Imaging Dementia—Evidence for Amyloid Scanning (IDEAS) Study:
A Coverage with Evidence Development Longitudinal Cohort Study

Directed by: Alzheimer's Association
Sponsored by: American College of Radiology
Managed by: American College of Radiology Imaging Network
Advised by: Centers for Medicare & Medicaid Services (CMS)

Protocol Amendment 1
Dated September 23, 2016

Summary of Changes

Section	**Description of Change**
Throughout	Minor typographical corrections
Cover page	• E-mail addresses updated for Barry A. Siegel, M.D. and Maria C. Carrillo, Ph.D. • Added Version Date (September 19, 2016) for Amendment 1
Table of Contents	Updated to reflect new header titles and page numbers
List of Abbreviations and Acronyms	Updated to include European Association of Nuclear Medicine, Physician Enrollment Chain and Ownership System, Society of Nuclear Medicine and Molecular Imaging
Schema	Schema replaced to clarify visit timepoints and data submission requirements
Study Objectives/Specific Aims	• Aim 1 revised to clarify participants for whom clinical data will be collected ("Clinical Data to address Aim 1 will be collected for the first 11,050 participants *completing both the amyloid PET scan and the Post-PET visit.*"). • Aim 2 revised to clarify source of claims data ("CMS Claims Data to address Aim 2 will be collected from all participants registered to the longitudinal study cohort [*for whom Medicare claims are available*] and from concurrent controls matched according to a validated algorithm.").
Eligibility	Eligibility criteria clarified to address requirement that Medicare must be a participant's primary health insurance: "Participants must be Medicare beneficiaries *with Medicare as their primary health insurance* and be referred by qualified dementia specialists who meet AUC for amyloid PET."
2.0	• Aim 1 revised to clarify participants for whom clinical data will be collected ("Clinical Data to address Aim 1 will be collected for the first 11,050 participants *completing both the amyloid PET scan and the Post-PET visit.*"). • Second paragraph clarifies that Medicare must be a participant's primary health insurance: "Analyses in Aim 2 will be restricted to participants enrolled in fee-for-service (FFS) Medicare *as their primary*

	insurance."
2.2.2	Added the following Secondary Aims: • Estimate and compare 12 month mortality rates in the amyloid PET known group versus the amyloid PET naïve control group. • Estimate and compare the 12 month rate of conversion from MCI to Alzheimer's disease and other dementia diagnoses in amyloid PET known group vs the amyloid PET naïve group. • Estimate the rate of changes in the use of Alzheimer's disease-specific medications (cholinesterase inhibitors and memantine) (pre-scan versus post-scan) in the subset of patients in the cohort with available Medicare Part D claims.
4.1	• Clarified criterion 4.1.2: "Medicare beneficiary *with Medicare as primary insurance"* • Revised criterion 4.1.4: Cognitive complaint ~~verified by~~ with objectively confirmed ~~cognitive~~ impairment
4.3	• Added the following sentence: "Clinicians who are board certified in other specialties but otherwise appear to meet the AUC definition of a dementia specialist may apply to the IDEAS study team for an exemption by submitting their CV and a letter of justification. Dementia specialists must be enrolled in the Medicare Patient Enrollment Chain and Ownership System (PECOS) to provide services to Medicare patients, even if they have opted to be non-participating physicians." • Added "practice" to clarify the following sentence: "Each participating dementia specialist *practice* will be included in a contractual agreement with the ACR" • Added the following sentence: "To be eligible to participate in the study the dementia specialist must complete the IDEAS "Clinical Applications and Best Practices" training video (link)."
4.4	• Added language to clarify PET Facility eligibility: "An eligible PET facility will have experience in PET brain imaging. Participating PET facility may be (1) free standing and accredited by either the American College of Radiology (ACR), the Intersocietal Accreditation Commission (IAC) or RadSite or (2) hospital based and accredited by the Joint Commission (*or another Medicare-approved hospital-based accrediting organization*) with or without additional accreditation by ACR, IAC or RadSite." • Added the following sentence: "Radiologists/nuclear medicine physicians also must be enrolled in the Medicare Patient Enrollment Chain and Ownership System (PECOS) to provide services to Medicare patients, even if they have opted to be non-participating physicians."
4.5	• Added the following sentence under "Screening and Responsibilities": "In order to ensure a diverse patient population in the study cohort, and in order to avoid potential bias related to disproportionate recruitment by a single dementia specialist, the maximum enrollment by any

	individual dementia specialist will be capped (refer to IDEAS-Study.org website for detail.)." • Added the following two sentences to the third paragraph under "Screening and Responsibilities": "Re-evaluation of a participant is not necessary if a participant signs the informed consent within 3 months of a formal evaluation. However, the positives and negatives of learning amyloid status, including potential psychological impact, should be discussed again at the time of consent if a formal re-evaluation is not performed." • Clarified the requirement for disclosing PET results in the third paragraph under "Screening and Responsibilities": "The dementia specialist will be responsible for completing the pre-PET CRF at the time of PET referral after formulation of the patient's intended management plan prior to PET, *for communicating the results of the amyloid PET scan to the patient after the scan is performed,* and for completing the post-PET CRF." • Clarified the timing and requirements of post-PET visits in the third paragraph under "Screening and Responsibilities": "The post-PET CRF should be completed at about 90 days (window: 75-105 days post PET) and submitted no later than 15 days following the post-PET clinical visit. At this post-PET follow-up, the actual management will be recorded in the post-PET form based on information collected during the in-person follow-up clinical visit."
5.3.1	Added link and description of amyloid PET imaging guidelines: "Participating PET facilities should follow the "Society of Nuclear Medicine and Molecular Imaging (SNMMI) Procedure Standard/EANM Practice Guideline for Amyloid PET Imaging of the Brain 1.0"
5.3.2	• Added amyloid PET disclosure language: "Amyloid PET disclosure: Disclosure of amyloid PET results to the patient and family should occur as part of clinical care, and no specific timeframe or parameters for accomplishing this are dictated in this protocol. However, best practices suggest that disclosure should be done as soon as possible after the scan results are available, based on physician and patient availability. In most cases it would not be appropriate to wait until Study Visit 3 (90 days post-PET) to disclose results. Results should be disclosed by the referring dementia specialist, and disclosure should not be delegated to non-clinical staff. In most cases it is preferred that scan results be disclosed in person, and every attempt should be made to avoid the patient receiving results directly from an electronic medical record portal. For more information about best practice recommendations for amyloid PET counseling and disclosure, please refer to the IDEAS "Clinical Applications and Best Practices" training video (http://training.alz.org/products/4035/amyloid-pet-clinical-applications-and-best-practice) and to "Development of a process to disclose amyloid imaging results to cognitively normal older adult research participants" (Harkins et al. 2015).

	As with disclosure of PET results, the referring dementia specialist should also recommend any subsequent changes in management that are clinically appropriate. There is no need to wait until the 90 day post-PET visit to make management recommendations. The goal of the 90 day case report form is to capture changes in management that have been implemented incorporating amyloid PET results."
5.4	Header revised to read: "90 Days (± 15 Days) After Amyloid PET VISIT 2 *and disclosure of PET Results*"
5.4.1	• Added language to describe procedures for disclosing PET results: "In rare instances in which the patient is not able to return for clinical follow-up within the allotted time (e.g., because of geographic distance from the dementia specialist), the post-PET visit may occur by telephone contact between the dementia specialist and the patient and family. The dementia specialist will need to document this protocol deviation in the post-PET CRF, and the IDEAS study team will contact the physician if the reason for telephone follow-up is deemed unacceptable or the frequency of telephone visits appears excessive. Under no circumstances is the dementia specialist permitted to delegate the post-PET contact (in person visit or telephone) to other staff." • Added the following sentence: "There is no need to wait until the 90-day post-PET visit to make management recommendations. The goal of the 90-day case report form is to capture changes in management that have been implemented incorporating amyloid PET results."
5.4.4	Clarified follow-up for deceased participants: "Any death also will prompt a direct call from *a member of* the study team to the dementia specialist to further ascertain the circumstances of death."
5.11	• Added column for "Disclosure of PET Results" • Added row for "Disclosure of PET results to patient by dementia specialist" • Added footnote 3: "Disclosure of the PET scan results to the patient, per standard of care, does not need to wait for the 90-day visit. The goal of the 90-day case report form is to capture changes in management that have been implemented incorporating amyloid PET results."
6.0	Conflict of interest policy revised to read: "Any IDEAS Study co-chair who has a conflict of interest with this study (such as patent ownership, royalties, or financial gain greater than the minimum allowable by ACR policy) must fully disclose the nature of the conflict of interest."
7.0	Section header revised to read "Data Access and Publication Policy" from "Publication & Data Sharing Policies".
8.4	Fourth paragraph revised to include ICD-10 code G31.84 (MCI).
8.7.5	Added sub-section for secondary objective: "Estimate and compare 12 month mortality rates in the amyloid PET known group versus the amyloid PET naïve control group."
8.7.6	Added sub-section for secondary objective: "Estimate and compare the 12

	month rate of conversion from MCI to Alzheimer's disease and other dementia diagnoses in amyloid PET known group vs the amyloid PET naïve group."
8.7.7	Added sub-section for secondary objective: "Estimate the rate of change in the use of Alzheimer's disease-specific medications (cholinesterase inhibitors and memantine) (pre-scan versus post-scan) in the subset of patients in the cohort with available Medicare Part D claims."
9.0	Added reference: "Harkins K, Sankar P, Sperling R, et al. (2015). "Development of a process to disclose amyloid imaging results to cognitively normal older adult research participants." Alzheimers Res Ther. 7(1):26."
Appendix V, Table 1	Row 1A: Clarified that 331.83 is an ICD-9 code and added code G31.84 (ICD-10); deleted ICD-9
Appendix V, Table 5	• Revised header to read "Diagnosis Codes Relevant for Matching" • Updated ICD-10 column to add ICD-10 codes • Applied formatting changes to entire table • Added the following note: "Code descriptions and code conversions between ICD9 and IC910 were derived from assistance using http://www.icd10codesearch.com/ and http://www.icd10data.com."
Appendix VIII	• Fifth paragraph: revised final sentence in paragraph to read "The ~~proposed~~ Steering Committee membership ~~will~~ *consists* of:" • Fifth paragraph, bulleted list: "ACR CEO or Designee" deleted from "Chair"; first item in the list now reads "Chair."