ISSUE BRIEF

Coverage for Evidence Development: A Conceptual Framework

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Is there an alternative to a straightforward "yes" or "no" coverage decision by payers when the risks and benefits of an emerging technology[1] remain unanswered? One alternative of interest to both U.S. and international payers is "Coverage for Evidence Development" (CED), which conditions coverage and payment for a technology on the collection of additional clinical evidence.[2]

Example: Proton Beam Radiation Therapy for Localized Prostate Cancer

Proton beam radiation supporters argue that protons can be delivered more precisely than traditional X-ray therapy and thus could reduce undesirable side effects. Others call such improvements theoretical, pointing out that the rates of side effects are already low for other approaches to treatment for common cancers such as localized prostate cancer. These experts question the significant investment in development of new proton beam centers currently underway. Proton beam therapy could double the costs of treating prostate cancer with uncertain benefits. A CED initiative that compares proton beam radiation to existing radiation therapy alternatives for prostate cancer could determine whether side effects differ among these treatment options, and define the magnitude of the clinical benefit to better inform treatment decisions.

In the United States, through the Medicare program, the Centers for Medicare & Medicaid Services (CMS) has used CED to provide access to potentially beneficial, yet unproven, medical technologies while encouraging the development of clinical evidence that will support more informed decision-making. Medicare first applied the CED concept in 1995 with lung volume reduction surgery (LVRS), a surgical treatment for emphysema. Medicare limited coverage to beneficiaries' being treated according to the protocol of the National Institutes of Health's (NIH's) National Emphysema Treatment Trial (NETT that compared the outcomes of comprehensive pulmonary rehabilitation with those of LVRS. The NETT trial found LVRS was riskier and provided no additional clinical benefit for the majority of candidates for the procedure. These findings dramatically reduced the use of this procedure and improved the quality of care for patients with emphysema.[3]

In the past, several private plans have also used CED for promising, but unproven technologies. A notable example in the late 90's was high-dose chemotherapy with autologous bone marrow transplant (ABMT) for patients with advanced breast cancer. Only after government agencies and insurers collaborated on a series of definitive trials was ABMT demonstrated to provide no benefit and a higher risk of early death over conventional therapy.[4]

Since the experience with LVRS and ABMT, Medicare and private plans have continued to explore ways to cover promising technologies while requiring prospective data

collection. In 2006, CMS formalized its CED policy through a guidance document which publically detailed the circumstances under which Medicare would use CED.[5] Medicare has issued several decisions using CED on a wide range of technologies including colorectal cancer chemotherapy and implantable cardioverter defibrillators.[6] Many policymakers, health plans, states, and healthcare purchasers also share an interest in promoting the use of CED. These stakeholders support making coverage contingent on participation in an organized program of clinical research[7] to encourage the development of stronger clinical evidence regarding new technologies. No decision-maker wants to repeat the experience with autologous bone marrow transplant for breast cancer, which was covered for a decade prior to understanding at high additional cost the procedure actually increased the risk of death among women with advanced disease.[8]

The Center for Medical Technology Policy (CMTP) convened a multi-stakeholder workgroup to address the complicated issues that pose a barrier to implementing CED more broadly. The group, funded by the California HealthCare Foundation and charged with creating the infrastructure that would allow private and public health plans to collaborate on a single CED initiative, has developed a conceptual framework for CED that includes:

- **A model** for CED development and implementation, including definition of the roles for different CED participants;
- **Criteria** to i) select appropriate technologies for CED development; ii) evaluate proposed research; and iii) guide the decisions of individual health plans and other purchasers (both public and private) on whether to participate in a particular CED initiative; and
- **Different approaches to incorporate CED** within existing health benefits programs.

CED Basics: What, How, Why and Should We?

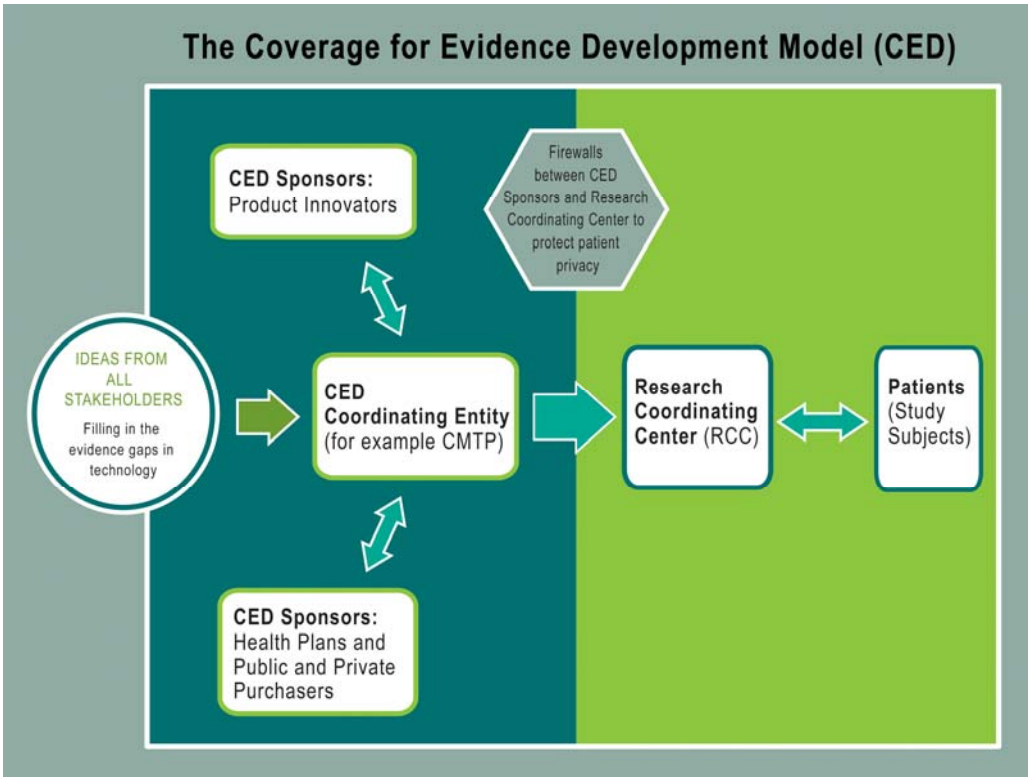
Definition

CED is a special plan provision or program that provides members with temporary coverage for medical technology deemed "experimental" or "investigational" and excluded from coverage. Coverage is contingent on the member's participation in an organized, payer approved, clinical research program.

Purpose

CED aims to generate clinical evidence to help patients, physicians and policymakers make informed decisions about the best use of selected emerging medical technologies. CED also seeks to improve the evidence base available to payers as they make their coverage decisions.

A CED Model



A health plan or other purchaser may choose to develop a CED initiative independently—by working directly with one or more product manufacturers—or to select from initiatives developed by an external coordinating entity. CMTP, as the coordinating entity, would act as the general contractor for the research, subcontracting the collection of data to a Research Coordinating Center (RCC). Within this coordinating entity, multi-stakeholder workgroups would agree on important emerging technologies and propose research protocols that address decision-maker questions. Each CED workgroup would include product innovators, health plans, patient and consumer advocates, practicing physicians, professional societies, and researchers. The model also assumes that health plans and other purchasers would typically split funding for the CED initiative with product innovators, with health plans reimbursing clinical costs for treatment, and product manufacturers funding study costs. Public or private grants might also make good funding sources.

All CED sponsors (health plans, public and private purchasers and product innovators) would make their own decisions on whether to participate. They would base their decision on independent evaluations of the technology's relevance, adequacy of the proposed research and factors like current coverage policy and cumulative financial commitment to CED initiatives already in progress.

Once an initiative is developed and funded, an independent and credible RCC would act as a subcontractor and do the actual research. The RCC would be responsible for obtaining the approvals of all appropriate Institutional Review Boards (IRBs) or for

creating a central IRB for compliance with the highest standards regarding the protection of human subjects in clinical research. The role of CMTP and the independent RCC would establish a firewall between CED sponsors and the conduct of actual research. The firewall would act to ensure the privacy of any research participant's individually identifiable data.

Once concluded, the RCC would publish the study results for health plans or other purchasers to then include in re-evaluating the technology for benefit coverage. Plans' individual re-evaluations might support broad or limited coverage under the usual terms and conditions of the plans, or these decision-makers could uphold their original decision not to extend coverage.

Why Do CED?

CED offers a number of advantages to payers, patients and the innovators bringing new medical technologies to market. Members and study participants potentially gain reimbursement for technologies that lack coverage, and they help to develop the clinical evidence to inform future patients and physicians about the benefits and risks of the technology. Payers begin to share responsibility for generating the evidence they need to make fair and informed coverage decisions when the market has failed to do so. Product manufacturers gain limited reimbursement to bridge the period between the date they obtain required regulatory approvals and when they can supply clinical evidence adequate to obtain a favorable coverage decision by payers.

How to Start: Selection Criteria

CMTP and a special multi-stakeholder workgroup define and apply transparent selection criteria to:

- Identify important emerging technologies that would make good potential candidates for a CED initiative;
- Determine whether the proposed research is likely to produce high-quality, relevant results; and
- Choose between competing high-quality initiatives in the face of resource constraints.

The project workgroup identified the types of criteria, outlined below, appropriate to each stage in the evaluation process. No individual criterion is mandatory; instead technologies and research with high cumulative scores would be considered most worthy of support.

Technology Selection Criteria

To identify new technologies (or new uses of existing technology), relevant, non-exhaustive criteria include whether:

- The technology has obtained any required governmental regulatory approval;

- Decision-makers have judged existing medical literature insufficient to answer key questions;
- The technology may potentially provide a clinically significant and substantial improvement in net health outcomes compared to the most effective alternative;
- The technology offers a cost effective alternative to existing treatments or offers significant cost savings to the plan;
- Market factors suggest that in the absence of a CED initiative, relevant evidence would not become available until after the technology is already in wide use; and
- A tentative study approach appears feasible for a CED initiative (credible, practical approach reasonable budget, etc.).

Research Design Criteria

In addition to satisfying the above criteria, the proposed research should address a high-priority evidence gap, and potential CED sponsors must believe the research results would reduce the identified uncertainties. The research design should score well against pre-established quality criteria, and rigorous conflicts of interest disclosure should be in place for key personnel involved in the design, conduct, management, review, reporting and funding of the studies. CMTP would oversee the timely publication of results, and transparency of adverse events to patients as well as appropriate regulatory authorities. The project workgroup rejected the notion of tying CED to a particular study design (e.g., only randomized controlled trials). Instead, the design should be appropriate to the research question, and promise a realistic chance of producing credible results, such as requiring feasible numbers of patients and showing realistic recruitment planning.

Sponsor Participation Criteria

At any given time, an individual CED sponsor may wish to have several CED initiatives in progress or none at all. Criteria by which a payer could manage its CED commitment include:

- Internal resource constraints, particularly around staffing, special provider contracting or member communications that might be required, or limited acceptance of CED expense by plans' contract holders;
- Potential benefit to both current and future patients;
- Relevance of initiatives offered for consideration to its particular customer or member demographics;
- Local coverage mandates or other regulations that affect the payer's ability to restrict coverage for a given technology to that available within a CED initiative; and
- Projected financial risk for an individual CED initiative or for the cumulative portfolio of CED initiatives.

CED Sponsors Act Independently, but Some Consistency Required

Not many individual health plans, self-insured employers or other payers would be large enough to generate credible research drawing only from its own covered population. Studies designed to compare the clinical utility of treatments may require patient populations in excess of one million members to work properly, even for highly prevalent conditions such as prostate cancer. The study may also need to recruit patients from relatively small geographic areas that surround the participating treatment centers. Although multiple health plans and purchasers would often need to participate to ensure timely study completion, if structured improperly, participation across health plans could provoke antitrust concern. CED sponsors must take care to operate well within both the formal constraints and the spirit of antitrust law.

Practically, this means that each health plan and purchaser would need to independently evaluate CED opportunities and decide at its sole discretion, whether to participate in any initiative. Payers would also be free to base evaluations on any criteria they want.

To facilitate research across payer populations, each sponsor deciding to support a particular initiative should accept certain common requirements, such as agreement to participate for the planned duration of the research and compliance with common study protocol provisions.

Individual, Flexible Approaches to Plan Language

Health plans and plan sponsors have multiple pathways to incorporate CED into the structure of an existing benefit plan or program. Deciding on a standard language and a uniform approach within each CED initiative would work best. Options include:

- Creating an exception to the plan's Experimental & Investigational exclusion that specifically permits such coverage; or
- Creating CED as a special program of extra-contractual payments, similar in concept to payments that might be allowed through case-management for catastrophic illnesses or injuries; or
- Including CED initiatives as part of their existing Clinical Trials Policy; or
- Defining CED within a Clinical Policy document specific to that technology; or
- Establishing CED outside of the benefit plan or structure in the form of a foundation to fund research or as a special project authorized by the health plan like BlueCross BlueShield's Demonstration Project for funding research on bone marrow transplants for breast cancer. [9]

Sample plan provisions below demonstrate how the first three options might be described in plan language or remain extra-contractual.

- **Option 1: Add language to the current Experimental & Investigational exclusion.** This exclusion would not apply with respect to a given medical technology (including drugs, devices, biologics of medical and surgical procedures, whether therapeutic or diagnostic) if all of the following requirements are met.
  - » [Health Plan], at its sole discretion, has elected to provide coverage for the technology in a specific clinical indication, under its CED program (described elsewhere in this certificate), and
  - » [Health Plan's] CED election remains in force on the date the patient's medical treatment with this item or service begins, and
  - » Patient agrees (in writing) to participate in the pre-approved program of clinical research that is required for coverage under the CED program, meets eligibility criteria established for the research and complies with all requirements for the research as specified in the research protocol.
  - » The physician or other provider of the service also participates in the approved program of clinical research and complies with all research protocol requirements.

- **Option 2: CED as extra-contractual payments.**
  This Plan participates in a CED program. CED temporarily provides reimbursement for a certain medical technology (including drugs, devices, biologics of medical and surgical procedures, whether therapeutic or diagnostic) that the Plan otherwise excludes from coverage as Experimental & Investigational for diagnosis or treatment of an indicated health condition. Reimbursement is contingent on the member's full participation in a formal program of organized clinical research that the Plan has approved in advance of making CED reimbursement for the technology available to its members. CED is available for only a small number of otherwise excluded technologies chosen by [Health Plan] at its sole discretion. [Health Plan] may impose a number of special requirements on members, patients and the treating provider before the service would qualify for reimbursement under this provision.

- **Option 3: CED as supplement to existing clinical trial language:10**
  To provide Company employees with access to the latest medical research and clinical developments on cancer, heart disease, arthritis, asthma and many other serious or chronic illnesses, [the Company] covers expenses for investigational or experimental treatments.

  Government-Sponsored Clinical Trials
  To be eligible for this coverage, you must qualify for, and participate in, a clinical research trial approved by the National Institutes of Health, the Food and Drug Administration, Centers for Disease Control and Prevention, the Agency for Health Care Research and Quality and the Department of Defense.

Other Clinical Trials

In addition, clinical trials sponsored by other entities may also be covered if approved by the benefits administrator, provided that the clinical trial has passed independent scientific review and has also been approved by an Institutional Review Board (IRB) that would oversee the trial; and the clinical trial must be conducted in a setting and by personnel who maintain a high level of expertise because of their training, experience and volume of patients. An IRB is an independent ethics committee usually associated with a university or physician-accrediting organization formally designated to approve, monitor and review biomedical and behavioral research involving humans with the aim to protect the rights and welfare of the subjects.

Why Not Start with Existing Clinical Trial Coverage Mandates?

CED has conceptual similarities to clinical trial coverage mandates employed in many states. Important differences in intent and approach however, suggest CED initiatives should be viewed as complementary to existing clinical trial policy legislation, rather than as a program that might supplant or modify these mandates.

The design of existing state legislation aims mainly to ensure coverage for experimental treatments for patients who have few other options. Twenty states have legislated that insurers and health plans cover the costs associated with participation in qualifying clinical trials, with thirteen of these restricting coverage to cancer clinical trials, six covering life-threatening conditions only, and one covering both cancer trials and chronic fatigue. Four states have arranged non-legislative agreements with the same intent.[11] Each non-legislative agreement is limited to the coverage of cancer clinical trials.

In contrast to state clinical trial coverage mandates, CED programs would not be limited by condition or type of treatment. CED is intended to develop stronger clinical evidence on many different types of unproven technologies, leading to better information about their risks and benefits, particularly compared to existing alternatives. Additionally, CED initiatives are not limited to traditional randomized clinical trials. While these represent the "gold standard" for clinical research, CED initiatives may wish to address evidence gaps for technologies that cannot be studied using randomized populations, or use a better-suited study design.

Next Steps for the CED Model Benefits Language Project

Members of the project workgroup are participating in CMTP's ongoing efforts to inform all stakeholders about the framework described by this Issue Brief. The workgroup also wants to test the concepts through implementation of a pilot CED project in 2009. Address any questions regarding these projects to info@cmtpnet.org.

Endnotes

[1] For purposes of this Issue Brief, the term medical technology includes all drugs, devices, biologics and surgical and medical procedures used in medical care.

[2] Medicare calls their policy "Coverage with Evidence Development." The authors prefer "Coverage for Evidence Development," but retain the same acronym of CED. For detailed discussion of the history and implications of Medicare and CED, please see Tunis S. and Pearson S., "Coverage Options for Promising Technologies: Medicare's Coverage with Evidence Development," Health Affairs 25 (2006): 1218-1230.

[3] Carino T., Sheingold, S., and Tunis, S., "Using Clinical Trials as a Condition of Coverage: Lessons from the National Emphysema Treatment Trial," Clinical Trials 1, no. 1 (2004): 108–121.

[4] Lippman, E., "High-Dose Chemotherapy plus Autologous Bone Marrow Transplantation for Metastatic Breast Cancer," New England Journal of Medicine 342, no. 15 (2000): 1119–1120; and Aubry, W.M., "False Hope: ABMT for Breast Cancer," Presentation at AcademyHealth Annual Research Meeting, San Diego, California, 2004. (www.academyhealth.org/2004/ppt/aubry.ppt)

[5] CMS, "Guidance for the Public, Industry, and CMS Staff National Coverage Determinations with Data Collection as a Condition of Coverage: Coverage with Evidence Development" (Baltimore: CMS, July 2006).

[6] CMS, "Coverage with Evidence Development," CMS website (http://www.cms.hhs.gov/CoverageGenInfo/03_CED.asp), last accessed December 22, 2008.

[7] For purposes of this Issue Brief, the term "organized program of clinical research" means research that has a written protocol describing a scientifically sound study, and that has been approved by all relevant institutional review boards (IRBs) before participants are enrolled.

[8] Rettig, R., Jacobson, P., Farquhar, C., and Aubry, W., "False Hope: Bone Marrow Transplantation for Breast Cancer," New York, Oxford University Press, 2007.

[9] The BlueCross BlueShield Association (BCBSA) in Chicago established the BlueCross BlueShield Demonstration Project to support patient care costs for high-priority, National Cancer Institute-sponsored, randomized controlled trials to evaluate high-dose chemotherapy with autologous bone marrow transplantation compared to conventional dose chemotherapy in the treatment of breast cancer. A small staff at BCBSA developed contracts with transplant facilities, determined patient eligibility for the contracted services, and paid transplant facilities discounted rates outside of usual contractual medical necessity provisions for the investigational care that was delivered. For more information, see Rettig et al., page 274.

[10] Sample plan language from a project workgroup member who has implemented a CED initiative. Emphasis added.

[11] Pettibone, K., Wallace, R., Field, R., and Arculi, R., "State Laws Concerning Clinical Trials and Off-Label Drug Use for Cancer Patients," Presentation at annual meeting of the American Public Health Association, Philadelphia, Pennsylvania, 2002. (http://www.scld-nci.net/presentations/soatweb.pps#257,3,Background)

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