

**Written Comments to the Medicare Evidence Development & Coverage Advisory  
Committee, Centers for Medicare & Medicaid Services**

Evidentiary Characteristics for Coverage with Evidence Development (CED)

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My comments on CMS coverage with evidence development (CED) programs are from the perspective of an approved site for a specific study, “Metabolic Cerebral Imaging in Incipient Dementia: Early and Long-Term Value of Imaging Brain Metabolism (MCI-ID)”, Daniel Silverman, M.D., Ph.D., Principal Investigator. There appear to be significant variations in the design of specific CED studies, so our experience may not be applicable to all existing CED studies. On the other hand, they do represent practical issues from the point of view of a participating site and thus should inform future CED programs. These comments are an expansion of a description submitted in a letter to Louis Jacques on February 15, 2012. I hope our experience will improve the conduct of future CED programs.

We have encountered significant barriers and unexpected challenges in participating in this study. It is not surprising that many potential sites have declined to participate in the MCI-ID study and that recruitment has been poor for our project at established sites. The ultimate success of this program of course depends upon sufficient, high quality and reliable data being accumulated over a reasonable time. Without a significant commitment to this program, the burdens would easily outweigh the benefits of participating. Indeed, we have expended significant time and expense to continue this program and there has been considerable internal discussion about whether we can continue. Nevertheless, we remain committed to the successful conduct of this project.

The CED mechanism need not be so onerous. It should be sufficient to allow a limited number of providers with expertise to collect data in the course of clinical care. Expertise could be demonstrated adequately through billing records available to CMS demonstrating experience with the technology in the appropriate context (such as using FDG-PET for suspected FTD). We recommend using the approach of previous successful CED imaging studies such as National Oncology Patient Registry (NOPR) rather than a longitudinal research study. Providing relevant data could simply be a condition for reimbursement. This is an accepted approach often used by insurers for reimbursement of imaging and diagnostic procedures. Finally, imaging for cognitive deficits should be done in the context of a clinical evaluation performed by a capable provider. CMS should solely reimburse for the scan in question and review medical records retrospectively. This will allow the procedure and patient monitoring to happen solely through clinical avenues and more accurately represent clinical practice, which is the goal of CED research.

The decision to require collection of data in the context of a clinical research study accounts for much of the difficulty. There are unreimbursed expenses to the site related to meeting regulatory requirements of a research study:

1. A study coordinator responsible for study procedures and documentation.
2. IRB application, reports, amendments and renewals
3. Radiation safety applications, reports and renewals
4. Now that FDG-PET is covered under IND and NDA applications, reports to FDA
5. Data monitoring and safety plans
6. Completion of consent forms, revision of consent forms and documentation of consent
7. Developing, updating, and maintaining case report forms and study binders

Because this project was conducted as a research study, study binders, managed by the study coordinator, were required. However, the study binders are redundant because, except for the blinded neuropsychological battery and nuclear medicine reports, the necessary data are already available and could be extracted from the patient's medical records.

In addition to the extensive requirements of a research study, we encountered many problems specific to this project that could have been avoided with adequate peer-review and guidance from CMS. The outcomes that presumably were of interest to CMS, such as quality of care and costs, were not well defined and/or available to investigators. We understood that CMS would be responsible for making final coverage / non-coverage decisions based upon their own analysis billing and coding records only available to them. Consequently, it

was impossible to focus on achieving project goals, or to know how to best respond to protocol issues that inevitably arose in the course of the study.

We found that the protocol, created at UCLA, was severely underdeveloped. This required multiple IRB amendments during the course of the study leading to site-specific alterations and therefore non-standard approaches throughout the nation. For example, visit windows were not addressed, clear study flow-charts were not created, no regulatory guidelines were recommended, no monitoring system was provided, and no query system was created for the data collection website. On top of this, communication with UCLA was difficult as the study coordinator changed 3 times and the amount of time needed from a local study coordinator was vastly underestimated. There also were difficulties with report forms that did not appear to reflect clinical decision-making or provide consistent longitudinal data collection (definitions could drift and medication names could change even though treatments were no different) and idiosyncratic entry criteria (a history of any thyroid disease was exclusionary). Ascertaining who had the right kind of Medicare coverage (part A and Part B) to qualify for the study was initially unclear and had to be worked out. Although patients with Medicare Advantage Plans are theoretically qualified for the same benefits and were being enrolled in the study, it was unclear whether or not we would be reimbursed for their PET scan. Only recently were we told that Medicare Advantage plans are not required to pay for CMS studies. Many items, such as enrollment of non-English speakers, the possibility of telephone follow-up for individuals traveling a great distance, or early withdrawal from the study were not considered in the protocol.

The neuropsychological (NP) battery was unnecessarily burdensome. Many subjects find this battery too challenging toward the end of the study due to the progressing of dementia. The 3-4 hour test is administered five times, which is taxing to the patient and does not yield any additional clinical information since these results are blinded from the physician. The NP battery is given at 6-month intervals and often interferes with standard of care (SOC) collection of cognitive measures due to scheduling conflicts and unintended practice effects with repeated measures between the study battery and SOC battery. Finally, no codes were developed in the protocol to capture a patient's cognitive inability to complete or attempt at cognitive measure leading to inaccurate data entry.

We also encountered problems with local Medicare coverage and institutional procedures. Many of these were due to this project being a hybrid of research and clinical care. Because this project had many unique aspects and did not fit in the usual institutional mode, even after we had worked out a practical solution, the problem would reappear and start again whenever there was a change in personnel in our billing department, clinic, radiology, Medicare Advantage plans or at the Medicare intermediary. This was extremely frustrating and required extensive unreimbursed effort that we had not planned for or envisioned on initiating the study.

Institutional procedures for patient scheduling did not accommodate this hybrid project easily. Visits were scheduled through our clinic, but there was concern about doing research or using clinical staff to conduct research. Because of the considerations of an active clinic, it was difficult to meet protocol requirements when the clinic received calls from the family to reschedule a visit or when there were standard of care (SOC) visits. We developed a complex system of joint clinic and study coordinator visit tracking that required much effort and redundancy.

Institutional procedures for clinical billing did not apply because this was a research project, and usual research billing procedures did not apply because there was an insurer rather than a research account. We found that institutional software could not accommodate this novel project, requiring considerable time of our study coordinator and many meetings with research and billing staffs at our institution. Our system bills primary and secondary insurance and then the balance becomes the responsibility of the patient. Since we found through trial and error that there is no way to automatically reverse the co-payment in the system, patients must contact our study coordinator to reverse the billed co-pay for project related procedures. In this patient population we encounter confusion and much difficulty with the billing details. Since the beginning of the study, occasionally patient "CED study" bills have gone to collections and SOC visits have been confused with CED study visits and patients have not paid properly. Patients have expressed extreme frustration with this process.

We have worked with our Clinical Research Compliance and Education (CRCE) Department and University billing to resolve these issues. Eventually, we were able to use the University's newly adopted uTRAC and Epic procedures for research and clinical study billing. This allowed our study coordinator to route and modify the qualifying bills with Q1 and Q0 and v70.7 modifiers to indicate Medicare approved research procedures. The details about billing procedures were not included in the original study protocol and we received no guidance about these issues directly from Medicare. As a result, our research staff and billing staff had to investigate these issues and devise solutions on our own. The research team continues to struggle with the billing for this study.

At the Medicare intermediary level there also has been a great deal of confusion requiring considerable effort on our part. CMS made the decision to cover FDG-PET in this study a population with mild cognitive impairment dx code 331.83. This was not communicated well to our intermediary Noridian and therefore not added to the local coverage determination (LCD). There also was misunderstanding on the part of Medicare Advantage plans. They routinely denied the bills we submitted without even sending them to Noridian. They did not seem to understand CED procedures or billing requirements of Noridian. Essentially, we found that they "wiped their hands" of the problems and were difficult to contact and had difficulty understanding the issues. All of this created a lot of billing difficulty and nearly 2 years to identify, address, and solve the problem. Our institution finally made the decision to quit enrolling participants with Medicare Advantage Plans. At one point we discovered almost by accident that Medicare had not reimbursed many PET scans. This tested the collaboration that we had established with nuclear medicine and they have closed our study until billing issues are resolved. Reimbursement offered at routine Medicare rates was not sufficient to justify contributions from radiology, which actually had the most to gain financially from the program. We recommend that Medicare in the future do a much better job of explaining CED procedures to private providers and intermediaries. We found that our intermediary Noridian was routinely denying reimbursement for study PET scans without looking at research modifiers or understanding that this was a qualified study, even after it had been reviewed and approved by Noridian's medical director before the study was initiated. In December 2011, our billing office met with Noridian to clarify study coding and reimbursement procedures. In February, we were told that retroactive reimbursement would occur for PET scans that had been denied for diagnostic code. At this time we are still uncertain about Medicare part B reimbursement for PET scans. In future studies, Medicare should provide billing guidance to sites and provide a national ombudsman to help resolve internal Medicare billing issues that arise during a CED study.

There also are burdens associated with a study of cognitive impairment. Unlike other CED studies, this study requires participation of a knowledgeable informant and scheduling needs to include coordination of travel and informant availability. Medicare needs to recognize with increased reimbursement the extra efforts required for data collection and coordination of studies in those with cognitive problems.

Despite the problems, I continue to believe this is a worthwhile project for our Center. As the only academic program for dementing diseases in the Intermountain West we are committed to high quality care and providing patients in our region access to the latest research advances. Furthermore as reflected in our Center's name, we are committed to increasing knowledge about the practical use of brain imaging in dementia care and providing leadership to the field. We strongly support the concept of CED and believe it is an important avenue of clinical discovery. We hope to participate in future CED programs, but hope that our experience will be used to design an improved approach.

In summary, at study initiation:

1. CMS should provide sites with funding for study coordination and regulatory management similar to other clinical trials.
2. Sites need to know who is required to pay for CED studies. Are Advantage plan participants excluded? Are only those with both Part A and Part B eligible?

3. Sites need to know the study outcomes that will be used to judge success. This will help to assure that study documentation and individual IRB requirements are consistent with study goals.
4. Whenever possible clinical medical records (often electronic) should be used for documentation. This would eliminate duplication and the need to assure that research and medical record documentation are consistent.
5. Consideration should be given to making health providers and their actions, rather than patients the subjects of the study. This would significantly decrease the burden of consent and consideration of competency, particularly when vulnerable populations are involved.
6. Studies should be at least revenue neutral. Involvement of treating physicians and their staff need to be recognized in reimbursement. Having co-pays waived recognizes and encourages subject participation, but if this is done, CMS should then cover the co-pay to the provider. As currently designed, CED studies are a money-loser, not just because of the extra costs of data collection and study management, but also for service reimbursement (already given at the promised lowest cost).
7. It is difficult to design CED studies for peer-review by other agencies and CMS. The standards and goals are different. If CMS uses other agencies, this should be in the context of a specific RFA that outlines CED needs.
8. Each CED study needs an assigned ombudsman within CMS to manage site questions and directly resolve billing issues with intermediaries and Advantage plans. The ombudsman should also make sure that Medicare intermediary concerns are addressed. Intermediaries such as Noridian are not aware of CMS CED decisions and do not have mechanisms to deal with coding requirements of CED submitted bills, or don't follow them. CMS should be in charge of making sure that all regional intermediaries are aware of CED studies. Sites should not have to work with multiple intermediaries in addition to CMS and the study coordinating center. Intermediaries and Advantage plans should not be able to re-review, revise and refuse participation.
9. CMS should conduct an information campaign about CED studies appropriate for institutions, investigators, and IRBs.
10. CMS should consider a central IRB mechanism for CED studies.

**Disclosures for Norman L. Foster, M.D.**

Within the past year, Dr. Foster has served as an advisory board member or consultant for GE Healthcare, Bristol-Myers Squibb, and Lilly USA.

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