration date	
Safety monitoring of new AD treatments	SAE; ARIA (including symptoms, radiological and clinical severity, management, and outcomes); infusion reactions; other events of interest	
Treatment discontinuation	Discontinuation reasons	
Extended dataset		
Cognitive, functional, and neurobehavioral assessments	SNSB; CERAD-K; LICA; K-IADL; S-IADL; GDS-15; GDS-30	
Brain MRI	Follow-up imaging data as indicated; identification of microbleeds; intracranial hemorrhages; superficial siderosis; evidence of brain edema; presence of lacunes; strokes involving major vascular territories; Fazekas score; amyloid beta-related angiitis, CAA-ri, and other significant intracranial findings potentially contributing to cognitive impairment; raw imaging data	
Amyloid PET	Follow-up imaging data when necessary (including radioligand type, positivity or negativity based on visual assessment, and raw imaging data); Centiloid values or SUVR	
CSF	Procedural details	Needle gauge; presence of traumatic tap; initial opening pressure; puncture site level
	Adverse effects	Assessment of severity and duration of adverse effects; documentation of associated symptoms
Laboratory assessments	*APOE* genotype; Aβ42 oligomerization potential	

CU: cognitively unimpaired, MCI: mild cognitive impairment, AD: Alzheimer's disease, K-MMSE-2: Korean-Mini-Mental State Examination-2, K-MoCA: Korean-Montreal Cognitive Assessment, CDR: Clinical Dementia Rating scale, FAQ: Functional Activity Questionnaire, AD8: Ascertain Dementia 8-Item Questionnaire, EQ-5D: European Quality of Life 5 Dimensions questionnaire, CGA-NPI: Caregiver-Administered Neuropsychiatric Inventory, MRI: magnetic resonance imaging, CAA-ri: cerebral amyloid angiopathy-related inflammation, PET: positron emission tomography, CSF: cerebrospinal fluid, p-tau: phosphorylated-tau, SAE: serious adverse event, ARIA: Amyloid-Related Imaging Abnormalities, SNSB: Seoul Neuropsychological Screening Battery, CERAD-K: Korean version of the Consortium to Establish a Registry for Alzheimer Disease, LICA: Literacy Independent Cognitive Assessment, K-IADL: Korean-Instrumental Activities of Daily Living, S-IADL: Seoul-Instrumental Activities of Daily Living, GDS-15: Geriatric Depression Scale-15 items, GDS-30: Geriatric Depression Scale-30 items, SUVR: Standardized Uptake Value Ratio, APOE: Apolipoprotein E, Aβ: amyloid-β.

type of living arrangement (such as living alone, or with spouse, children, grandchildren, relatives, caregivers, or others), and family history of dementia. The presence of a primary caregiver or support person is also recorded. A detailed medical history, including vascular risk factors such as hypertension, diabetes mellitus, and dyslipidemia, will be obtained.

Lifestyle-related factors, including smoking status, alcohol consumption, nutrition, and physical activity level, will also be collected. Physical activity and nutritional status will be assessed using the International Physical Activity Questionnaire[20] and the Nutrition Quotient for the Elderly,[21] respectively. Vital signs, such as blood pressure and pulse, along with height, weight, and body mass index will be measured at each study visit. Detailed information on both current and past medical conditions will be reviewed regularly, with particular focus on cerebrovascular, psychiatric, autoimmune, and endocrine disorders.

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Table 4. Minimum and extended dataset for each visit

Visit	Screening visit 1	Baseline visit 2	Follow-up visit 3	Follow-up visit 4	Follow-up visit 5	Follow-up visit 6–13
Weeks	−8 week~−1 day	0 day	26-week (±2 week)	52-week (±2 week)	78-week (±2 week)	104-week, assessed annually (±4 week)
Minimum dataset						
Demographic characteristics	X					
Weight		X	X	X	X	X
Medical history/Concomitant medication	X	X	X	X	X	X
Clinical diagnosis		X	X	X	X	X
Lifestyle factors		X				X*
Blood pressure, heart rate		X	X	X	X	X
K-MMSE-2, K-MoCA		X	X	X	X	X
CDR		X	X	X	X	X
FAQ, K-AD8		X	X	X	X	X
EQ-5D		X		X	X	X
CGA-NPI		X		X	X	X
New AD treatment dosage/schedule		X†	X†	X†	X†	X†
New AD treatment safety-adverse events/ ARIA events		X†	X†	X†	X†	X†
End of study participation						X‡
Extended dataset						
SNSB, CERAD-K or LICA		O		O		O
K-IADL or S-IADL		O		O		O
GDS-15 or GDS-30		O		O		O
Brain MRI evaluation		X	O	O	O	O
Alzheimer's biomarker (amyloid PET or CSF)		X	O	O	O	O
Plasma biomarkers of AD		O	O	O	O	O
Additional blood collection		O§			O§	

X: required form, O: collect when available, K-MMSE 2: Korean-Mini-Mental State Examination-2, K-MoCA: Korean-Montreal Cognitive Assessment, CDR: Clinical Dementia Rating scale, FAQ: Functional Activity Questionnaire, K-AD8: Korean version of the Ascertain Dementia 8-Item Questionnaire, EQ-5D: European Quality of Life 5 Dimensions questionnaire, CGA-NPI: Caregiver-Administered Neuropsychiatric Inventory, AD: Alzheimer's disease, ARIA: Amyloid-Related Imaging Abnormalities, SNSB: Seoul Neuropsychological Screening Battery, CERAD-K: Korean version of the Consortium to Establish a Registry for Alzheimer Disease, LICA: Literacy Independent Cognitive Assessment, O: optional form, K-IADL: Korean-Instrumental Activities of Daily Living, S-IADL: Seoul-Instrumental Activities of Daily Living, GDS-15: Geriatric Depression Scale-15 items, GDS-30: Geriatric Depression Scale-30 items, MRI: magnetic resonance imaging, PET: positron emission tomography, CSF: cerebrospinal fluid.
*Completed every 2 years; †Participants receiving approved New AD treatments; ‡To be completed at the end of study participation; §Applicable only for participants who give consent.

A detailed record of concomitant medications, including cognitive or behavioral therapies such as cholinesterase inhibitors, memantine, antiplatelet agents, antidepressants, and antipsychotics, will be maintained. For each drug, specific details such as class, agent, dosage, route of administration, start and stop dates, and clinical indication will be documented to characterize real-world treatment patterns and assess potential drug interactions.

Clinical diagnoses will be abstracted from clinical records according to inclusion criteria, categorizing participants as CU, MCI, AD dementia (early, moderate, severe stage), or other types of dementia. Initial cognitive symptoms as well as additional clinical features suggestive of potential co-pathologies will be recorded.

EDS

No additional specific demographic or clinical variables will be included in the EDS. All demographic-related information, such as patient profile, vital signs, lifestyle factors, and medical history, will be collected as part of the MDS.

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Cognitive, functional, and neurobehavioral assessments

MDS

Cognitive function will be evaluated using the Korean-Mini-Mental State Examination-2[22] and the Korean-Montreal Cognitive Assessment,[23] administered in clinical practice by trained personnel. Global cognitive severity will be determined using the CDR scale.[24] Everyday functional abilities will be assessed via the Functional Activities Questionnaire,[25] and early cognitive decline will be detected using the informant-rated Ascertain Dementia 8-Item Questionnaire.[26] Behavioral and psychological symptoms of dementia will be assessed through the Caregiver-Administered Neuropsychiatric Inventory Questionnaire.[27] Quality of life will be evaluated using the European Quality of Life 5 Dimensions questionnaire (EQ-5D),[28] which is collected for the economic analysis of the new drug.

EDS

If more detailed annual assessments of cognition, Instrumental Activities of Daily Living (IADL), or mood are routinely performed at each center, these data will be collected. IADL will be recorded using the results of the Seoul IADL[29] or Korean-IADL.[30] Comprehensive neuropsychological assessment outcomes, such as the Seoul Neuropsychological Screening Battery,[15] the Korean version of the Consortium to Establish a Registry for Alzheimer Disease,[31] or the Literacy Independent Cognitive Assessment,[32] will be obtained if these are available. Mood status will be recorded based on the Geriatric Depression Scale (GDS)-15 or GDS-30.[33]

Brain MRI

MDS

Brain MRI data acquired within one year prior to the enrollment date, or if this is not available, the most recent data obtained thereafter, will be collected from clinical records and used as baseline MRI data. Imaging sequences including fluid attenuated inversion recovery, gradient echo sequences or susceptibility-weighted imaging, and diffusion-weighted imaging are required. MRI findings such as microbleedings, macrohemorrhages, superficial siderosis, brain edema, lacunes, stroke involving major vascular territory, and Fazekas scores will be documented based on radiology reports interpreted at each participating institution.

EDS

Baseline 3D T1-weighted images will be sourced from clinical imaging data when available. Follow-up brain MRI data obtained for clinical indications after baseline will be included if accessible. Any changes in MRI findings from baseline will be documented according to radiology reports at each participating institution.

AD diagnostic work-up

MDS

Historical amyloid PET imaging data utilizing MFDS-approved radioligands (F^{18}-florbetaben, F^{18}-flutemetamol, or F^{18}-fluorapronol), as well as CSF results for Elecsys Aβ42 and Elecsys p-tau181, will be collected from clinical records at baseline if these investigations were previously performed for the diagnosis of AD. Binary results (positive or negative) based on visual evaluation by a nuclear medicine physician will also be extracted from clinical reports.

EDS

Follow-up amyloid PET imaging data will be collected if clinically indicated. When available, quantitative assessments of amyloid burden, such as Centiloid values and standardized uptake

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value ratio, will be obtained. Detailed information regarding the lumbar puncture procedure (e.g., needle size, occurrence of traumatic tapping) and any reported side effects (e.g., headache, back pain) will also be extracted from clinical documentation when available. Plasma biomarkers of AD that later receive Korean MFDS approval will be evaluated for their clinical relevance using real-world evidence collected as an EDS through JOY-ALZ following approval.

Blood samples

MDS

There is no MDS requirement for new blood sample collections beyond that needed for clinical indications.

EDS

Additional blood samples—including plasma, serum, and DNA—will be collected for research purposes based on separate informed consent. Samples will be obtained at both baseline and week 78 and stored in a centralized biobank according to standardized procedures. APOE genotyping results will be integrated into the dataset if previously available in clinical records, or acquired anew with consent specifically for genetic analysis. Blood-based Aβ42 oligomerization tendency values will be retrieved from existing laboratory data when available.[20]

New AD treatments and safety monitoring

MDS

The use of DMTs, including monoclonal antibodies targeting Aβ, will be closely monitored throughout the observation period via clinical records. At each visit, comprehensive information on DMT administration—such as dosage, route, frequency, adherence, and discontinuation—will be extracted from routine documentation. AEs, serious AEs, and ARIA events related to these treatments will be systematically documented based on data recorded in routine clinical care.

EDS

No additional items concerning AD treatments or safety monitoring will be included in the EDS.

Data management plan

The JOY-ALZ platform will be developed to align with the Findable, Accessible, Interoperable, and Reusable data principles, facilitating optimal data use for future clinical, translational, and policy-oriented research.[34] The system architecture will support real-time monitoring, automated quality assurance, secure data governance, and integration with national and international databases.

All clinical, imaging, and biomarker data will be entered into a centralized, role-based EDC system by trained study personnel. Immediately upon entry, the system's integrated data validation system will conduct logic and consistency checks to detect discrepancies, outliers, or missing values. Designated statisticians will perform extensive data audits twice annually, generating descriptive tables, assessing variable distributions, and identifying anomalies. Where relevant, automated correction algorithms will be utilized. Any unresolved queries will be flagged within the EDC system for further resolution.

To maintain longitudinal consistency and comparability across study sites, a predefined Data Quality Index (DQI) will be implemented for clinical, laboratory, and neuroimaging data.

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This DQI framework, uniquely customized for JOY-ALZ and harmonized with Korea's national brain health research standards, supports continuous evaluation and benchmarking of data quality. Modifications to DQI parameters and associated quality control criteria will be subject to version control and meticulous logging to uphold transparency and enable reproducibility.

Data standardization remains a critical objective for the platform. Laboratory values and clinical measurements will be mapped wherever possible to internationally accepted terminology sets such as Logical Observation Identifiers Names and Codes.[35] This method will support semantic interoperability and allow integration with external databases, including the National Health Insurance Service (NHIS), Health Insurance Review and Assessment Service (HIRA), and Korea Disease Control and Prevention Agency (KDCA), as well as international consortia such as Alzheimer's Network for Treatment and Diagnostics (ALZ-NET) and the Global Alzheimer's Association Interactive Network. For data elements not directly mappable to international standards, comprehensive metadata will be provided with variable definitions, units, and formats to support both data interpretation and cross-study comparison.

All data, including imaging and biospecimen metadata, will be securely archived and subject to stringent de-identification procedures in accordance with the Personal Information Pseudonym Processing Guidelines issued by the Personal Information Protection Committee of Korea and the Health and Medical Data Utilization Guidelines from the Ministry of Health and Welfare. Identifiable information will be segregated from analytical datasets, with access to the data system regulated by rigorous access control protocols and audit-logging. Oversight responsibilities will rest with the JOY-ALZ Data Oversight Committee in conjunction with the Institutional Review Boards (IRBs) of each participating site.

Statistical analysis

Continuous variables will be described as mean ± SD and compared using independent *t*-tests or Wilcoxon rank-sum tests, based on their distribution. Categorical variables will be reported as frequencies and percentages, and group comparisons will use the χ^2 test or Fisher's exact test, depending on suitability. Patterns of missing data will be evaluated to classify them as Missing Completely At Random, Missing At Random (MAR), or Missing Not At Random. When data are considered MAR, multiple imputation via chained equations will be implemented. For continuous variables, predictive mean matching will be applied, fitting a linear regression model to the observed cases and using predicted values to identify similar observed values; an observed value is then randomly selected for imputation. Binary variables will be handled using logistic regression, while multinomial logistic regression will be utilized for categorical variables with more than 2 categories.

The cumulative incidence of clinical events will be estimated using the Kaplan–Meier method, and groups will be compared with log-rank tests.[36] Time-to-event outcomes will be analyzed with Cox proportional hazards models,[37] and results will be reported as hazard ratios with 95% confidence intervals. For analyses that emulate target trials, propensity score-based approaches such as propensity score matching and inverse probability weighting will be used to adjust for baseline confounding. Propensity scores will be calculated using logistic regression models incorporating all covariates available at the index date.[38] Additional outcomes, including quality of life, will be assessed using linear mixed-effects models, which will include fixed effects for visit time points and visit-by-group interaction terms, with random intercepts accounting for baseline between-subject

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variability. Cost-effectiveness analyses will conform to the Consolidated Health Economic Evaluation Reporting Standards.[39] Results will be quantified in terms of quality-adjusted life years (QALYs),[40] combining survival and health-related quality of life according to utility weights. The cost-effectiveness of DMTs will be determined by incremental cost-effectiveness ratios, calculated as the difference in total costs divided by the difference in cumulative QALYs between treatment groups.

Ethics statement

This study will adhere to the International Conference on Harmonization Good Clinical Practice Guideline. This study has received Institutional Review Board (IRB) approval from 40 institutions, including Inha University Hospital (IRB No. 2025-01-005), and IRB review is planned at 6 other institutions. Participating institutions and IRB approval numbers are listed in **Supplementary Table 1**. Any protocol modifications will be reported to and must receive approval from the corresponding institutional IRB. Written informed consent, along with supplementary consent for the collection and use of biological specimens, will be obtained from all potential participants by a designated study physician before study enrollment. The confidentiality of participants' names and personal information will be maintained, with identification limited to numbers assigned during the study.

The JOY-ALZ registry will be accessible to all participating investigators to promote transparency and foster collaborative research. From the third year onward, anonymized data may be provided to external investigators, contingent upon submission of a research proposal, evaluation and approval by the JOY-ALZ data access committee, legal verification by IRBs, and execution of a formal data use agreement. Furthermore, the study incorporates comparative analyses and data sharing with international registries to enable cross-cohort validation and improve the applicability of findings globally. The registry may also serve regulatory objectives; specifically, select JOY-ALZ data will support the post-marketing commitment study (PMS) of lecanemab, contingent upon approval by appropriate regulatory authorities (**Supplementary Data 1**). Only data from participants receiving lecanemab, and who have provided distinct written informed consent for their data's use in the PMS, will be included in the PMS analysis. Study findings will be published in peer-reviewed journals, presented at national and international conferences, and shared on public platforms to optimize scientific contribution and societal impact.

DISCUSSION

The JOY-ALZ registry represents the first nationwide, prospective, real-world evidence platform dedicated to AD treatment and diagnostics in Korea. By enrolling participants spanning the entire AD continuum—from CU individuals at risk to those with dementia—and by tracking them for up to ten years, JOY-ALZ addresses the gap between the relatively short, controlled settings of RCTs and the variability of clinical practice. The registry strengthens evidence generation in 4 key ways. First, it encompasses the broad clinical heterogeneity typically excluded from RCTs, such as very old adults, individuals with multiple comorbidities, and patients managed in community hospitals. For example, the Appropriate Use Recommendations for lecanemab by the Korean Dementia Association advise prioritizing treatment for patients with MCI due to AD or mild AD dementia, and recommend caution for those with findings like multiple microbleedings or those on concomitant anticoagulant therapy.[12] In clinical settings, however, treatment may be extended beyond

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these recommended indications, and JOY-ALZ has been structured to capture these real-world practices through systematic documentation. This demonstrates how the registry's wider inclusion criteria account for clinical diversity not typically represented in RCTs or guideline-based cohorts, highlighting both the limitation in strict comparability and the unique strength of JOY-ALZ as a RWD resource. Second, its adaptive, tiered approach to data collection mirrors how diagnostics and DMTs are utilized in practice, permitting pragmatic evaluation of effectiveness, safety, adherence, and cost. Third, by deterministically linking to national health-insurance and mortality databases, it provides a long-term, population-level view unavailable in RCTs. Fourth, JOY-ALZ uniquely incorporates diverse populations seen in practice, including non-AD dementia control groups, AD patients not treated with lecanemab, and individuals with mixed pathology. JOY-ALZ enrolls individuals with clinically suspected AD who are scheduled for AD biomarker assessment to evaluate lecanemab treatment eligibility. If amyloid pathology is not found, the final diagnosis may be vascular dementia or frontotemporal dementia, which supports the inclusion of such data. Patients without AD pathology are categorized as non-AD dementia and may serve as a control group. If AD pathology coexists with other brain diseases, the patient is classified as having mixed pathology or atypical AD.

A notable strength of the JOY-ALZ platform is its design, which is prospective, longitudinal, and multi-modal. The registry combines structured clinical evaluations with MRI, amyloid PET, fluid biomarkers, genomic information, and patient-reported outcomes (e.g., EQ-5D). Aligning the timing of data collection with routine clinical visits reduces participant burden while preserving temporal accuracy. Real-time data validation procedures incorporated in the EDC system, along with a prespecified DQI, contribute to maintaining internal validity as the registry expands. Additionally, optional EDS such as research-only components, including collection of blood specimens, provide adaptability for sites with advanced capabilities and support long-term sustainability of the platform. The centralized biobank, applying standardized pre-analytical methods, serves as a reliable resource for pharmacogenomic research and facilitates the investigation of ARIA predictors.

JOY-ALZ was intentionally designed to address interoperability, scalability, and data harmonization. Standardized assessments, uniform imaging protocols, and consistent biospecimen collection procedures are used across more than 40 participating sites. The registry accommodates both a core set of data and optional extensions based on the resources of each site, allowing for participation at varying levels of complexity. In addition, linkage with national sources such as the NHIS, HIRA, and KDCA will allow for extended follow-up beyond the planned study duration and supports thorough assessment of long-term outcomes, patterns of healthcare utilization, and evaluations of cost-effectiveness.

The inclusive structure of the registry is intended to mitigate disparities in access to diagnostics and treatment. By engaging a spectrum of healthcare institutions, including both high-level academic hospitals and regional general hospitals, JOY-ALZ ensures representation of patients from a wide range of demographic and geographic groups. This diversity strengthens external validity and enables analyses focused on equity in the Korean setting, for example by examining whether factors such as insurance coverage or region influence access to biomarker assessment or initiation of DMT.

Consistent with international trends, JOY-ALZ incorporates key structural and methodological elements found in prominent real-world AD registries, such as

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ALZ-NET[41] and International Registry for Alzheimer's Disease and Other Dementias (InRAD).[42] Mirroring these programs, JOY-ALZ places emphasis on systematic longitudinal RWD collection to evaluate the safety, effectiveness, and clinical application of novel therapeutics and diagnostics. The registry employs a modular, tiered dataset design (MDS and EDS), facilitates biomarker integration, and upholds stringent data standardization to promote interoperability. Nevertheless, JOY-ALZ is distinguished by its comprehensive integration with Korea's healthcare infrastructure and its tailored adaptation to local clinical practices. ALZ-NET, by contrast, is directly integrated with regulatory and payer structures in the USA, with a primary focus on assessing the safety and effectiveness of recently approved treatments and connectivity with Medicare and electronic medical records. InRAD, by comparison, operates as a globally adaptable platform emphasizing cross-country interoperability and milestone-driven tracking of AD trajectories, focusing on disease progression and healthcare access rather than drug-specific outcomes. JOY-ALZ demonstrates several unique characteristics. It utilizes culturally validated neuropsychological measures and is structured to connect with Korea's NHIS and mortality databases, supporting robust population-based research. Its inclusive criteria for participants, which encompass both DMT users and non-users, allow for comprehensive analysis of diagnostic pathways and future innovations within the AD spectrum. Additionally, with defined biannual and annual follow-up and a projected 10-year observation period, JOY-ALZ is uniquely placed to generate high-quality, East Asian-specific real-world evidence for the international AD research field.

The U.S. Food and Drug Administration (FDA) has recently approved the Lumipulse G p-tau217/Aβ42 plasma ratio[43] and the Elecsys plasma p-tau181 assay to support the diagnosis of AD. Upon approval of these assays by the MFDS in Korea, JOY-ALZ will collect real-world clinical data to assess their diagnostic value. In addition, as new AD therapeutics attain future MFDS approval, JOY-ALZ will also facilitate RWD collection to monitor their longterm efficacy, safety, and cost-effectiveness. The FDA has also recently authorized a subcutaneous formulation of lecanemab for use as an at-home autoinjector in the maintenance treatment of early AD. Should the MFDS authorize the subcutaneous lecanemab formulation, JOY-ALZ will similarly gather real-world clinical data to evaluate its longterm efficacy, safety, and cost-effectiveness.

While the JOY-ALZ registry is structured to comprehensively capture RWD across the AD continuum, several limitations should be considered. First, consistent with other observational registry studies, the risk of residual confounding and selection bias persists, despite the application of statistical adjustment methods such as propensity score analysis and inverse probability weighting. Second, differences in site-level resources and infrastructure may result in variable completeness and quality of data, especially for optional modules like advanced neuroimaging or biomarker testing. Third, variability in real-world diagnostic practices—including disparities in biomarker availability, clinician experience, and institutional protocols—may affect diagnostic classification and treatment approaches, introducing potential site-level biases. Fourth, missing data represent a persistent challenge in longitudinal registry studies. Even though the JOY-ALZ platform utilizes real-time data validation and structured imputation, attrition or logistical issues may still result in data loss over time. Fifth, lecanemab is not currently covered by NHIS in Korea, which restricts access and typically confines treatment to major urban centers; this may impact the demographic and clinical characteristics of JOY-ALZ participants. Sixth, there is currently no institutional participation from Chungcheongbuk-do in the JOY-ALZ, highlighting a need

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for greater involvement from this province to achieve nationwide representation. Currently, lecanemab is prescribed at 85 hospitals, and approximately 54% of these have joined the JOY-ALZ. Efforts will be made to further expand recruitment of institutions across more regions. Finally, although the registry is intended to facilitate broad national representation, its applicability to populations outside Korea may be constrained by distinct healthcare policies and cultural considerations relevant to dementia care.

The JOY-ALZ registry offers a nationally integrated, future-oriented platform for the acquisition of high-quality RWD regarding AD diagnosis, therapeutic interventions, and patient outcomes in Korea. By systematically collecting clinical, imaging, biomarker, genomic, and safety data from a broad spectrum of healthcare environments, it facilitates a thorough assessment of DMTs in actual clinical settings. Constructed with a modular, scalable framework and culturally tailored assessment tools, JOY-ALZ accurately represents the context of dementia care in Korea and enables large-scale analyses by linking with national health databases. Notably, its adherence to international standards and alignment with global initiatives such as ALZ-NET and InRAD significantly strengthen opportunities for international comparisons and collaborative research. With Korea experiencing an increasing dementia prevalence, JOY-ALZ is well positioned to advance precision medicine, inform health policy, and foster multicenter research to improve Alzheimer's care both nationally and internationally.

SUPPLEMENTARY MATERIALS

Supplementary Data 1

Data submitted for the post-marketing commitment study, covering 2025 through 2030

Supplementary Table 1

IRB approval number for each institution

REFERENCES

1. Kamatham PT, Shukla R, Khatri DK, Vora LK. Pathogenesis, diagnostics, and therapeutics for Alzheimer's disease: breaking the memory barrier. Ageing Res Rev 2024;101:102481. PUBMED | CROSSREF
2. Long JM, Holtzman DM. Alzheimer disease: an update on pathobiology and treatment strategies. Cell 2019;179:312-339. PUBMED | CROSSREF
3. Dickerson BC, Bakkour A, Salat DH, Feczko E, Pacheco J, Greve DN, et al. The cortical signature of Alzheimer's disease: regionally specific cortical thinning relates to symptom severity in very mild to mild AD dementia and is detectable in asymptomatic amyloid-positive individuals. Cereb Cortex 2009;19:497-510. PUBMED | CROSSREF
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. PUBMED | CROSSREF
5. 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;330:512-527. PUBMED | CROSSREF
6. Rissman RA, Langford O, Raman R, Donohue MC, Abdel-Latif S, Meyer MR, et al. Plasma Aβ42/Aβ40 and phospho-tau217 concentration ratios increase the accuracy of amyloid PET classification in preclinical Alzheimer's disease. Alzheimers Dement 2024;20:1214-1224. PUBMED | CROSSREF
7. Ashton NJ, Janelidze S, Mattsson-Carlgren N, Binette AP, Strandberg O, Brum WS, et al. Differential roles of Aβ42/40, p-tau231 and p-tau217 for Alzheimer's trial selection and disease monitoring. Nat Med 2022;28:2555-2562. PUBMED | CROSSREF

8. Klunk WE, Koeppe RA, Price JC, Benzinger TL, Devous MD Sr, Jagust WJ, et al. The centiloid project: standardizing quantitative amyloid plaque estimation by PET. Alzheimers Dement 2015;11:1-15.e1. PUBMED | CROSSREF
9. Collij LE, Bollack A, La Joie R, Shekari M, Bullich S, Roé-Vellvé N, et al. Centiloid recommendations for clinical context-of-use from the AMYPAD consortium. Alzheimers Dement 2024;20:9037-9048. PUBMED | CROSSREF
10. Öhman F, Hassenstab J, Berron D, Schöll M, Papp KV. Current advances in digital cognitive assessment for preclinical Alzheimer's disease. Alzheimers Dement (Amst) 2021;13:e12217. PUBMED | CROSSREF
11. Staffaroni AM, Tsoy E, Taylor J, Boxer AL, Possin KL. Digital cognitive assessments for dementia: digital assessments may enhance the efficiency of evaluations in neurology and other clinics. Pract Neurol (Fort Wash Pa) 2020;2020:24-45. PUBMED
12. Park KH, Kim GH, Kim CH, Koh SH, Moon SY, Park YH, et al. Lecanemab: Appropriate Use Recommendations by Korean Dementia Association. Dement Neurocogn Disord 2024;23:165-187. PUBMED | CROSSREF
13. Chen C, Katayama S, Lee JH, Lee JY, Nakagawa M, Torii K, et al. Clarity AD: asian regional analysis of a phase III trial of lecanemab in early Alzheimer's disease. J Prev Alzheimers Dis 2025;12:100160. PUBMED | CROSSREF
14. Albert MS, DeKosky ST, Dickson D, Dubois B, Feldman HH, Fox NC, et al. The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement 2011;7:270-279. PUBMED | CROSSREF
15. Ryu HJ, Yang DW. The Seoul Neuropsychological Screening Battery (SNSB) for comprehensive neuropsychological assessment. Dement Neurocogn Disord 2023;22:1-15. PUBMED | CROSSREF
16. Jessen F, Amariglio RE, van Boxtel M, Breteler M, Ceccaldi M, Chételat G, et al. A conceptual framework for research on subjective cognitive decline in preclinical Alzheimer's disease. Alzheimers Dement 2014;10:844-852. PUBMED | CROSSREF
17. Petersen RC, Smith GE, Waring SC, Ivnik RJ, Tangalos EG, Kokmen E. Mild cognitive impairment: clinical characterization and outcome. Arch Neurol 1999;56:303-308. PUBMED | CROSSREF
18. McKhann GM, Knopman DS, Chertkow H, Hyman BT, Jack CR Jr, Kawas CH, et al. The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement 2011;7:263-269. PUBMED | CROSSREF
19. Wang MJ, Yi S, Han JY, Park SY, Jang JW, Chun IK, et al. Oligomeric forms of amyloid-β protein in plasma as a potential blood-based biomarker for Alzheimer's disease. Alzheimers Res Ther 2017;9:98. PUBMED | CROSSREF
20. Oh J, Yang YJ, Kim B, Heon KJ. Validity and reliability of Korean Version of International Physical Activity Questionnaire (IPAQ) short form. Korean J Fam Med 2007;28:532-541.
21. Lim YS, Lee JS, Hwang JY, Kim KN, Hwang HJ, Kwon S, et al. Revision of Nutrition Quotient for Elderly in assessment of dietary quality and behavior. J Nutr Health 2022;55:155. CROSSREF
22. Song M, Jahng S, Kim S, Kang Y. A normative study of the full version of story memory in the Korean-Mini Mental State Examination, 2nd edition: expanded version (K-MMSE-2: EV). Dement Neurocogn Disord 2020;19:161-169. PUBMED | CROSSREF
23. Kang Y, Park J, Yu KH, Lee BCA. Reliability, Validity, and Normative Study of the Korean-Montreal Cognitive Assessment (K-MoCA) as an Instrument for Screening of Vascular Cognitive Impairment (VCI). Kor J Clin Psychol 2009;28:549-562. CROSSREF
24. Morris JC. The Clinical Dementia Rating (CDR): current version and scoring rules. Neurology 1993;43:2412-2414. PUBMED | CROSSREF
25. Pfeffer RI, Kurosaki TT, Harrah CH Jr, Chance JM, Filos S. Measurement of functional activities in older adults in the community. J Gerontol 1982;37:323-329. PUBMED | CROSSREF
26. Galvin JE, Roe CM, Powlishta KK, Coats MA, Muich SJ, Grant E, et al. The AD8: a brief informant interview to detect dementia. Neurology 2005;65:559-564. PUBMED | CROSSREF
27. Kang SJ, Choi SH, Lee BH, Jeong Y, Hahm DS, Han IW, et al. Caregiver-Administered Neuropsychiatric Inventory (CGA-NPI). J Geriatr Psychiatry Neurol 2004;17:32-35. PUBMED | CROSSREF
28. Devlin NJ, Brooks R. EQ-5D and the EuroQol group: past, present and future. Appl Health Econ Health Policy 2017;15:127-137. PUBMED | CROSSREF
29. Ku HM, Kim JH, Kwon EJ, Kim SH, Lee HS, Koh HJ, et al. A study on the reliability and validity of Seoul-Instrumental Activities of Daily Living(S-IADL). J Korean Neuropsychiatr Assoc 2004;43:189-199.

30. Chin J, Park J, Yang SJ, Yeom J, Ahn Y, Baek MJ, et al. Re-standardization of the Korean-Instrumental Activities of Daily Living (K-IADL): clinical usefulness for various neurodegenerative diseases. Dement Neurocogn Disord 2018;17:11-22. PUBMED | CROSSREF
31. Lee JH, Lee KU, Lee DY, Kim KW, Jhoo JH, Kim JH, et al. Development of the Korean version of the Consortium to Establish a Registry for Alzheimer's Disease assessment packet (CERAD-K): clinical and neuropsychological assessment batteries. J Gerontol B Psychol Sci Soc 2002;57:P47-P53. PUBMED | CROSSREF
32. Choi SH, Shim YS, Ryu SH, Ryu HJ, Lee DW, Lee JY, et al. Validation of the Literacy Independent Cognitive Assessment. Int Psychogeriatr 2011;23:593-601. PUBMED | CROSSREF
33. Bae JN, Cho MJ. Development of the Korean version of the Geriatric Depression Scale and its short form among elderly psychiatric patients. J Psychosom Res 2004;57:297-305. PUBMED | CROSSREF
34. Wilkinson MD, Dumontier M, Aalbersberg IJ, Appleton G, Axton M, Baak A, et al. The FAIR guiding principles for scientific data management and stewardship. Sci Data 2016;3:160018. PUBMED | CROSSREF
35. Khan AN, Griffith SP, Moore C, Russell D, Rosario AC Jr, Bertolli J. Standardizing laboratory data by mapping to LOINC. J Am Med Inform Assoc 2006;13:353-355. PUBMED | CROSSREF
36. Goel MK, Khanna P, Kishore J. Understanding survival analysis: Kaplan-Meier estimate. Int J Ayurveda Res 2010;1:274-278. PUBMED | CROSSREF
37. Bender R, Augustin T, Blettner M. Generating survival times to simulate Cox proportional hazards models. Stat Med 2005;24:1713-1723. PUBMED | CROSSREF
38. Garrido MM, Kelley AS, Paris J, Roza K, Meier DE, Morrison RS, et al. Methods for constructing and assessing propensity scores. Health Serv Res 2014;49:1701-1720. PUBMED | CROSSREF
39. Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, et al. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement. Int J Technol Assess Health Care 2013;29:117-122. PUBMED | CROSSREF
40. Torrance GW, Feeny D. Utilities and quality-adjusted life years. Int J Technol Assess Health Care 1989;5:559-575. PUBMED | CROSSREF
41. Alzheimer's Association launches ALZ-NET: a long-term data collection and sharing network for new treatments. Alzheimers Dement 2022;18:1694-1695. PUBMED | CROSSREF
42. Perneczky R, Darby D, Frisoni GB, Hyde R, Iwatsubo T, Mummery CJ, et al. Real-world datasets for the International Registry for Alzheimer's Disease and Other Dementias (InRAD) and other registries: an international consensus. J Prev Alzheimers Dis 2025;12:100096. PUBMED | CROSSREF
43. Hu S, Yu H, Gao J. The pTau217/$A\beta_{1-42}$ plasma ratio: The first FDA-cleared blood biomarker test for diagnosis of Alzheimer's disease. Drug Discov Ther 2025;19:208-209. PUBMED | CROSSREF