Imaging Dementia—Evidence For Amyloid Scanning

The IDEAS Study – PET Imaging Update

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CAMD Annual Regulatory Meeting

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ACR® American College of Radiology

alzheimer's association®

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IDEAS Study

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

- **Directed by:** Alzheimer's Association
- **Sponsored &** American College of Radiology Imaging (ACR)
  Managed by: American College of Radiology Imaging Network (ACRIN)
- **Advised by:** Centers for Medicare & Medicaid Services (CMS)
- **Tracer Agnostic: All tracers can be used**
  - florbetaben (*Neuraceq*, Piramal Imaging)
  - florbetapir (*Amyvid*, Eli Lilly and Company)
  - flutemetamol (*Vizamyl*, GE Healthcare)

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IDEAS Research Team

IDEAS Steering Committee

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Maria Carrillo, Alzheimer's Association
Constantine Gatsonis, Brown University
Bruce Hillner, Virginia Commonwealth U
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Rachel Whitmer, Kaiser Permanente

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Rosemarie Hakim, CMS
Meridith Johnson, GE Healthcare
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Study Overview

- An open-label, longitudinal cohort study that will assess the impact of brain amyloid PET imaging on patient outcomes under Coverage with Evidence Development (CED) in patients meeting Appropriate Use Criteria (AUC)[1,2]

- **The primary hypothesis** is that, in diagnostically uncertain cases, knowledge of amyloid status as determined by brain amyloid PET will lead to significant changes in patient management, and this will translate into improved medical outcomes

1. *J Nucl Med* 2013;54:476-490
2. *Alzheimers Dement* 2013:9:e1-e16

IDEAS Aim 1

- To assess the impact of brain amyloid PET imaging on the management of patients meeting Appropriate Use Criteria (AUC) at 90 days
    - Patient management plans recorded in pre and post-PET case report forms completed by the Dementia Specialist

Aim 1 Study Primary Objective

- Test whether amyloid PET imaging will lead to a ≥ 30% change between *intended* and *actual* patient management within ~90 days in a composite measure of at least one of the following:
  - AD drug therapy;
  - Other drug therapy; and
  - Counseling about safety and future planning
- The hypothesis will be tested separately for MCI and dementia.

Impact on Management in the Literature (Aim 1)

- **31%** change in AD drug therapy and **7%** change in non AD drug therapy in 229 patients (intended management)[1]
- **35%** change in cholinesterase inhibitor or memantine use in 140 patients (retrospective) [2]
- **37%** change in patient management (prospective study of 211 patients)[3]
- Prospective study of 618 patients randomly assigned to immediate or delayed (1 y) disclosure of brain amyloid PET showed **immediate disclosure lead to significantly more changes in management vs delayed**.[4]

1. Grundmann et al. *Alzheimer Dis Assoc Disord.* 2013;(1):4-15.
2. Sanchez-Juan et al. *Neurology*. 2014 Jan 21;82(3):230-8.
3. Zwan et al. Presented at AAIC, July 19, 2015.
4. Pontecorvo et al. Presented at AAIC, July 22, 2015.

IDEAS Aim 2

- To assess the impact of brain amyloid PET on hospital admissions and emergency room visits in study patients (*amyloid PET-known*) compared to matched patients not in the study (*amyloid PET-naïve*) over 12 months
    - CMS Claims Data to address Aim 2 will be collected for all study participants and from concurrent controls matched according to a validated algorithm

Aim 2 - Rationale

- Individuals with dementia at increased risk for hospitalizations & ED visits compared to those without dementia [1]
  - Annual hospitalizations: 26.7% vs. 18.7% [1]
  - Annual ED visits: 34.5% vs. 24.5% [1]
  - *Two-thirds deemed preventable (*CHF exacerbation, bacterial pneumonia, UTI) [2]
- Dementia associated with increased mortality and shorter survival after hospitalizations
- Preliminary data from Kaiser shows targeted dementia plan led to 18% reduction in ED visits and 11% reduction in hospitalizations[3]

1. Feng et al. *Health Aff.* 2014;33(4):683-690.
2. Phelan et al. *JAMA*. 2012;307(2): 165-172.
3. Whitmer RA. Unpublished data.

Overall Rationale (Aim 1 and 2)

Diagnostic clarity helps:

- Prompts physicians, individuals and their families to develop targeted strategies to manage medical co-morbidities
- Develop care plan to better protect personal safety in the setting of cognitive impairment

Increased diagnostic clarity will lead to targeted care plan, which will translate into decreased hospitalizations and ER visits

When should brain amyloid imaging be considered per the AUC?

For patients with all of the following core elements:[1,2]

1. A cognitive complaint with objectively confirmed impairment.
2. Alzheimer's disease is a possible diagnosis, but the diagnosis remains uncertain upon comprehensive evaluation by a Dementia Specialist.
3. The presence or absence of amyloid would increase certainty in the diagnosis and alter the treatment plan.

1. Johnson et al. *J Nucl Med* 2013;54:476-490
2. Johnson et al. *Alzheimers Dement* 2013:9:e1-e16

Appropriate Clinical Indications

- Patients with progressive unexplained MCI
- Patients with possible AD but unclear clinical presentation due to an atypical course or comorbid conditions

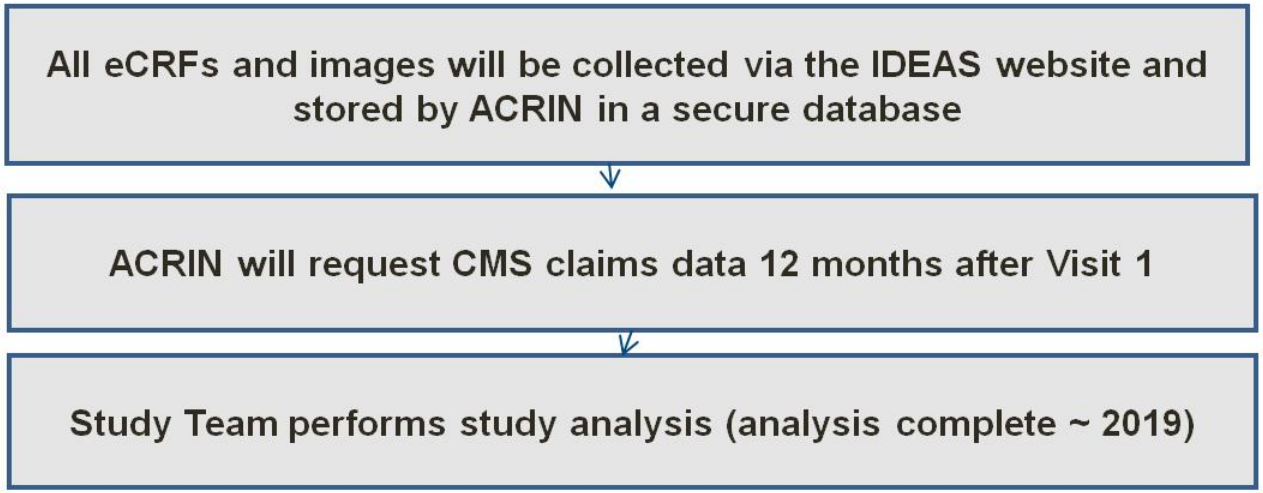
Disclaimer

- Brain amyloid PET imaging detects one of the key pathologic processes in Alzheimer's disease – **Beta-amyloid**
- Brain amyloid PET(alone) does not diagnose AD nor predict the risk or rate of progression to AD dementia
- Negative brain amyloid PET indicates few to no amyloid plaques. If there is cognitive impairment, the cause is likely to be something other than AD.

IDEAS Study Data Analysis

Goal = 18,488 study patients over **24 months**

- **Aim 1 and Aim 2 = 11,050**
- **Aim 2 = 18,488**
  - Additional 7,438 for Aim 2; 90-day visit clinical assessment not required
- **At least 400 Dementia Specialists refer 2-3 cases/month**



Clinical Site Locations

- Patients referred by Dementia Specialists must have access to a study PET Imaging facility.
- PET Imaging facility must be within 3-4 hours of an amyloid tracer supplier.
- Upon patient enrollment (January 2016), a listing of Dementia Specialists and Imaging sites will be available.

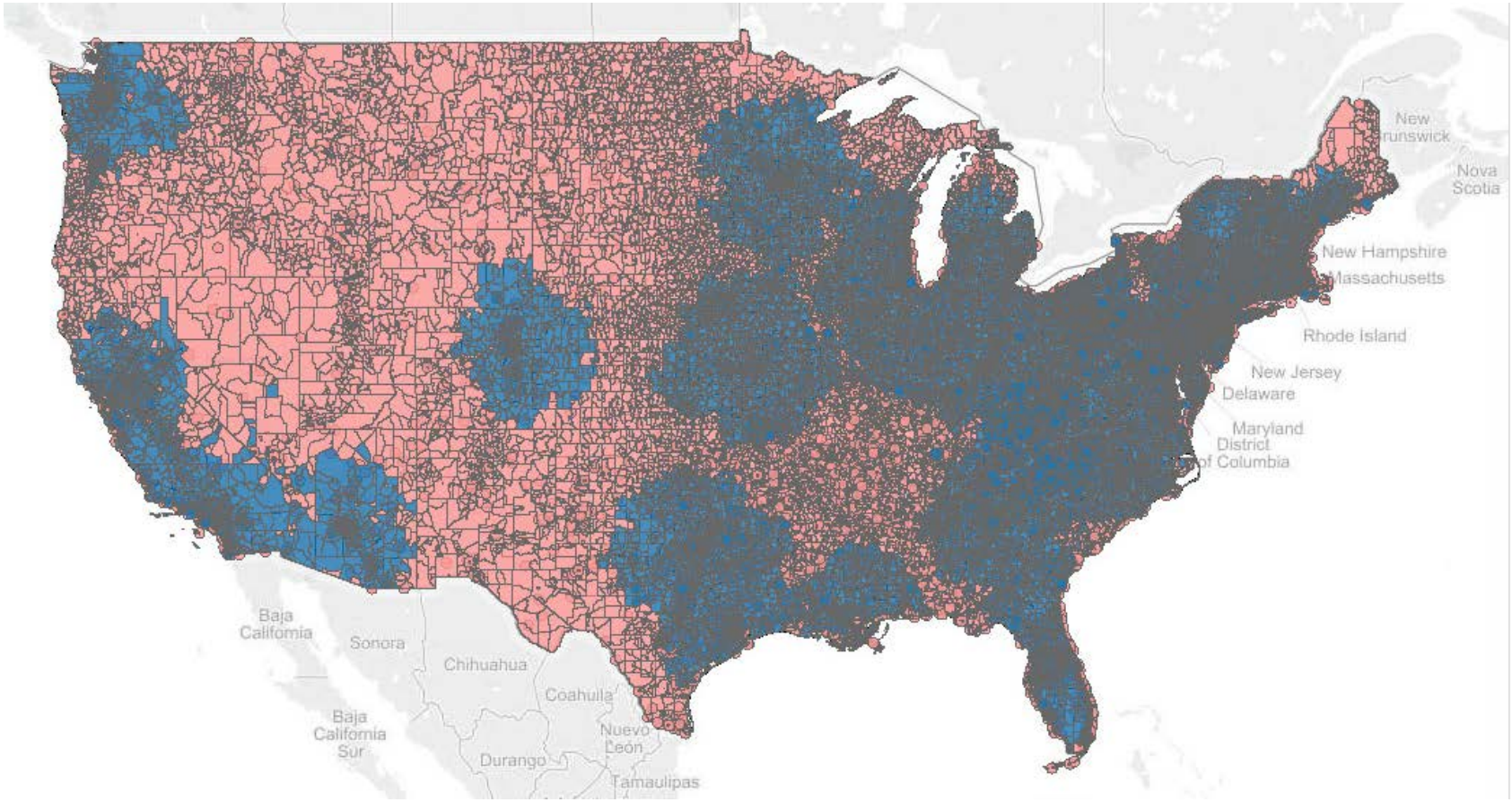
IDEAS Study: Funding Sources

Amount ($)	Funding Source
1,000,000	Alzheimer's Association
924,400	PET facility Payments
16,965,420	Amyloid Tracer Manufacturers*
~80,000,000	CMS Coverage of Amyloid Brain PET Scans

~$100 Million in Total Funding

*florbetaben (*Neuraceq*, Piramal Imaging)
florbetapir (*Amyvid*, Eli Lilly and Company)
flutemetamol (*Vizamyl*, GE Healthcare)

Where are PET amyloid agents available in USA?



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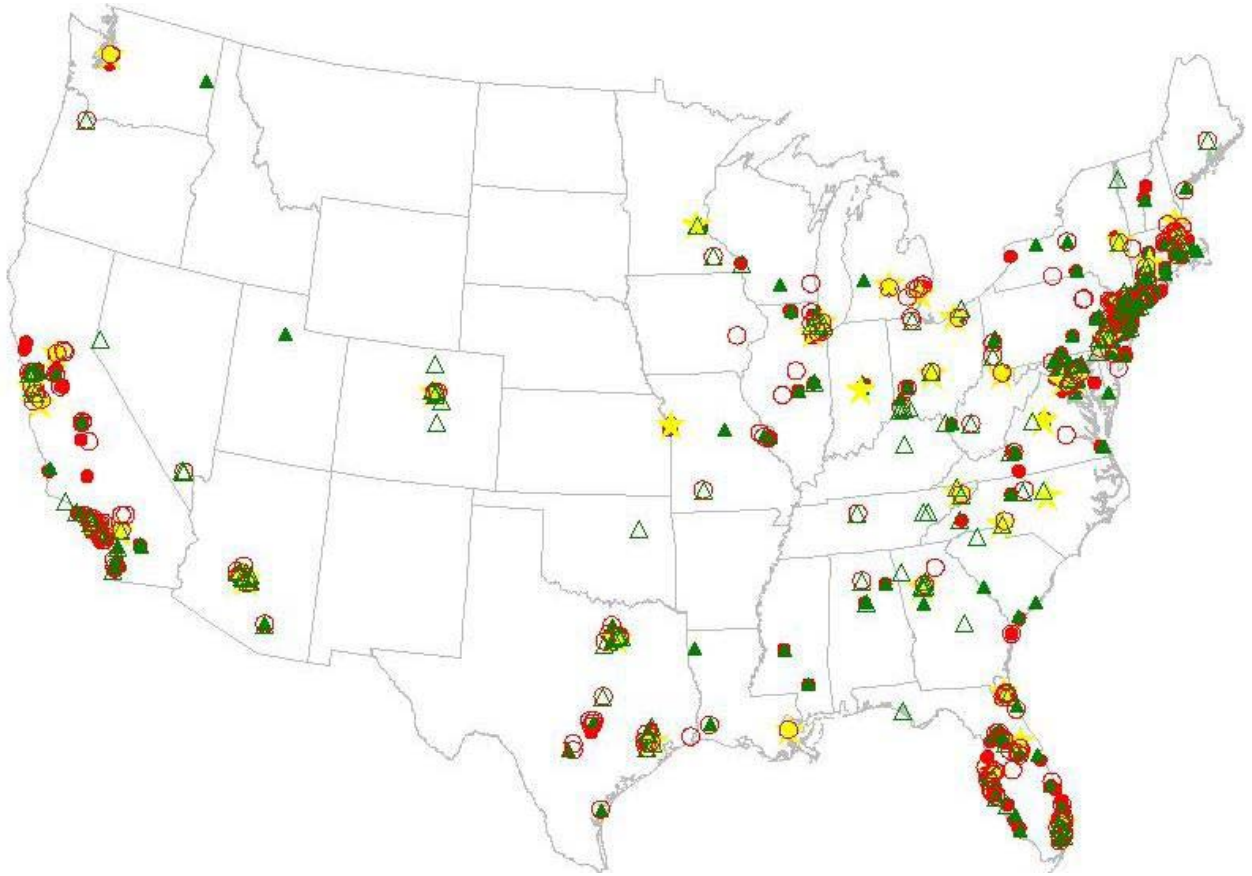
IDEAS Study Participation



● Active Clinic ○ Registered Clinic ▲ Active Facility △ Registered Facility ★ Suppliers

as of 8/31/16

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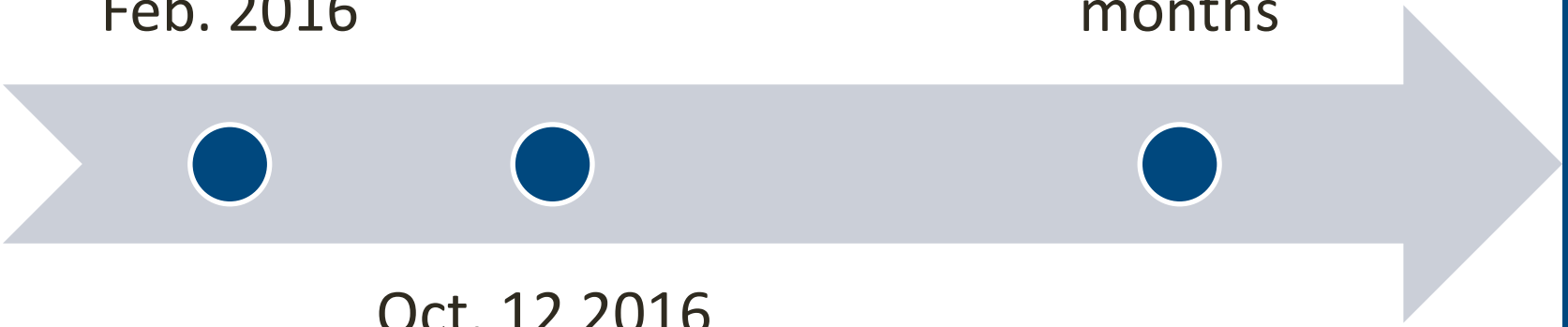
IDEAS Progress



380 Dementia clinics activated

268 PET centers activated

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For Information and Registration

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IDEAS Add-On Studies

- **Brain Health Registry (IDEAS-BHR)**
  - Aim: to use BHR online platform to collect longitudinal health, lifestyle, cognitive data and caregiver measures in IDEAS participants (**as many subjects as possible**)
  - PI: Mike Weiner (UCSF); Funder: Alzheimer's Association
- **Amyloid Neuroimaging and Genetics Initiative (ANGI)**
  - Aim: to study genetic information from IDEAS participants through collection saliva DNA from **3,333** subjects
  - PI: Andy Saykin (Indiana); Funder: Alzheimer's Association
- **Caregivers' Reactions and Experience (CARE-IDEAS)**
  - Aim: interview **3500** IDEAS patient-caregiver dyads regarding attitudes about diagnostic testing, treatment, planning, health attitudes and values
  - PI: Vince Mor (Brown); Funder: NIA

IDEAS Add-On Study: BrainHealth REGISTRY

- **Specific Aims**
  1. To collect longitudinal health, lifestyle, and cognitive data from IDEAS participants using the Brain Health Registry (BHR)
     - Self-report online questionnaires
     - Self-administered online neuropsychological tests
  2. To collect longitudinal data from study partners of IDEAS participants through a Caregiver and Study Partner (CASP) Portal within the BHR
  3. To implement the TABCAT line orientation task for IDEAS participants within the BHR
  4. To elucidate the associations between brain amyloid (Aβ) and online measures using data collected from IDEAS participants by the BHR
  5. To share all data collected by BHR with the IDEAS project (both Add-On Study specific and general BHR data)

IDEAS Add-On Study:

BrainHealth REGISTRY

- **BHR/IDEAS Sub-study tasks** (every 6 months)
  1. *Participants*
     a. BHR questionnaires
        - ECog, Med Hx, ADLs, medications, mood, lifestyle
     b. Lumos Neurocognitive Performance Test
        - memory, attention, processing speed
     c. TABCAT Line Orientation
        - visuospatial perception
  2. *Study Partners (SP)*
     a. About the participant
        - Cognitive function, ADLs
     b. About the SP
        - Caregiver burden

Amyloid Neuroimaging and Genetics Initiative (ANGI)

- The study of genetic information from IDEAS participants through the collection of saliva for DNA extraction from 3,333 subjects.
- The APOE gene is strongly associated with amyloid on PET as well as rate of amyloid accumulation over time. In addition to APOE, previous research has identified over 20 candidate genes associated with risk for or protection against AD. However, the possible role of these genes in amyloid deposition has not been well-studied.
- NCRAD will ensure DNA is obtained according to NIH sharing guidelines and will allow all ***samples and resulting data to be shared broadly.***
- **The Alzheimer's Association is currently funding the collection and storage of the samples.**

Caregivers' Reactions and Experience: Imaging Dementia - Evidence for Amyloid Scanning (CARE IDEAS) Study

Survey 3500 patients and their care partners as they traverse the diagnosis and treatment process. The purpose of the current study is to:

1. To design telephone interviews to be administered to Medicare beneficiaries and their care partners covering topics ranging from demographics, history of seeking diagnostic information about the source of their symptoms of dementia, health care decision making, advanced care planning and health care preferences;
2. Recruit 3500 patients, including oversampling minority patients, enrolled in the IDEAS study along with their care partners (spouses, children or others knowledgeable about the patient's treatment) to participate in telephone surveys;
3. To obtain consent to access longitudinal Medicare health insurance claims information as well as other relevant financial data from CARE IDEAS study patients and their care partners who are eligible for Medicare;
4. To create complete data files of patient and care partner survey responses in a form amenable for analysis.

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