



National Institutes of Health: Comparative Effectiveness Research

The Department of Health and Human Services (HHS) received funding for comparative effectiveness research (CER) under the American Recovery and Reinvestment Act (Recovery Act) of \$1.1 billion, of which \$300 million is for the Agency for Healthcare Research and Quality (AHRQ), \$400 million is for the National Institutes of Health (NIH), and \$400 million is for allocation at the discretion of the Secretary.

This implementation plan focuses on the \$400 million of funds in the Recovery Act for NIH as part of a trans-agency research effort in CER.

A. Funding Table

(Dollars in millions)

Program/ Project/Activity	Total Appropriated	FY 2009 Actual Obligations	FY 2010 Estimated Obligations
<i>Comparative Effectiveness Research</i>	\$400.0	\$176.5	223.5

B. Objectives

The overarching goal of this program is to improve health outcomes by providing evidence to enhance medical decisions made by patients and their medical providers. NIH uses the definition of comparative effectiveness research as set forth by the Federal Coordinating Council:

Comparative effectiveness research is the conduct and synthesis of systematic research comparing different interventions and strategies to prevent, diagnose, treat and monitor health conditions. The purpose of this research is to inform patients, providers, and decision-makers, responding to their expressed needs, about which interventions are most effective for which patients under specific circumstances. To provide this information, comparative effectiveness research must assess a comprehensive array of health-related outcomes for diverse patient populations. Defined interventions compared may include medications, procedures, medical and assistive devices and technologies, behavioral change strategies, and delivery system interventions. This research necessitates the development, expansion, and use of a variety of data sources and methods to assess comparative effectiveness. Systematic research methods can include randomized controlled trials, meta-analyses, observational cohort analyses, and other new and emerging methodologies.

NIH's objective is to target funding to support scientific research opportunities that help support the goals of the Recovery Act. The projects support Recovery Act by



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conducting CER that aims to enhance patient and clinician decision-making and to improve “real world” health outcomes for the Nation. The NIH objective specifically supports the HHS Strategic Plan.

C. Activities

As a member of the Federal Coordinating Council for Comparative Effectiveness Research (FCC), which was authorized by and established pursuant to the Recovery Act, NIH coordinated its research plan with other agency members and consulted with the FCC to ensure consistency with the HHS-wide plan.

To support scientific research opportunities that help achieve the goals of the Recovery Act, NIH has and will continue to obligate resources across several major activities, including:

1. **Previously Peer-Reviewed and Approved Projects.** NIH is supporting peer-reviewed and approved, highly-meritorious grant applications from investigators across the Nation that were not funded in FY 2008 and grant applications that would not otherwise likely be funded in FY 2009 or FY 2010.
2. **New and Competing Research Efforts.** NIH also is supporting new types of activities that fit into the structure of the Recovery Act. For example, the new NIH Challenge Grant and Grand Opportunities programs focus on health and science problems where significant progress can be made within a two-year time frame.
3. **Continuations.** NIH also is supporting acceleration of ongoing science via NIH’s supplement programs known as “administrative supplements” or expansion of the scope of current research through “competitive revisions” for support of additional infrastructure (e.g., equipment costing less than \$100,000) and personnel.

As of March 2010, NIH had committed \$342 million (M) to the following categories:

- \$144.9M for 31 Grand Opportunity Grants;
- \$76.5M for 82 Challenge Grants;
- \$55.0M for 12 Pay-line Expansions;
- \$39.2M for 5 Other Actions (contracts, interagency agreements, etc);
- \$7.3M for 7 Competitive Revisions; and,
- \$19.1M for 29 Administrative Supplements.

Note that while this represents \$342M in commitments, the amount of money actually obligated so far is \$207.5M (see table below); the difference relates to the second year of two-year ARRA CER grants. Those funds are already committed, but will not be obligated until later this year.

NIH plans to commit the remaining \$58M to the following categories:

- \$10M for Methodology Development in CER;
- \$15M for CER on Upper Endoscopy in Gastro-Esophageal Reflux Disease. Eradication Methods for Methicillin-Resistant Staphylococcus Aureus (Staph) Infection, and Dementia Detection and Management Strategies;
- \$25M for CER Mentored Career Development Awards; and,
- \$8M for Administrative Supplements for CER Workforce Development.



D. Characteristics

In general, NIH is funding competitive awards based on peer review, scientific opportunity and the potential impact of the proposal on biomedical research and public health priorities related to CER. To date, approximately 38% of the recipients are “Institutions of Higher Learning,” and 62% are “Non-profit” organizations (these entities include hospital systems, research institutions, centers, foundations, etc.). In order to avoid duplicative databases, each project that involves database establishment, expansion, and/or maintenance must detail the rationale and need for the database work proposed. Senior NIH and Science Implementation officials continue to meet regularly with senior Department officials to ensure that projects are meeting their program goals, assessing and mitigating risks, ensuring transparency, and incorporating corrective actions.

The \$400M in CER ARRA funds has allowed NIH to expand its portfolio of landmark CER to fund additional comparisons within ongoing clinical trials, support new CER projects, and bolster CER infrastructure and training—all in a trans-agency context. Some highlights of the ARRA-funded CER include:

- 1) “SPRINT Senior” adds an older adult population to the original “SPRINT” trial to compare control of systolic blood pressure (BP) to 140 versus 120 for possible beneficial and adverse effects in this age group (over 75) on multiple real-world end-points, including cardiovascular, renal and cognitive function.
- 2) The Oregon lottery study analyzes how insurance affects health care utilization and health by comparing low income participants selected for enrollment in Oregon’s public health insurance program through a lottery with non-participants.
- 3) A follow-up to the diabetes prevention study, which showed dramatic effects of lifestyle and/or drugs in preventing onset of diabetes, will determine effects on relevant health end-points associated with diabetes complications.
- 4) Recovery After an Initial Schizophrenia Episode (RAISE) is the first step for transforming treatment for schizophrenia by engineering rapid adoption of an effective early treatment package consisting of both pharmacologic and psychosocial interventions.
- 5) Additional studies compare the effectiveness of:
 - Breast imaging strategies in community practice;
 - Interventions for chronic pain management;
 - FIT (fecal immunochemical test for occult blood) vs. colonoscopy for cancer screening;
 - Surgery vs. medical management in patients with atrial fibrillation and stroke;
 - Minimally invasive surgical pulmonary vein isolation vs. medical management in patients with atrial fibrillation and stroke; and,
 - Conservative vs. dialytic management in Stage V Chronic Kidney Disease.



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6) Multiple registries will allow tracking of populations for variables including outcomes and relationship to treatment:

- Community-based Autism Spectrum Disorders disease registry; and,
- Kaiser Permanente Autoimmune Disease Registry.

7) CER Centers to support research, training and dissemination of evidentiary knowledge:

- Center for CER in Cancer Genomics - “CancerGen;”
- Comparative Effectiveness and Outcomes Improvement Center; and,
- Clinical and Translational Science Awards

E. Delivery Schedule

Status of ARRA CER Obligations ¹
As of 3/31/2010
 (\$ in millions)

Research	Type of Award	Obligations	Unobligated Balance	Total
Previously Peer-Reviewed and Approved Projects	Grants	\$16.9	\$18.9	\$35.8
Challenge Grants	Grants	38.6	37.9	76.5
GO Grants	Grants	76.8	68.2	145.0
Administrative Supplements	Grants	17.6		17.6
Competing Revisions	Grants	7.3		7.3
High Impact Research / Infrastructure	Grants		25.0	25.0
Institutional Mentored Career Development	Grants		25.0	25.0
Administrative Supplements for Workforce Development	Grants		8.9	8.9
Other Activities (interagency agreements, grants, and contracts)	Grants/ Contracts/ IAA	35.3	23.6	58.9
Total CER Recovery Act Obligations		\$192.5	\$207.5	\$400.0



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¹ Note that while this represents \$342M in commitments, the amount of money actually obligated so far is \$207.5M (see table below); the difference relates to the second year of two-year ARRA CER grants. Those funds are already committed, but will not be obligated until later this year.

NIH has accomplished the following milestones over the past 16 months:

- Began publishing Recovery Act specific funding announcements (March 2009)
- Assessed highly meritorious CER applications that expanded the pay-line (May/June 2009)
- Conducted peer review for Challenge and Grand Opportunity Program Grants to determine which were CER-related (May-July 2009)
- Awarded all FY 2009 Challenge and Grand Opportunity Program Grants (August – September 2009)
- Issued four additional CER-specific funding announcements – CER Methodology, CER Research Gaps, and 2 CER Training announcements (October – December 2009)
- Awarded “Administrative supplements for CER Workforce Development” (May 2010)
- NIH plans to award the remaining CER fund by August 2010.

NIH expects to obligate an additional \$110.6M by August 2010 and the remaining \$96.5M by September 2010. NIH expects to have obligated all \$400M by the end of 2010.

Research results with significant impacts are expected to begin being generated in FY 2011-FY 2012 (see Section G—Measures below.)

F. Environmental Review Compliance

Consistent with the provisions of the National Environmental Policy Act (NEPA), NIH has procedures in place to ensure that Federal officials properly take into account potential environmental consequences when taking actions. Section 1609 (c) of the Recovery Act requires that the President report to the Senate Environment and Public Works Committee and the House Natural Resources Committee every 90 days following the date of enactment until September 30, 2011 on the status and progress of projects and activities funded by the Act with respect to compliance with NEPA requirements and documentation. The Council on Environmental Quality (CEQ) promulgated reporting requirements in a March 11, 2009 document that described specific procedures and a reporting template that NIH completes regularly and provides to the HHS Office of Facilities Management and Policy (OFMP).

Most research grants qualify for a categorical exclusion from detailed NEPA review, as promulgated in the Federal Register on January 19, 2000: “NIH is providing notice of the actions that will normally be categorically excluded from further environmental review because individually and cumulatively they will not have a significant effect on the human environment. If a proposed action is included in one of the categories but extraordinary circumstances as described in section D of this notice apply, an environmental review will be performed.” In other words, whereas most research grants qualify for the categorical exclusion, NIH is required to conduct oversight to ensure that all proposals are reviewed for extraordinary circumstances or triggers



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that might warrant additional environmental review. To meet this responsibility, NIH has included NEPA related reviews in its award and progress reporting processes.

G. Measures

HHS is working to develop cross-cutting outcome measures for comparative effectiveness research activities across the Department. In addition, the measures below will be reported quarterly and help HHS track progress toward the program's goals and objectives. NIH recently developed outcome measures as indicated in the last five measures presented below. NIH will develop targets for these measures over the next few months by analyzing the funded CER projects (which will be finalized in July 2010). The targets will be developed by the end of September 2010. Outcomes are expected to be generated starting in FY 2011.

Each of the targets for the various measures was developed through either evaluating CER efforts in 2009 (i.e., the number of CER Coordinating Committee meetings) or analyzing the portfolio of funded projects in order to determine the likely product/result of each project. Actual outcomes are calculated through tracking actual events, and will be confirmed through communications with the funding recipients. Measures of outcomes, in particular, will be generated based on grantee reporting and validation of those reports; greater measures specificity will be available as the grantees' work progresses and NIH is able to initiate outcome measurements.

NIH is using the following measures for this program:



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Outcome / Achievement	Units	Type	9/30/09	12/31/09	3/31/10	6/30/10	9/30/10	12/31/10	3/31/11	6/30/11	9/30/11	Program End
# applications received ¹	#	TARGET				445	N/A	N/A	N/A	N/A	N/A	
		ACTUAL	304	304	395	442	N/A	N/A	N/A	N/A	N/A	
# meritorious grants awarded	#	TARGET					216	N/A	N/A	N/A	N/A	
		ACTUAL	166	166	166	185		N/A	N/A	N/A	N/A	
# of CER-related meetings , including FCC, AHRQ CER, VA CER ²	#	TARGET						33				
		ACTUAL	27	27	27	29						
# of NIH CER Coordinating Committee meetings	#	TARGET						23				
		ACTUAL	14	14	16	18						

¹ No targets were estimated for this particular measure. The earliest target developed was 445 – which is the total of applications received in 2009 plus the applications anticipated to be received in 2010. The additional 138 applications in March 2010 include the following:

- (1) 31 applications in response to **RFA-OD-10-008** “Comparative Effectiveness Research on Upper Endoscopy in Gastroesophageal Reflux Disease, Eradication Methods for Methicillin Resistant Staphylococcus aureus and Dementia Detection and Management Strategies,” and
- (2) 60 applications in response to **RFA-OD-10-009** “Methodology Development in Comparative Effectiveness Research.”
- (3) 26 applications in response to **RFA-OD-10-011** “Institutional CER Mentored Career Development Award.”
- (4) 21 applications in response to **NOT-OD-10-037** “Administrative supplements for CER Workforce Development.”

² The measure in the March 2010 FOR, “# of coordinating meetings, including FCC, AHRQ CER, VA CER,” has been split into the following two measures: “# of CER-related meetings including FCC, AHRQ CER, VA CER,” and “# of NIH CER Coordinating Committee meetings.” The measure was split in order to emphasize the difference between the two types of meetings – the first measure represents meetings at the federal level where coordination and information sharing between agencies is occurring, the second measure looks at meetings internal to NIH (these meetings are where the additional review of ARRA-funded CER projects at NIH occurs).



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Full Implementation Phase Measures (FY 2011-2012)³

Outcome / Achievement	Units	Type	3/31/11	6/30/11	9/31/11	12/31/11	3/31/12	6/30/12	9/30/12	12/31/12	3/31/13	Program End
Number of interventions whose relative effectiveness as compared to other interventions is identified by CER studies		TARGET	TBD	TBD	TBD	TBD	TBD	TBD	TBD	TBD	TBD	
		ACTUAL										
Number of dissemination efforts (programs/tools) to translate CER findings to clinicians, consumers, and policy-makers		TARGET	TBD	TBD	TBD	TBD	TBD	TBD	TBD	TBD	TBD	
		ACTUAL										
Increase evidence available to policy-makers, providers and consumers		TARGET	TBD	TBD	TBD	TBD	TBD	TBD	TBD	TBD	TBD	
		ACTUAL										
Number of sources available for CER		TARGET	TBD	TBD	TBD	TBD	TBD	TBD	TBD	TBD	TBD	
		ACTUAL										
Number of research networks developed for CER		TARGET	TBD	TBD	TBD	TBD	TBD	TBD	TBD	TBD	TBD	
		ACTUAL										

This information will be available to the public on the Recovery Act website.

³ This table includes new measures developed by NIH. No targets are reported for these measures until 2011 because significant outcomes, as demonstrated through these measures, are not expected until then. Over the next few months, NIH will develop targets for each of these measures by analyzing the projects funded with the \$400 million in CER funds. Until all awards are made, targets representing the full portfolio cannot be established.



H. Monitoring and Evaluation

All Recovery Act programs are assessed for risk to ensure that appropriate internal controls are in place throughout the entire lifecycle of the program. These assessments are done consistent with the statutory requirements of the Federal Manager's Financial Integrity Act and the Improper Payments Information Act, as well as OMB's circular A-123 "Management's Responsibility for Internal Control" (including Appendices A, B & C).

NIH's risk management process fits within the overall governance structure established at HHS to address Recovery Act program risks. The HHS Risk Management and Financial Oversight Board provides executive leadership and establishes accountability for the risk assessment process related to internal controls over financial reporting, and the HHS Senior Assessment Team ensures that risk assessment objectives are clearly communicated throughout the Department. NIH's Senior Assessment Team in coordination with the NIH Risk Management Program carries out comprehensive annual assessments of its Recovery Act programs to identify risks and develop strategies to address them, including those associated with selecting recipients, awarding and overseeing funds, and achieving program goals. It meets quarterly to monitor and assess the effectiveness of mitigation strategies and identify emerging risks.

In addition, NIH has presented its high level risks to the Recovery Act Implementation Team. Chaired by the Deputy Secretary and comprised of senior policy officials from throughout the Department, the Implementation Team convenes monthly to monitor progress in carrying out Recovery Act programs and address the obstacles and risks that could impact on their success.

The National Institutes of Health through the Extramural Grants Management Advisory Committee (GMAC), and the Contract Management Advisory Committee (CMAC), has established policies and procedures to assure a consistent and integrated approach to oversight practices that monitor extramural grantee activities for NIH contracts, grants, and cooperative agreements. These committees meet approximately twice a month. Guidance for progress tracking, financial management, and administrative management of NIH grants includes OMB Circular A-110, OMB Circular A-123, *Management's Responsibility for Internal Control*, sections of the Recovery Act including Section 1512, and the *Updated Implementing Guidance for the Recovery Act of 2009*.

In addition, the NIH Office of Management Assessment (OMA) and the Office of Financial Management (OFM) have established the NIH risk management framework for identifying, assessing, and testing of operational and financial risks and internal controls associated with implementing Recovery Act requirements. OFM and OMA conduct risk and control assessments in compliance with the statutory requirements of the Federal Managers' Financial Integrity Act, the Improper Payments Information



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Act, and OMB's Circular A-123 *Management's Responsibility for Internal Control*. OMA works with NIH offices that are responsible for implementing programs receiving Recovery Act funding to: identify and score the Recovery Act risks, assess controls related to the identified the Recovery Act risks, remediate controls as needed, monitor the inventory of the Recovery Act risks, and report on the risks and controls to NIH and HHS leadership. OFM uses its existing process for assessing internal control over financial reporting related to using and tracking Recovery Act funds and take into account any control deficiencies.

Progress reports are required for all active projects annually. The reports are reviewed by both program and grants management staff as required in the respective NIH Manual Chapters. The review process includes a project officer completing a review checklist for each project that covers: progress, scope, planning, any project changes, safety, outputs, and reporting requirement. The checklist requires additional information for any identified risk or challenge areas. Mitigating or corrective actions are documented and trigger additional review as required. Outputs are reviewed by program officials to confirm appropriate progress. Progress standards are based on planned activities and milestones within the grant application.

Grants management specialists monitor disbursements from the grantee project accounts as reported in the quarterly SF272 (Cash Transaction Report) to assure that the drawdowns from the Division of Payment Management System are appropriate for the effort described in the application. When disbursements are outside of planned parameters, grants management specialists contact the grantee for additional information, and confer with NIH program staff to determine whether the project may be at risk. Decisions to limit disbursements based on actual charges to the project may be required, if project funds are determined to be at risk. Additional funds may be withheld if progress is not satisfactory, and continued concerns may lead to suspension or termination of award.

NIH conducts technical assistance visits for oversight of grantee organizations when deemed necessary by the grants management specialist based on a GMAC Risk Assessment analysis. Criteria that trigger additional site visits can include challenges or risk factors for progress, financial, or administrative management. Site visits and reviews are tailored to the specific circumstance of use for each Grantee Institution, with the participation of grant and / or program management as needed.

Although science validates itself statistically, other forms of evaluations occur on a regular or as needed basis. The findings from evaluability assessments, evaluations and system assessments are used to improve or to eliminate activities. Assessment type activities often are conducted by external contractors; however, trained evaluation NIH staff separate from a project or program can conduct the assessment as well.

For a current assessment of the risks associated with NIH's CER program, refer to the program's latest Risk-Executive Summary and Detailed Summary available from the NIH Office of Management Assessment.



I. Transparency

NIH is open and transparent in all of its grants competitions that involve spending of Recovery Act funding consistent with statutory and OMB guidance. NIH ensures that recipient reports required by Section 1512 of the Recovery Act are submitted and reviewed for material omissions and significant errors that would mislead or confuse the public. NIH informs recipients of their reporting obligation through standard terms and conditions, grant announcements, contract solicitations, and other program guidance. NIH provides technical assistance to grantees and contractors and fully utilizes project officers to ensure compliance with reporting requirements. To ensure recipient cost and performance requirements are reported, all awards issued with Recovery Act funding have special accounting numbers and codes to track the funds and awards. All Recovery Act funds must be awarded separately from the normal appropriation funds. The awards must comply with both existing NIH reporting requirements and the Recovery Act reporting requirements. Grants include special terms and conditions based on guidance provided by OMB and HHS.

NIH links to Recovery.gov on its website at <http://recovery.nih.gov/>.

NIH is open and transparent in all of its contracting and grant competitions and regulations depending on what is appropriate for program activities that involve spending of Recovery Act funding consistent with statutory and OMB guidance.

NIH ensures that recipient reports required by Section 1512 of the Recovery Act are submitted and reviewed for material omissions and significant errors that would mislead or confuse the public. NIH informs recipients of their reporting obligation through standard terms and conditions, grant announcements, contract solicitations, and other program guidance. In addition, NIH provides key award information to recipients and other technical assistance to grantees and contractors and fully utilizes project officers to ensure compliance with reporting requirements.

J. Accountability

To ensure that managers are held to high standards of accountability in achieving program goals under the Recovery Act, NIH has built upon and strengthened existing processes. Senior NIH officials meet regularly with senior Department officials to ensure that projects are meeting their program goals, assessing and mitigating risks, ensuring transparency, and incorporating corrective actions. The personnel performance appraisal system also incorporates Recovery Act program stewardship responsibilities for program and business function managers.

The project officer's annual review requires additional information for any identified risk or challenge areas. Mitigating or corrective actions are documented and trigger additional review as required. Outputs are reviewed by program officials to confirm appropriate progress. Progress standards are based on planned activities and milestones within the grant application. Grants management can limit disbursement of funds for any funding improprieties and if progress is not satisfactory.



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The NIH Office of Management Assessment and Office of Financial Management are coordinating efforts to ensure that existing risk management processes are fully used as NIH implements the provisions of the Recovery Act. Terms and conditions of award notices also are amended so that awardees are fully aware of the reporting requirements associated with these funds.

K. Barriers to Effective Implementation

NIH does not anticipate any significant barriers to implementation.

NIH participates on the Federal Coordinating Committee for CER and has also reached out to other agencies across the Department and with the Federal Coordinating Council, (including the Food and Drug Administration (FDA) and the Veterans Administration (VA)) to ensure that research efforts are not duplicative and that research is pursued on topics of interest to stakeholders.

L. Federal Infrastructure

The infrastructure that are supported through these funds are primarily data bases, patient registries and other health information technologies, which are not subject to energy efficiency or green building requirements. No construction will be carried out with these funds.

Summary of Significant Changes:

- Expanded funding table to show three year obligations and outlays (Section A. Funding Table)
- Addition of itemized actual and planned commitments (Section C. Activities)
- Shifted emphasis from process description of award review/ control to active process management efforts and listing of CER awards already made (Section D. Characteristics)
- Replacement of delivery schedule development plans with status of obligations by research type to date and plans for remaining obligations (Section E. Delivery Schedule)
- Replacement of the listing of environmental review compliance “extraordinary circumstances” and efforts made to communicate compliance efforts to-date (May 2009) within NIH with the addition of National Environmental Policy Act (NEPA)-related reviews in awards and progress reports (F. Environmental Review Compliance)
- Detailing of Developmental Phase Measures and addition of Full Implementation Phase Measures (Section G. Measures)
- Added information on NIH’s proactive risk assessment and mitigation efforts and their connection to OMB required internal controls (Section H. Monitoring and Evaluation)
- Expanded transparency efforts by making contractors and awardees aware of their transparency requirements under the Recovery Act; added link to recovery website (Section I. Transparency)