

Guidance for the Public, Industry, and CMS Staff

National Coverage Determinations with Data Collection as a Condition of Coverage: Coverage with Evidence Development

Document Issued on July 12 , 2006

For questions about this guidance, please contact Rosemarie Hakim, PhD, at (410) 786-3934.

For questions about specific National Coverage Determinations, please see the Coverage and Analysis Group's website:<http://www.cms.hhs.gov/center/coverage.asp> or call the Coverage and Analysis Group's main number, at (410) 786-2281.

Public comments may be submitted via the Coverage website at http://www.cms.hhs.gov/InfoExchange/06_contactus.asp#TopOfPage. Please refer to this guidance document when submitting comments.

This guidance represents the Centers for Medicare & Medicaid Services' (CMS') current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind CMS or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, please contact CMS staff responsible for implementing this guidance. If you cannot identify the appropriate CMS staff, call the number listed on the title page of this guidance.

I. Purpose of this guidance document

This guidance document describes national coverage determinations (NCDs) that include, as a condition of payment, the development and capture of additional patient data to supplement standard claims data. Congress has instructed the Secretary of Health and Human Services to develop guidance documents that make available to the public the factors that CMS considers in making coverage determinations of whether an item or service is reasonable and necessary.¹ This guidance does not establish legislative rules that have the force and effect of law or that is binding on the public.

We received a large number of comments in response to the draft guidance document entitled "Coverage with Evidence Development: National Coverage Determinations Requiring Data Collection as a Condition of Coverage", which was posted on CMS' website on April 7, 2005. This revised guidance responds to concerns raised by the public about the meaning of CED and clarifies the statutory basis for CED.

The purpose of CED is to generate data on the utilization and impact of the item or service evaluated in the NCD, so that Medicare can a) document the appropriateness of use of that item or service in Medicare beneficiaries under current coverage; b) consider

future changes in coverage for the item or service; c) generate clinical information that will improve the evidence base on which providers base their recommendations to Medicare beneficiaries regarding the item or service.

In this document, we describe two arms of CED and introduce a new concept of conducting research under section 1862(a)(1)(E) to add to the existing body of medical evidence. We are again requesting public comments.

II. Background

CMS makes NCDs based on requests for national coverage from individuals or entities that identify an item or service as a potential benefit (or to prevent potential harm) to Medicare beneficiaries. The requestor may be a Medicare beneficiary, manufacturer, provider, supplier, medical professional association, health plan, or another party who requests our consideration of a particular issue for an NCD. CMS may also initiate an NCD internally.

Whether externally or internally generated, NCDs help ensure that access to advances in health technologies that may result in improved health care are available to Medicare beneficiaries when those items and services are reasonable and necessary. NCDs may also be used to bar payment for specific items or services that are not reasonable and necessary as described in the Medicare Act. The NCD process facilitates the rapid and uniform diffusion of beneficial technologies, items, and services.

In most instances, CMS, through the NCD process determines whether the item or service is “reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.”² In making NCDs under section 1862(a)(1)(A), CMS considers medical and scientific evidence and provides an opportunity for public comments on our proposed decisions. Because an NCD must be supported by a record, we attempt to gather and discuss all relevant medical and scientific information about a given topic and present our analysis for public scrutiny to ensure transparency. An aggrieved person can challenge an NCD pursuant to the procedure established by statute and regulation.³ In this guidance document, we describe a second statutory provision that may permit Medicare payment in some circumstances. If the evidence is not adequate for coverage under section 1862(a)(1)(A), an item or service may be considered for coverage under the CMS Coverage with Evidence Development (CED) policy in which “reasonable and necessary” is established under 1862(a)(1)(E) of the Act. Section 1862(a)(1)(E) is linked to Section 1142 of the Social Security Act, which allows CMS to work jointly with the Agency for Healthcare Research and Quality (AHRQ) to evaluate and empower CMS to pay for the clinical costs of this research.

III. National Coverage Determinations

Under the authority of section 1862(a)(1)(A), the NCD process may result in one of the following coverage decisions:

1. No change in coverage. Current coverage, whether local or national, will remain unchanged.
2. Non-coverage. The medical evidence is not adequate to conclude that the item or service is reasonable and necessary under section 1862(a)(1)(A) and coverage is not allowed for Medicare beneficiaries.
3. Coverage without special conditions. The medical evidence is adequate to conclude that the item or service is reasonable and necessary under section 1862(a)(1)(A) for all Medicare beneficiaries.
4. Coverage with special conditions. The medical evidence is adequate to conclude that the item or service is reasonable and necessary under section 1862(a)(1)(A) only under one or more of the following circumstances:
 - a. The item or service is covered only for patients with specific clinical or demographic characteristics.
 - b. The item or service is covered only when provided by physicians and/or facilities that meet specific criteria.
 - c. The item or service is covered only when specific data are submitted in addition to claims data to demonstrate that the item or service was provided as specified in the NCD.
5. Under the authority of section 1862(a)(1)(E), the NCD process may result in coverage if the item or service is covered only when provided within a setting in which there is a pre-specified process for gathering additional data, and in which that process provides additional protections and safety measures for beneficiaries, such as those present in certain clinical trials.

Conditions 4(c) and 5 are components of coverage with evidence development (CED), which is the focus of this guidance. There are two sub-types of CED that distinguish between 4(c) and 5 above. Coverage conditioned on specific additional data collection (4c) is referred to as Coverage with Appropriateness Determination (CAD). Coverage conditioned on care being delivered in a setting with a pre-specified data collection process and additional protections in place such as are present in some research studies (5) is referred to as Coverage with Study Participation (CSP).

IV. Strength of evidence for national coverage determinations

When making national coverage determinations, CMS evaluates relevant clinical evidence to determine whether the evidence is of sufficient quality to support a finding that an item or service that falls within a benefit category is reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. This critical appraisal of the evidence enables us to determine whether: 1) assessment questions specific to the process of the evidence evaluation can be answered conclusively; and 2) the investigational item or service will improve health

outcomes for patients. An improved health outcome is one of several considerations in determining whether an item or service is reasonable and necessary.

When CMS assesses the clinical evidence of an item or service, we take the following three factors into account: 1) the quality of the individual studies; 2) the relevance of findings from individual studies to the Medicare population; and 3) overarching conclusions that can be drawn from the body of the evidence about the direction and magnitude of the risks and benefits of the item or service under investigation.

V. Coverage with Evidence Development

A. Coverage with Appropriateness Determination (CAD)

If the evidence for an item or service being evaluated is adequate to determine that the item or service is reasonable and necessary under section 1862(a)(1)(A), CMS may determine that the item is covered under Medicare. Given the importance of the patient's factual circumstances in determining the appropriate treatment, coverage without conditions is rare. Most NCDs have restrictions that ensure that appropriate patients are receiving care by competent providers. CMS may have concerns that beneficiaries receiving the item or service meet the conditions specified in the NCD. In these cases CMS could require CAD, which allows CMS to ensure that new technology is provided appropriately to patients meeting specific characteristics as described in the NCD.

In the application of CAD, CMS may decide that there is adequate evidence to determine that an item or service is reasonable and necessary under section 1862(a)(1)(A), but that additional clinical data is needed that is not routinely available on claims forms to ensure that the item or service is being provided to appropriate patients in the manner described in the NCD. The extra data supplements the information gathered routinely through claims for services rendered and is collected by providers when the service is provided. For the most part, providers will submit extra data to databases or registries specifically designed for collecting data specified in the NCD in question. Our agreements with entities establishing the registries will include protections to ensure that Medicare health information is protected.

CAD will only be invoked when there is adequate evidence to determine that the item or service is to be covered. However, when an NCD requires CAD, only items or services for patients who are included in the data collection are covered. CAD will be required when CMS is concerned that the data collected on a claims form is insufficient to determine that the item or service was appropriately provided as outlined in the NCD. The following are some concerns that may lead to a coverage decision that requires CAD as a condition of coverage:

1. If the newly covered item or service should be restricted to patients with specific conditions and criteria.
2. If the newly covered item or service should be restricted for use by providers with specific training or credentials.

3. If there is concern among clinical thought leaders that there are substantial opportunities for misuse of the item or service.
4. If the coverage determination significantly changes how providers manage patients utilizing this newly covered item or service.

CMS does not intend to routinely develop, oversee, or maintain these databases or registries that contain information about provision of an item or service. However, CMS will only accept data from registries that conform to accepted standards to ensure that the data collected is sufficient to determine if the item or service is reasonable and necessary for Medicare coverage under section 1862(a)(1)(A). In particular, the registries must have qualified scientific oversight; tested and validated data collection methods; adequate patient safety and monitoring; quality assurance and data protection; and appropriate human subjects protections.

B. Coverage with Study Participation (CSP)

CSP will allow coverage of certain items or services for which the evidence is not adequate to support coverage under section 1862(a)(1)(A) and where additional data gathered in the context of clinical care would further clarify the impact of these items and services on the health of Medicare beneficiaries. In the past, this level of evidence would have prompted non-coverage decisions.

CSP allows CMS to determine that an item or service is only reasonable and necessary when it is provided within a research setting where there are added safety, patient protections, monitoring, and clinical expertise. If CMS decides that there is limited existing evidence to support a decision to cover the item or service under review and more evidence is needed for CMS to determine whether that item or service meets the evidentiary standards for reasonable and necessary, then the item or service is found to not be reasonable and necessary for Medicare coverage under section 1862(a)(1)(A). CMS may then consider whether coverage of the item or service is reasonable and necessary for Medicare coverage under section 1862(a)(1)(E)⁴ of the Act.

This section states:

(a) Notwithstanding any other provision of this title, no payment may be made under part A or part B for any expenses incurred for items or services—

(E) in the case of research conducted pursuant to section 1142, which is not reasonable and necessary to carry out the purposes of that section,

Section 1142⁵ describes the authority of the Agency for Healthcare Research and Quality (AHRQ). As part of section 1142, AHRQ assures that research priorities appropriately reflect the needs and priorities of the Medicare program under Title XVIII, as set forth by the CMS Administrator.

Using section 1862(a)(1)(E) authority, the CED/CSP concept considers the item or service to be reasonable and necessary only while evidence is being developed. Under section 1142, research may be conducted on the outcomes, effectiveness, and appropriateness of health care services and procedures to identify the manner in which diseases, disorders, and other health conditions can be prevented, diagnosed, treated, and managed clinically.⁶

In addition, evaluations of the comparative effects, health and functional capacity; alternative services and procedures utilized in preventing, diagnosing, treating, and clinically managing diseases, disorders, and other health conditions may be conducted.⁷

When the evidence is inadequate to determine that the item or service is reasonable and necessary under section 1862(a)(1)(A), Medicare coverage may be extended to patients enrolled in a clinical research study. In this case, the research is conducted under section 1862(a)(1)(E). The following list includes some of the evidentiary findings that might result in CMS issuing an NCD for items and services that do not have sufficient evidence for coverage under section 1862(a)(1)(A) that would provide payment only for Medicare patients enrolled in a research study:

1. Available evidence may be a product of otherwise methodologically rigorous evaluations but may not have evaluated outcomes that are relevant to Medicare beneficiaries.
2. The available clinical research may have failed to address adequately the risks and benefits to Medicare beneficiaries for off-label or other unanticipated uses of a drug, biologic, service or device.
3. Available clinical research studies may not have included specific patient subgroups or patients with disease characteristics that are highly prevalent in the Medicare population.
4. New applications may exist for diagnostic services and devices that are already on the market, but there is little or no published research that supports a determination of reasonable and necessary for Medicare coverage at the time of the request for an NCD.
5. Sufficient evidence about the health benefits of a given item or service to support a reasonable and necessary determination is available only for a subgroup of Medicare patients with specific clinical criteria and/or for providers with certain experience or other qualifications. Other patient subgroups or providers require additional evidence to determine if the item or service is reasonable and necessary.

CSP research conducted may include a broader range of studies than randomized clinical trials to include observational research. However, all studies must conform to the standards that will be developed by the Clinical Research Policy.

In rare instances, for some items or services, CMS may determine that the evidence is very preliminary and not reasonable and necessary for Medicare coverage under section 1862(a)(1)(A), but, if the following criteria are met, CSP might be appropriate:

- a. The evidence includes assurance of basic safety;
- b. The item or service has a high potential to provide significant benefit to Medicare beneficiaries; and
- c. There are significant barriers to conducting clinical trials.

These research studies will be rigorously designed and meet standards to be developed in a reconsideration of the current Clinical Trial Policy established under a 2000 NCD.

New evidence that assists in the Medicare coverage process for the item or service is one of the desired results of CSP. However, a more important outcome is the production of evidence that will influence clinical practice and help Medicare beneficiaries and providers make the most appropriate diagnostic and therapeutic decisions. If the research results are published in a peer-reviewed journal, the evidence will be used in an NCD reconsideration to determine if a change in Medicare coverage is appropriate under section 1862(a)(1)(A).

VI. Data sources

A. Registries

CMS may issue an NCD that requires data to be sent to a centralized database. Formal registries with qualified oversight ensure that data will be uniform, valid, and consistent with accepted standards and definitions. Medicare data from the database will be provided to CMS for the purposes outlined in the coverage determination. Data collected in this manner may be linked with Medicare claims data to confirm that data are submitted for patients receiving the item or service. Collection and use of this data will meet all relevant patient protections including the Privacy Act HIPAA, and 45 CFR Part 46.

Data collected under CAD will commonly be submitted to an approved registry. This data will then be sent to CMS to ensure that the item or service was provided in accordance with the NCD. This data is payment data collected under section 1862(a)(1)(A).

Data submission to a registry may also be necessary within clinical studies required under CSP. Collection and use of this data, though in a registry, is for the purposes of research and will meet all relevant patient protections including the Privacy Act, HIPAA, and 45 CFR Part 46.

While CMS will use the information to meet specific CAD and/or CSP determinations for Medicare beneficiaries, the information is likely to be of great interest to other government and non-government researchers for many purposes. Registry data may be useful in evaluating patient safety and health benefits, comparative effectiveness, utilization and diffusion of the item or service, and variations in outcomes among providers or patients. The data may also be used to evaluate long term outcomes and patient management issues; issues not ordinarily addressed in clinical trials. The claims-linked data can be used to follow outcomes such as mortality and post-coverage utilization of services. The data may be also linked to other data sets or other patient information to conduct controlled observational studies. Use of this data will meet all conditions of the Privacy Act, HIPAA, and patient protections set forth in 45 CFR Part 46.

B. Research studies

If CMS determines that the evidence for coverage of certain items or services is inadequate to establish Medicare coverage under 1862(a)(1)(A), Medicare may still reimburse for that item or service for Medicare beneficiaries enrolled in a research study that provides data and information to be used to evaluate that item or service, as well as reimburse for the routine costs incurred by Medicare beneficiaries in the study.

To qualify for reimbursement, such a study must be designed to produce evidence that could be used in a future national coverage decision that would focus on whether the item or service should be covered by Medicare under 1862(a)(1)(A). Payment for the items and services provided in the study will be restricted to the Medicare qualified patients involved as human subjects in the study.

CMS will not routinely be involved in the design, review, or execution of research studies. CMS will only provide payment for clinical research that meets the standards of a qualified trial as will be outlined in the revision of the Clinical Trial Policy. We anticipate this NCD will include the following principles:

1. The primary purpose of the trial is to test whether the intervention potentially improves the participants' health outcomes.
2. The trial is well supported by available scientific and medical information or is intended to clarify or establish the health outcomes of interventions already in common clinical use.
3. The trial does not duplicate existing studies unjustifiably.
4. The trial design is appropriate to answer the research question being asked in the trial.
5. The trial is sponsored by a credible organization or individual capable of executing the proposed trial successfully.
6. The trial is in compliance with Federal regulations relating to the protection of human subjects.
7. All aspects of the trial are conducted according to the appropriate standards of scientific integrity.

8. The trial is listed in the National Library of Medicine clinical trials database.
9. The sample of study subjects in the trial should include individuals representative of the Medicare population with the condition described in the NCD.

VII. Principles governing the application of CED:

- | | |
|--------------|--|
| Principle 1. | NCDs requiring CED will occur within the NCD processes, which is transparent and open to public comment. |
| Principle 2. | CED will not be used when other forms of coverage are justified by the available evidence. |
| Principle 3. | CED will in general expand access to technologies and treatments for Medicare beneficiaries. |
| Principle 4. | CMS expects to use CED infrequently. |
| Principle 5. | CED will lead to the production of evidence complementary to existing medical evidence. |
| Principle 6. | CED will not duplicate or replace the FDA's authority in assuring the safety, efficacy, and security of drugs, biological products, and devices. |
| Principle 7. | CED will not assume the NIH's role in fostering, managing, or prioritizing clinical trials. |
| Principle 8. | Any application of CED will be consistent with federal laws, regulations, and patient protections. ⁸ |

VIII. Ending CED-required data collection

A. Research studies

In research studies, the end to data collection is predetermined in the study protocol. After the study ends, Medicare coverage reverts to the pre-NCD coverage policy. Because NCD analyses are normally based on a review of publicly available evidence, the results of the trial should be published in the peer reviewed literature to be considered in an NCD reconsideration.

B. Registries

The length of data collection by registries will be determined by the requirements of the NCD. For those registries collecting data under CAD in which the length of time for data collection is not specified in the NCD, CMS will evaluate the data on an ongoing basis to determine when the requirements of the NCD have been met and data collection is longer necessary. The data collection requirement will be removed through reconsideration of the NCD.

For registries collecting data under CSP, the length of data collection by registries depends on factors related to the hypotheses upon which the data collection is based.

Sufficient data should be collected to satisfy the hypotheses. Similar to results of clinical trials, evidence from analyses of registry data should be published in peer-reviewed journals if CMS is considering ending the NCD-required registry data collection

The key factors that CMS will consider in its decision to end registry data collection include the following:

1. Data from the registry provides satisfactory answers to the questions posed in the NCD that were used to establish the registry.
2. Stronger evidence of a health benefit of the item or service published in peer-reviewed literature after the original NCD.
3. Evidence that the item or service does not provide a health benefit in the long term.
4. Evidence of an unacceptable level of adverse events beyond that found in the published literature during the NCD analysis.

IX. How researchers may access CMS' CED data

CMS may link CED data to the Medicare enrollment database and Medicare claims data. Individuals or groups may have access to the data in accordance with the applicable System of Record's Routine Uses if they enter into a Data Use Agreement (DUA) with CMS.⁹ CMS retains ownership of the data. The DUA contract identifies a custodian for the data, contains a declaration that the protocol is accurate, prohibits the user to sell or grant access to the data without authorization, and defines a termination date for use of the data.

Those applying to use CMS data must prepare a proposal that includes:

1. A statement of purpose and goals;
2. A description of how the project will improve the quality of care for Medicare beneficiaries or the administration of the Medicare program;
3. Background information with appropriate literature review;
4. A description of the methods with definitions of outcomes, files, and variables needed;
5. An analytic plan;
6. A description of human subjects to be applied, if relevant;
7. A listing of key personnel qualifications;
8. A work plan; and,
9. A dissemination plan.
10. The user must provide CMS with a final report when the DUA expires [10.11](#)

X. Funding data collections to meet CED requirements

A. Clinical trials

CMS will exercise discretion in determining the research that will be funded under section 1862(a)(1)(E). CMS may pay for the investigational and or routine clinical costs of an item or service for a trial in an NCD requiring CED as described in the revision of the Clinical Trial Policy. CMS will not fund the non-clinical research costs.

B. Registries

CMS will pay for the clinical costs of patient care for Medicare beneficiaries for which data collection is required. CMS will not provide financial support for registry development and maintenance. However, CMS may reimburse registries for data submission to CMS. CMS encourages stakeholders to work together to provide additional support for data collection efforts. These stakeholders include manufacturers, health care providers and facilities, professional societies, foundations, and health plans. To allay the cost of data collection, CMS recommends that CED take place in the context of existing data systems when feasible.

XI. Other uses of data collected under CED

While the goals of CED include the consideration of changes in Medicare coverage as well as the documentation of the appropriateness of care for Medicare beneficiaries, others outside of the Medicare program may find these data useful. The information gathered under CED will be made available for public use in accordance with usual Medicare rules for claims and clinical information. Potential studies with these data may:

- Stimulate industry product development with a focus on technology for patients with specific characteristics. This evidence could allow industry to build on existing technology and help provide new directions for innovation.
- Be used by health plans for quality improvement programs, conducting cost analyses, or establishing clinical criteria.
- Be used by providers to track short-term adverse outcomes, such as postoperative complications or in-hospital mortality. This information can be used to evaluate the safety of the item or service; compare side effects and adverse events with published clinical trial results; or compare outcomes among providers or to a gold standard.
- Be used by hospitals and facilities to monitor performance.
- Serve as a cohort to create longitudinal databases by linking it with claims data or by following up patients enrolled in the registry.
- Be used by investigators for post coverage analyses, including head to head comparisons, case control studies, or nested case control studies.
- Be used to develop clinical criteria and contraindications (risk stratification).

¹ Congress further instructed CMS to model the guidance documents on similar guidance documents issued by the FDA. The established procedures for making these guidance documents are in 69 Fed. Reg. 57325 (September, 24, 2004).

<http://a257.g.akamaitech.net/7/257/2422/06jun20041800/edocket.access.gpo.gov/2004/pdf/04-21197.pdf>

² Social Security Act §1862(a)(1)(A).

³ § 1869(f) of the Social Security Act; 42 CFR Part 426.

⁴ http://www.ssa.gov/OP_Home/ssact/title18/1862.htm

⁵ http://www.ssa.gov/OP_Home/ssact/title18/1142.htm

⁶ §1142(a)(1)(A)

⁷ §1142(a)(2)

⁸ These protections include: 1) the Paperwork Reduction Act (PRA) of 1995 (35 U.S.C. 3501), which requires Federal agencies to be accountable for reducing the burden of Federal paperwork requirements; 2) the Privacy Act of 1974 (5 U.S.C. 552a), which requires that the Agency inform the public that CMS is maintaining information about individuals, institutions, or other groups such as state or local governments; and 3) the HHS protection of human subjects regulation (45 CFR Part 46).

⁹ <http://www.cms.hhs.gov/privacyact/requests/cmsdua.pdf>

¹⁰

http://www.resdac.umn.edu/docs/CMS_STUDY_PROTOCOL_FORMAT_Feb2004.pdf

¹¹ The Research Data Assistance Center (ResDAC) provides free assistance to researchers in the academic, non-profit, and government sectors who are interested in using CMS data for research. See <http://www.resdac.umn.edu/>.