DEPARTMENT OF HEALTH & HUMAN SERVICES

Agency for Healthcare Research and Quality

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Louis Jacques, MD
Director, Coverage and Analysis Group
Center for Clinical Standards and Quality
Centers for Medicare & Medicaid Services
7500 Security Blvd.
Baltimore, MD 21244

Dear Dr. Jacques,

The Agency for Healthcare Research and Quality (AHRQ) understands that the Centers for Medicare & Medicaid Services (CMS) will cover the use of positron emission tomography (PET) amyloid-beta (Aβ) imaging (one PET Aβ scan per patient) only for beneficiaries enrolled in a CMS-approved clinical research study.

Clinical study objectives must be to (1) develop better treatments or prevention strategies for AD, or, as a strategy to identify subpopulations at risk for developing AD, or (2) resolve clinically difficult differential diagnoses (e.g., frontotemporal dementia (FTD) versus AD) where the use of PET Aβ imaging appears to improve health outcomes.

Clinical studies must involve subjects from appropriate populations, be comparative, prospective and longitudinal, and use randomization and postmortem diagnosis as the endpoint where appropriate. The studies must address one or more of the following questions. For Medicare beneficiaries with cognitive impairment suspicious for AD, or who may be at risk for developing AD:

1. Do the results of PET Aβ imaging lead to improved health outcomes? Meaningful health outcomes of interest include: avoidance of futile treatment or tests; improving, or slowing the decline of, quality of life; and survival.

2. Are there specific subpopulations, patient characteristics or differential diagnoses that are predicitive of improved health outcomes in patients whose management is guided by the PET Aβ) imaging?

3. Does using PET Aβ imaging in guiding patient management, to enrich clinical trials seeking better treatments or prevention strategies for AD, by selecting patients on the basis of biological as well as clinical and epidemiological factors, lead to improved health outcomes ?

We understand that CMS is requiring and will assume an oversight role to assure that covered studies meet the following standards:

a. The principal purpose of the research study is to test whether a particular intervention potentially improves the participants' health outcomes.
b. The research study is well supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use.
c. The research study does not unjustifiably duplicate existing studies.
d. The research study design is appropriate to answer the research question being asked in the study.
e. The research study is sponsored by an organization or individual capable of executing the proposed study successfully.
f. The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects found at 45 CFR Part 46. If a study is regulated by the Food and Drug Administration (FDA), it must be in compliance with 21 CFR parts 50 and 56.
g. All aspects of the research study are conducted according to appropriate standards of scientific integrity (see http://www.icmje.org).
h. The research study has a written protocol that clearly addresses, or incorporates by reference, the standards listed here as Medicare requirements.
i. The clinical research study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Trials of all medical technologies measuring therapeutic outcomes as one of the objectives meet this standard only if the disease or condition being studied is life threatening as defined in 21 CFR § 312.81(a) and the patient has no other viable treatment options.
j. The clinical research study is registered on the ClinicalTrials.gov website by the principal sponsor/investigator prior to the enrollment of the first study subject.
k. The research study protocol specifies the method and timing of public release of all pre-specified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 24 months of the end of data collection. If a report is planned to be published in a peer reviewed journal, then that initial release may be an abstract that meets the requirements of the International Committee of Medical Journal Editors (http://www.icmje.org). However a full report of the outcomes must be made public no later than three (3) years after the end of data collection.
l. The research study protocol must explicitly discuss subpopulations affected by the treatment under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria effect enrollment of these populations, and a plan for the retention and reporting of said populations on the trial. If the inclusion and exclusion criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary.
m. The research study protocol explicitly discusses how the results are or are not expected to be generalizable to the Medicare population to infer whether Medicare patients may benefit from the intervention. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.

Consistent with section 1142 of the Social Security Act, AHRQ supports clinical research studies that CMS determines meet the above-listed standards and address the above-listed research questions.

Sincerely,

Jean R. Slutsky
Director, Center for Outcomes and Evidence