

## **Assessing the Impact of AHRQ Evidence-based Practice Center (EPC) Reports on Future Research**



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# *Methods Future Research Needs Report*

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## Number 7

# Assessing the Impact of AHRQ Evidence-based Practice Center (EPC) Reports on Future Research

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**Prepared by:**

RTI International–University of North Carolina Evidence-based Practice Center  
Research Triangle Park, NC

**Investigators:**

Meera Viswanathan, Ph.D.  
Patrick Nerz, B.A.  
Barbara Dalberth, M.A.  
Christiane Voisin, M.S.L.S.  
Kathleen N. Lohr, Ph.D.

**Other contributors:**

Lucia Rojas-Smith, Ph.D.  
Douglas Kamerow, M.D.  
Elizabeth Tant, B.A.  
Marianne Kluckman, M.A.  
Carol Woodell, B.A.  
Dan Jonas, M.D., M.P.H.  
Timothy Carey, M.D.

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## Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies and strategies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To improve the scientific rigor of these evidence reports, AHRQ supports empiric research by the EPCs to help understand or improve complex methodologic issues in systematic reviews. These methods research projects are intended to contribute to the research base and be used to improve the science of systematic reviews. They are not intended to be guidance to the EPC program, although may be considered by EPCs along with other scientific research when determining EPC program methods guidance.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality. The reports undergo peer review prior to their release as a final report.

We welcome comments on this Methods Research Project. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by e-mail to [epc@ahrq.hhs.gov](mailto:epc@ahrq.hhs.gov).

Carolyn M. Clancy, M.D.  
Director  
Agency for Healthcare Research and Quality

Jean Slutsky, P.A., M.S.P.H.  
Director, Center for Outcomes and Evidence  
Agency for Healthcare Research and Quality

Stephanie Chang, M.D., M.P.H.  
Director  
Evidence-based Practice Program  
Center for Outcomes and Evidence  
Agency for Healthcare Research and Quality

Sonia Tyutyulkova, M.D., Ph.D.  
Task Order Officer  
Center for Outcomes and Evidence  
Agency for Healthcare Research and Quality

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## **Peer Reviewers**

Mei Chung, M.P.H.  
Tufts Medical Center Evidence-based Practice Center  
Boston, MA

Jeanne-Marie Guise, M.D., M.P.H.  
Oregon Evidence-based Practice Center  
Portland, OR

Joseph Lau, M.D.  
Tufts Medical Center Evidence-based Practice Center  
Boston, MA

Naomi Aronson, Ph.D.  
BC/BS Evidence-based Practice Center, Technology Evaluation Center  
Chicago, IL

# Assessing the Impact of AHRQ Evidence-based Practice Center (EPC) Reports on Future Research

## Structured Abstract

**Objectives.** To evaluate the impact of EPC systematic reviews on solicited or funded research and to identify barriers and facilitators to the impact of these documents on future research.

**Data Sources.** ISI Web of Science, MEDLINE<sup>®</sup>, reviews of citations from updated systematic reviews, National Institutes of Health Guide for Grants and Contracts Web site, key informant interviews, and data from AHRQ on dissemination.

**Methods.** We selected two systematic reviews as case studies to evaluate their impact on future research. We identified key citations generated by these reports and traced forward to identify their impact on subsequent studies through citation analysis. We reviewed requests for application and program announcements and dissemination data from AHRQ to identify impact. We conducted interviews with 13 key informants to help identify short-, medium- and long-term impacts of the EPC reports.

**Results.** The impact of the selected EPC case studies is demonstrably greater on short-term outcomes (greater awareness of the issues) than on medium-term (such as the generation of new knowledge) or long-term outcomes (such as changes in patient practice or health outcomes). The extent of impact of an EPC report varies based on factors such as the topic and the timing of the report relative to the development of the field. The degree to which the new research can be directly attributed to the AHRQ reports remains unclear. Key informants discussed several benefits stemming from the EPC reports, including providing a foundation for the research community on which to build, heightening awareness of the gaps in knowledge, increasing the quality of research, and sparking new directions of research. However, the degree to which these reports were influential and well received hinged on several factors including marketing efforts, the very nature of the reports, and other influences external to the EPC domain.

**Conclusions.** Our findings illustrate the importance of the breadth, specificity, and readiness of the topic for more research; ongoing developments in the field; availability of funding; and active engagement of champions. AHRQ and the EPCs may be able to improve the likelihood of impact by creating more targeted products, planning for and expanding dissemination activities, improving the readability and other attributes of the reports themselves, and actively involving funders early on and throughout the process of creating and publishing the reviews.

# Contents

<b>Executive Summary</b> .....	ES-1
<b>Introduction</b> .....	1
Background .....	1
Objectives .....	1
Definitions of Outcomes and Impact of Future Research Documents .....	1
Potential Pathways for Impact .....	2
Key Questions .....	5
Selected Case Studies .....	5
Organization of the Remainder of the Report .....	8
<b>Methods</b> .....	9
Methodological Considerations and Approaches .....	9
Implications of Methodological Constraints on Project Methods .....	10
Data Sources for Bibliometric Analysis .....	12
Update Searches .....	15
Selection and Interviews of Key Informants .....	15
Analysis of Key Informant Interviews .....	17
Other Sources of Information .....	17
<b>Results</b> .....	18
Organization of Results .....	18
Impact of EPC Reports (KQ 1): The Literacy and Health Outcomes Case Study .....	18
Impact of EPC Reports (KQ 1): The Omega-3 and Cardiovascular Disease Case Study .....	24
Factors Influencing the Impact of EPC Reports (KQ 2) .....	30
<b>Discussion</b> .....	34
Impact of EPC Reports on Future Research Funding (KQ 1) .....	34
Elements That Contribute to the Impact of EPC Reports (KQ 2) .....	35
Development of a Dissemination Plan .....	38
Consideration of Audience and Impact When Scoping the Topic .....	38
Balanced Investigative Team .....	38
Targeted Dissemination to Funders and Investigators .....	38
Outreach to Other Funding Agencies .....	38
Limitations .....	39
Conclusions .....	40
<b>References</b> .....	41
<b>Tables</b>	
Table A. Ongoing and Newly Proposed Changes to Future Research Sections of Systematic Reviews .....	ES-9
Table 1. Indicators of Research Outcomes and Impact from Future Research Sections in EPC Reports .....	11
Table 2. Data Sources for Bibliometric Analysis .....	13
Table 3. AHRQ Systematic Review and Related Citations .....	14
Table 4. Questions for Key Informants .....	16
Table 5. Citations From the Updated Health Literacy Report: Reasons for Citing the 2004 AHRQ Report .....	19

Table 6. Citations From the Updated Omega-3 and Cardiovascular Risk Factors and Intermediate Markers Report: Reasons for Citing the 2004 AHRQ report .....	25
Table 7. Ongoing and Newly Proposed Changes to Future Research Sections of Systematic Reviews.....	35

**Figures**

Figure 1. Analytic Framework: Processes and Activities Leading to Impact of EPC Reviews on Future Research .....	3
Figure 2. Evaluation Logic Model for Evaluating Impact of EPC Reports on Research Outcomes .....	4
Figure 3. Weight and Interconnectedness of Health Literacy Citations to the AHRQ Report and Derived Articles .....	19
Figure 4. Web-Based Metrics: Literacy and Health Outcomes .....	20
Figure 5. Weight and Interconnectedness of Omega-3 Citations to the AHRQ Report and Derived Articles .....	26
Figure 6. Web-Based Metrics: Effects of Omega-3 Fatty Acids on Cardiovascular Disease .....	27
Figure 7. Web-Based Metrics: Effects of Omega-3 Fatty Acids on Cardiovascular Risk Factors and Intermediate Markers of Cardiovascular Disease .....	28
Figure 8. Analytic Framework of the Processes and Activities Leading to Impact of the 2004 Report on Literacy and Health Outcomes on Future Research.....	36
Figure 9. Analytic Framework of the Processes and Activities Leading to Impact of the Omega-3 and Cardiovascular Disease Reports on Future Research.....	37

**Appendixes**

Appendix A. Case Study Identification	
Appendix B. Sources Searched for Assessment of Impact of an EPC Report	
Appendix C. Potentially Relevant National Institutes of Health (NIH) Requests for Applications and Program Announcements	
Appendix D. Results of Update Search	
Appendix E. Key Informant List	



# Executive Summary

## Introduction

The mission of the Agency for Healthcare Research and Quality (AHRQ) to improve “the quality, safety, efficiency, and effectiveness of health care for all Americans” places AHRQ’s Effective Health Care (EHC) Program squarely in the realm of translating research into practice. Recent increases in funding in comparative effectiveness research have fueled the urgency of widening the pipeline from the EHC Program’s research portfolio to actionable policy, whether that policy is framed in terms of addressing patient care issues or filling gaps in evidence with new research.

This methods project has two key questions (KQs). KQ 1 evaluates the impact of Evidence-based Practice Center (EPC) systematic reviews on solicited or funded research (i.e., research funding opportunities or ongoing or completed studies). KQ 2 examines best practices, contextual variables, and other factors that are likely to increase the impact of these documents in the future. Thus, this project presents a unique and timely opportunity to evaluate this aspect of EPC work as changes in the program are unfolding. Specifically, the commissioning of *Research Needs* pilot documents (the first wave was completed in late 2010) represents a change in AHRQ’s expectations for and investment in the EPC program for specifying future research priorities.

The effects of EPC reports can have short-, medium-, or long-term outcomes (often taken to be 1–3 years, 4–6 years, and 7–10 years, respectively). For this task, we will focus primarily on short- and medium-term outcomes of future research sections; we anticipate that impact (longer-term outcomes) will be difficult to identify.

## Methods

Two basic approaches can be used to answer questions of research impact: *historical tracing* or *forward tracing*. With historical tracing, evaluators first identify key advances and then determine the bodies of evidence that influenced the key advances. This particular approach relies heavily on bibliometric techniques (e.g., weight and interconnectedness of citations). Forward tracing starts with specific research and can use a variety of methods, such as case studies, interviews, questionnaires, and bibliometric techniques, to identify both the effects and the pathways for those effects. The historical tracing technique requires a comprehensive bibliographic source, without which results are likely to be biased. The forward tracing technique, through its narrower focus on the specific report for which effects are to be determined, uses a more targeted bibliographic search than historical tracing but may be particularly susceptible to biases relating to attribution. An additional concern with case study analyses, which are often used in forward tracing, is that of selection bias in identifying the cases, which may lead to focusing excessively on positive rather than negative findings or conclusions. We elected to use the forward tracing method and attempted to address specific methodological concerns.

Methodological concerns in identifying the effects of EPC reviews on research (opportunities, priorities, studies begun, and/or studies completed) include the following: (1) attributing impact to the EPC report itself, given that other factors may be influencing policy decisions or changes in research directions or opportunities; (2) accounting for the time lag

between the report and the change in research funding priorities or actual investigations; and (3) taking into consideration what might have occurred in the absence of the EPC report. We attempted to answer the two project questions using forward tracing for two case studies. We used a combination of methods: key informant interviews, Web searches, and bibliometric techniques for citation analysis.

In addressing the two key questions and accounting for potential biases, we took the following tasks to be critical: (1) developing an analytic framework to depict and separate, when possible, the pathways for attribution of impact directly to the systematic review as contrasted with its contribution to a larger set of factors that impact future research; (2) stating the considerations weighed in selecting case studies; and (3) carrying out some assessment of funding priorities before and after the publication of the report to avoid a focus on overly positive findings.

Regarding the development and revision of the analytic framework, we explicitly asked each key informant for feedback on the analytic framework and used their input to revise our hypothesized pathways for impact.

We sought nominations for case studies from EPC directors to identify EPC reports known to have had some impact. We identified 16 potential reports. In evaluating each nomination, we highlighted studies that were either so recent or so old as to raise concerns regarding the measurement or attribution of impact. We also identified studies with the potential for a conflict of interest (i.e., the authors of the systematic review would be intimately involved in this evaluation). We consulted with senior AHRQ staff to narrow the selection further.

Two important additional considerations influenced the final selection of the topics: ongoing update activities and variation in the topic. The 2004 report on literacy and health outcomes and the 2004 reports on omega-3 fatty acids and cardiovascular issues were in the process of updates, either formally or as part of a methods project. In addition, each of these projects represented very different types of topics. Health literacy is a broad topic that influences many different substantive areas; omega-3, by contrast, is a much more focused topic. The variation in topics presented an opportunity to explore different pathways for impact.

We addressed the assessment of funding priorities before and after the systematic reviews through reviews of federal Requests for Applications (RFAs) and Program Announcements (PAs) from 1993 to 2010 (a period that includes 11 years of funding before release of the reports and 6 years thereafter). We also asked funders who offered anecdotal evidence of changes in funding priorities to describe the contribution of the AHRQ report to these changes.

## **Data Sources for Bibliometric Analysis**

**Published Literature.** We used information provided by our key informants to obtain a list of “first-generation” references—that is, references that were derived directly from the report (peer-reviewed publications drawing upon the reports). We then used ISI Web of Science and PubMed Central sources to obtain information on the weight (i.e., the number of articles referring to the report and first-generation sources) and interconnectedness of citations. We ran searches in these sources for each of the original citations and first-generation citations to obtain the list of second-generation citations.

**Solicitations.** We searched the National Institutes of Health [NIH] Guide for Grants and Contracts Web site for funding opportunity announcements. The Web site is limited in its search functionality: no date limits can be set if inactive solicitations are requested. A search for “health

literacy” yielded 92 requests for applications (RFAs) and program announcements (PAs) since 1993. Four separate searches of terms related to omega-3 (“omega 3,” “fish oil,” “n-3 fatty acids,” and “omega-3 fatty acid”) yielded 34 unique RFAs and PAs since 1993.

## **Update Searches**

One methodological limitation of the forward tracing approach is its focus on positive results. Searches for studies in ISI Web of Science or PubMed provide information on weight and interconnectedness of citations, but they cannot provide information on the *extent* to which the systematic review and its byproducts influenced future research. To understand the extent to which systematic reviews have had impact, a denominator, that is, the number of studies that could potentially have cited the systematic review, is required. As noted earlier, we selected both case studies because they were in the process of being updated. We obtained updated search results for both case studies through personal communication with the update teams. The health literacy update team conducted a full update of the literature and identified 177 new citations from 2003 to 2010 that met inclusion criteria. For omega-3, we understood from personal communication with the team that the update search was an abbreviated search for the 2004 Balk et al. report on cardiovascular risk factors and intermediate markers alone (i.e., the update search did not focus on the Wang et al. report). The intent of the update search was conducted primarily to understand signals for whether the report was ready to be updated rather than to serve as an update of the results. The update team conducted searches only in key journals; these searches yielded 66 new citations that met inclusion criteria.

We obtained full-text articles for each article and reviewed each article for evidence of citation of the systematic review or associated articles. We abstracted data showing how each article cited the systematic review or associated articles. We also reviewed each article and abstraction dually and recorded the context and purpose of the citation.

## **Selection and Interviews of Key Informants**

We used snowball recruitment to identify and recruit key informants. We intended to interview at least two investigators of the original report, two funders, and two external experts. We began our interviews with the investigators of the reports and were guided by their input in the selection of subsequent key informants. We interviewed a total of six key informants for the literacy and health outcomes case study and seven for the omega-3 case study. The chief purpose of the interviews was to identify (1) relevant funding solicitations and investigator-initiated funding and (2) barriers and facilitators to the use of past reports for developing funding agendas or solicitations. We used NVivo to analyze the data.

## **Other Sources of Information**

We obtained information from AHRQ on the number of downloads from the AHRQ Web site and orders from the AHRQ clearinghouse.

## Results

### Impact of EPC Reports (KQ 1): The Literacy and Health Outcomes Case Study

**Inputs.** The American Medical Association (AMA) requested the report on literacy and health outcomes; AHRQ funded it. Principal authors included systematic review expert Nancy Berkman, Ph.D., of RTI International, and substantive experts Darren DeWalt, M.D., M.P.H., and Michael Pignone, M.D., M.P.H., of UNC.

**Outputs.** In January 2004, AHRQ released the report on literacy and health outcomes. The authors also produced two journal articles.

**Short-term impact: Increased awareness of issues.** Our analysis of the short-term impact of this report comes from several sources: evidence of citation of the report through searches from the updated reports, ISI Web of Science, and PubMed Central; dissemination through downloads and orders of the AHRQ report; qualitative reports of media interest; and heightened collaboration in the field.

*Citation of the report.* Our analysis of the literature from the health literacy update report suggests widespread citation of the 2004 report. More than one-third of the articles (60 of 168) in the update of the report cited the 2004 report or its derived articles.

*Media coverage.* The 2004 report on literacy and health outcomes generated some media interest. EPC investigators, along with authors of a report from a committee of the Institute of Medicine (IOM) on health literacy, presented their findings at the National Press Club in Washington, D.C.

*Dissemination of the AHRQ report.* Over time, interest in the executive summary in both PDF and HTML formats continues to be quite high (2004 through October 2010) through downloads (3500-4900)

*Collaboration.* EPC investigators were able, despite some constraints, to collaborate to fill research gaps following publication of the report. Some key informants believed that the EPC investigators were not funded either to disseminate the reports more broadly or to maintain systematic contact with policymakers or key stakeholders; this problem made it difficult for them to build on report findings. However, several of the EPC investigators were in a position, as a result of their prominence in the field independent of the report, to collaborate on future health literacy research.

**Short-term impact: Influence on funding priorities.** Of the 92 RFAs and PAs identified through our searches, 17 (funded by a variety of agencies within NIH and AHRQ) preceded the release of the report. This tally suggests that the funders were pursuing active support of this field even before the release of the systematic review. Of the remaining 75 RFAs and PAs, 4 cite the AHRQ report.

In keeping with these findings, although key informants believed that the EPC report had a role in increasing funding for health literacy, generally they were unable to identify many specific requests for funding or funding prioritization documents that referred to the report. They noted several reasons: first, report findings were not compatible with future research. Second, the very nature of the topic is difficult to translate into funded research. Health literacy is relevant across the entire health care continuum, but it is not specific to any particular clinical area. Third, dissemination could have been planned better and targeted to end users. Fourth, the report itself could have been easier to use.

**Short-term impact: Influence on policy or practice guidelines.** Key informants noted that although some organizations have developed policies about health literacy since 2004, these developments are difficult to attribute to the EPC report. Key informants noted that the report's failure to change policy and practice guidelines in any substantial way may be more the result of the then-nascent state of research and literature on health literacy than the shortcoming of the report.

**Medium-term impact: Knowledge generation.** Key informants repeatedly referred to the AHRQ EPC report as a foundational document. We found that 13 of 168 citations in the update search referred to the 2004 report as a means of illustrating that their research addressed a gap identified by the report. An additional three studies referred to the AHRQ report and its products to support their own conclusions for future research.

In addition to the impact on other investigators, the report had an impact on the future research of the EPC investigators who wrote it. Independent of the EPC report, the EPC content experts were pursuing research in health literacy. However, their involvement in the report had two impacts. First, it helped to clarify for them the status of health literacy research and the gaps that needed to be filled. Second, it was one of many reports that provided them with a strong reputation for health literacy research. They were able to parlay their experience into future work and prominence in the field: serving on review panels, writing editorials, and presenting and planning major conferences.

**Long-term impact: Changes in clinical or patient practice.** In general, key informants felt that the report's impact on clinical and patient practice was tangential at best. Most key informants saw the report as several steps removed from changes at the clinical or patient practice level. Some of the reasons that the report has not changed clinical or patient practice can be attributed to the report itself. Several key informants noted that the report was not written for clinicians; the comprehensive review of literature is helpful for researchers but unwieldy for clinicians. One key informant suggested the creation of complementary documents created specifically with clinicians in mind.

**Long-term impact: Changes in health outcomes.** The key informants generally agreed that if the report had any effect on health outcomes, it was indirect.

## Impact of EPC Reports (KQ 1): The Omega-3 and Cardiovascular Disease Case Study

**Inputs.** The omega-3 reports on CVD were part of a series of reports requested and funded by the Office of Dietary Supplements (ODS), National Institutes of Health; two focused on humans and a third on animals and isolated/cell cultures.

This methods project used the two reports (Balk et al. 2004 and Wang et al. 2004) focusing on outcomes in humans, with the exception of one indicator for short-term impact (citation of the report or articles) and one for medium-term impact (knowledge generation). For these two indicators, we derived information from an ongoing update of the literature by Balk and colleagues for the Balk et al. 2004 report. No similar resource was available for the Wang et al. report; conducting an update of the literature for the Wang et al. report would have been outside of the scope of this Methods Future Research Needs project.

**Outputs.** In March 2004, AHRQ released both omega-3 reports on CVD and on CVD risk factors. The CVD report led to a journal article. The CVD risk factors report resulted in two journal articles. The team then published a methods paper on systematic reviews of nutrition topics based on several omega-3 reports.

After the release of the EPC reports, ODS (the report funder) and the National Heart, Lung, and Blood Institute (NHLBI) organized two workshops to discuss priorities for future funding.

**Short-term impact: Increased awareness of issues.** We evaluated four measures of short-term impact: citation of the report, media coverage, dissemination of the AHRQ report, and collaboration.

*Citation of the report.* Our analysis of the literature from the omega-3 update search suggests some citation of the 2004 report. Of 49 articles, seven cite the omega-3 report or subsequent journal articles. Most articles cite the report and the articles to place their findings in context or to establish the state of the science.

*Media coverage.* AHRQ and ODS orchestrated a press release, which received some media publicity. Several key informants noted coverage from popular media as well as scientific media. Key informants also noted that omega-3 fatty acids have received substantial coverage overall concerning their positive effects.

*Dissemination of the AHRQ report.* AHRQ's record of downloads through HTML and PDF formats since the publication of the reports through October 2010 show a peak of interest in the year following the report (with more than 14,000 downloads of the full report on cardiovascular disease); interest leveled off after that point. For both reports, the executive summary remains the most consistently sought-after product.

*Collaboration.* The coinvestigators on this topic who were content experts had substantial expertise before their involvement in the report; thus, the report did not serve as a mechanism to create opportunities for collaboration with their peers on the topic.

Co-investigators who were methodologists (i.e., EPC investigators) did not pursue additional work in this content area, so they did not seek opportunities for collaboration on this specific

topic. They did, however, make connections with nutrition experts at Tufts as a result of this work and so expanded their capacity to do nutrition-related reviews.

**Short-term impact: Influence on funding priorities.** We found 9 RFAs and 25 PAs that cited the term “omega-3,” “fish oil,” “n-3 fatty acids,” or “omega-3 fatty acids.” Four RFAs and two PAs preceded the release of the report. None cited the EPC reports or articles. The low yield of RFAs and PAs was validated by key informants who cited the importance of investigator-initiated research in this field.

As for influence of the report on funding solicitations, as noted earlier, NHLBI and ODS collaborated on two workshops. NHLBI’s first workshop proposed a large clinical trial, but the lack of funding support prevented further evolution of the proposal. The second workshop resulted in a peer-reviewed journal article that was cited by three articles in the update search for the Balk et al. 2004 report and was reported by key informants to be influential in investigator-initiated funding ideas. Our review of citations using ISI Web of Science and PubMed Central found that 39 studies cited the article from the NHLBI workshop. In addition, the workshop served as means of convening experts in the field, who then went on to submit investigator-initiated awards.

ODS conducted an assessment in 2010 of the effect of EPC omega-3 reports on their grant portfolio and found that only one of 20 grants cited the AHRQ report (personal communication). One possible reason for the citation could be that the sole investigator who cited the AHRQ report was involved in the workshop and knew about the reports beforehand.

Key informants noted that the reports lacked specificity, particularly when compared to other reports (e.g., from the IOM) that separate “major” knowledge gaps from noncritical research gaps.

**Short-term impact: Influence on policy or practice guidelines.** Key informants generally did not believe that the EPC reports had impact on policy and practice guidelines for several reasons. First, the American Heart Association (AHA) guidelines on eating oily fish preceded the reports; the AHA did not change their guidelines based on the reports. Second, no translation of the AHRQ report to clinical recommendations exists. A third explanation is that the evidence base is not compelling to guideline developers. Third, one key informant noted that guideline developers may not always be driven by evidence.

**Medium-term impact: Knowledge generation.** Two sets of authors cited one of the AHRQ report and two journal articles to illustrate how their studies filled gaps identified by the AHRQ review.

Investigators on the EPC team expanded their portfolio of research in the area of systematic reviews of nutrition topics. Content experts became more involved in systematic review work and related activities, serving on a Technical Expert Panel and on guideline committees. Additionally, the methodological challenges of conducting systematic reviews in the nutrition field spurred the Tufts team to seek additional funding on methods from NIH.

External constraints included funding, the state of current patient practice, and the existing knowledge base among funders and reviewers.

**Long-term impact: Changes clinical or patient practice.** Key informants noted a substantial change in clinical practice and cited the commonplace use of omega-3 supplements. They noted,

however, that this change is attributable not to a single report, but to a body of evidence, with a slow accumulation of data on benefits from 1985 onward (when the *New England Journal of Medicine* published three studies on omega-3) and limited evidence of harms.

**Long-term impact: Changes in health outcomes.** Key informants uniformly agreed that they could not make a judgment on whether the EPC report has had an impact on health outcomes. They cited the difficulty of attribution of effect to the EPC report in particular.

## **Factors Influencing the Impact of EPC Reports (KQ 2)**

Key informants discussed several benefits of the EPC reports. Among these were steps such as providing a foundation for the research community to build on, heightening awareness of the gaps in knowledge, increasing the quality of research, and sparking new directions of research. However, the degree to which these reports were influential and well-received hinged on several factors including marketing efforts, the very nature of the reports, and various other influences external to the EPC domain.

Dissemination involves using multiple venues and media and identifying “champions.” The reports themselves were not easy to read. Key informants suggested expanding the intended reach of reports, improving recommendations for future research, and building on strengths of the systematic review approach. External factors such as the lack of evidence supporting a clear direction for future research, the difficulty of funding research in basic science, and restrictions in the size of the field and number of investigators or lack of overall funding may not be as amenable to change. Key informants did note the heightened impact of AHRQ reports when their release converges with other seminal reports.

## **Discussion**

### **Impact of EPC Reports on Future Funding (KQ 1)**

The impact of EPC reports on future funding can be conceptualized narrowly, as being limited to knowledge generation, that is, new studies inspired by the gaps identified by the systematic review. A more comprehensive framework, and one that key informants reinforced, specifies pathways for impact that include other outcomes such as increased awareness or changes in policy and practice that may then spur new research.

The impact of the selected EPC case studies is demonstrably greater on short-term outcomes, that is, greater awareness of the issues, than on medium-term (such as the generation of new knowledge) or long-term outcomes (such as changes in patient practice or health outcomes). Articles identified in the relevant updates of the literature searches cited reports and articles from both case studies in high numbers.

We did not uncover evidence of impact of EPC reports on long-term outcomes; however, long-term effects may take longer than the 6 years that have elapsed since the publication of the reports for the two case studies. Attributing impact related to long-term outcomes to the EPC reports may be poorly documented.

Our evaluation suggests that the extent of impact of an EPC report will vary based on factors such as the nature of the topic and the timing of the report relative to the development of the field. Systematic reviews that cover a broad scope will likely be cited more frequently than more



narrowly specified topics. Reports that summarize findings for an emerging field serve as foundational material for subsequent work.

The degree to which the new research can be directly attributed to the AHRQ reports remains unclear. Neither the literacy report nor the omega-3 reports directly resulted in allocation of dedicated funds for future research for that topic. In the case of health literacy, for example, the initial PAs did not cite the AHRQ report until the second round of funding. Nevertheless, the reports did influence the way that the EPC investigators, other investigators, and funders approached the topics.

## Elements That Contribute to the Impact of EPC Reports (KQ 2)

Our interviews with key informants suggest that factors that contribute to or detract from the impact of EPC report are associated with the report itself, its dissemination, and the environment into which it is issued. AHRQ has already identified some of these challenges and has instituted (or is in the process of implementing) several specific solutions. Some appear in the new round of funding for future research documents; others are steps that EPCs can take by following revised methods for systematic reviews and comparative effectiveness reviews (Table A).

**Table A. Ongoing and newly proposed changes to future research sections of systematic reviews**

<b>Ongoing changes</b>
<ul style="list-style-type: none"> <li>Greater specificity in future research needs (including providing a sense of relative urgency about specific recommendations)</li> </ul>
<ul style="list-style-type: none"> <li>Greater involvement of funders and stakeholders in the research recommendations</li> </ul>
<ul style="list-style-type: none"> <li>Improvements in readability of the systematic review</li> </ul>
<ul style="list-style-type: none"> <li>Greater specificity in future research needs (including providing a sense of relative urgency about specific recommendations)</li> </ul>
<b>Additional changes suggested by key informants and results of the report</b>
<ul style="list-style-type: none"> <li>Newly proposed changes</li> </ul>
<ul style="list-style-type: none"> <li>Dissemination plan that involves EPC investigators and a “champion” funder</li> </ul>
<ul style="list-style-type: none"> <li>Careful consideration of likely audience and impact when scoping the topic</li> </ul>
<ul style="list-style-type: none"> <li>Balanced investigative team</li> </ul>
<ul style="list-style-type: none"> <li>Targeted dissemination to funders and investigators</li> </ul>
<ul style="list-style-type: none"> <li>Outreach to other funding agencies</li> </ul>
<ul style="list-style-type: none"> <li>Greater funding support of journal articles (the most widely cited source of AHRQ-support research)</li> </ul>

## Limitations

The two case reports selected for this methods project represent different types of content areas and, therefore, provide some variation in understanding how EPC reports may have impact on future research. Nevertheless, these two case studies are limited in applicability to other reports in the EPC program.

The methods used in this report are best suited to identifying impacts through short-term and medium-term pathways. Our methods and timeframe may have influenced our ability to find evidence of long-term impacts.

## Conclusions

The case studies of literacy and health outcomes and omega-3 fatty acid supplements illustrate the multiple and often nonlinear pathways by which EPC reports can have short- to long-term impact on future research. Although these pathways are not entirely predictable,

common themes emerged from our work along several dimensions: the importance of the breadth, specificity, and “readiness” of the topic for more research; ongoing developments in the field; availability of funding; and the active engagement of champions. AHRQ and the EPCs may be able to improve the likelihood of impact by creating more targeted products, planning for and expanding dissemination activities, improving the readability and other attributes of the reports themselves, and actively involving funders early on and throughout the process of creating and publishing the reviews.

## **References**

Please refer to the reference list in the full report for documentation of statements contained in the Executive Summary.

# Introduction

## Background

The mission of the Agency for Healthcare Research and Quality (AHRQ) to improve “the quality, safety, efficiency, and effectiveness of health care for all Americans” (Clancy and Slutsky, 2007, p. xii)<sup>1</sup> places AHRQ’s Effective Health Care (EHC) Program squarely in the realm of translating research into practice. Recent increases in funding in comparative effectiveness research have fueled the urgency of widening the pipeline from the EHC Program’s research portfolio to actionable policy, whether that policy is framed in terms of addressing patient care issues or filling gaps in evidence with new research.

The latter expectation (filling research gaps) from the EHC products and from the Evidence-based Practice Centers (EPCs) is relatively new; it has been codified in terms of production of *Research Needs* documents. An assessment of the first decade of AHRQ’s outcomes and effectiveness research, which was published in 2000, includes a lengthy list of policy-level change agents that may be influenced by AHRQ reports (“health plans, professional organizations, legislative bodies, regulators, accrediting bodies, the media, industry, and patients”), but it does not mention research funders (Stryer et al. 2000, p. 985).<sup>2</sup> By 2005, researchers recognized the potential impact of EPC reports on funders and provided anecdotal<sup>3</sup> or qualitative<sup>4</sup> evidence that they had influenced a variety of stakeholders. We have not, however, uncovered any systematic consideration of barriers to the use of AHRQ’s EPC reports for developing future funding agendas or empirical evidence of the impact of EPC reports on federal, foundation, or industry funding solicitations.

The United Kingdom’s National Institute for Health and Clinical Excellence (NICE), in grappling with the issue of raising the influence of their systematic reviews, published recommendations in 2006 that systematic reviews offer research recommendations in the “EPICOT” framework, that is, evidence, population, intervention, comparator, outcomes, and timestamp of recommendation.<sup>5</sup> We are not aware of any empirical assessment of the NICE recommendations.

## Objectives

This methods project has two objectives. The first is to evaluate the impact of EPC systematic reviews on solicited or funded research. The second is to identify factors that are likely to increase the impact of these documents in the future. Thus, this project presents a unique and timely opportunity to evaluate this aspect of EPC work as changes in the program are unfolding. Specifically, the commissioning of *Research Needs* pilot documents (the first wave was completed in late 2010) represents a change in AHRQ’s expectations for and investment in the EPC program for specifying future research priorities. We anticipate that although these changes will anticipate some of the insights contained in this report, other conclusions from the report will continue to have relevance as the program evolves.

## Definitions of Outcomes and Impact of Future Research Documents

This task is related to a larger question of identifying the outcomes and impact of research, broadly defined. Stryer and Tunis frame research impacts for AHRQ as a triangle, with the base representing studies that result in knowledge generation, or Level 1 impacts. Attribution of

impact to these studies is commonly acknowledged to be difficult to do.<sup>2,6</sup> Higher level impacts include changes in programs or policies (Level 2), changes in clinical or patient practice (Level 3), and changes in health outcomes as the apex (Level 4).<sup>2</sup>

For our task, we focus on lower-level impacts of EPC systematic reviews. By this, we mean effects seen through research that has been either solicited or funded, and changes occurring in federal, state, and private sector (such as hospital or professional society policies and guidelines) programs and policies (Levels 1-2) . We are not examining the impact of systematic reviews or comparative effectiveness reviews on either clinical decisionmaking or health outcomes (Levels 3-4) *per se*; our interest in these changes is to consider their effect on future research.

The effects of EPC reports can have short-, medium-, or long-term outcomes (often taken to be 1–3 years, 4–6 years, and 7–10 years, respectively).<sup>7</sup> Evaluations typically reserve the word “impact” for long-term outcomes. For this task, we will focus on short- and medium-term outcomes of future research sections; we anticipate that impact (longer-term outcomes) will be difficult to identify.

## Potential Pathways for Impact

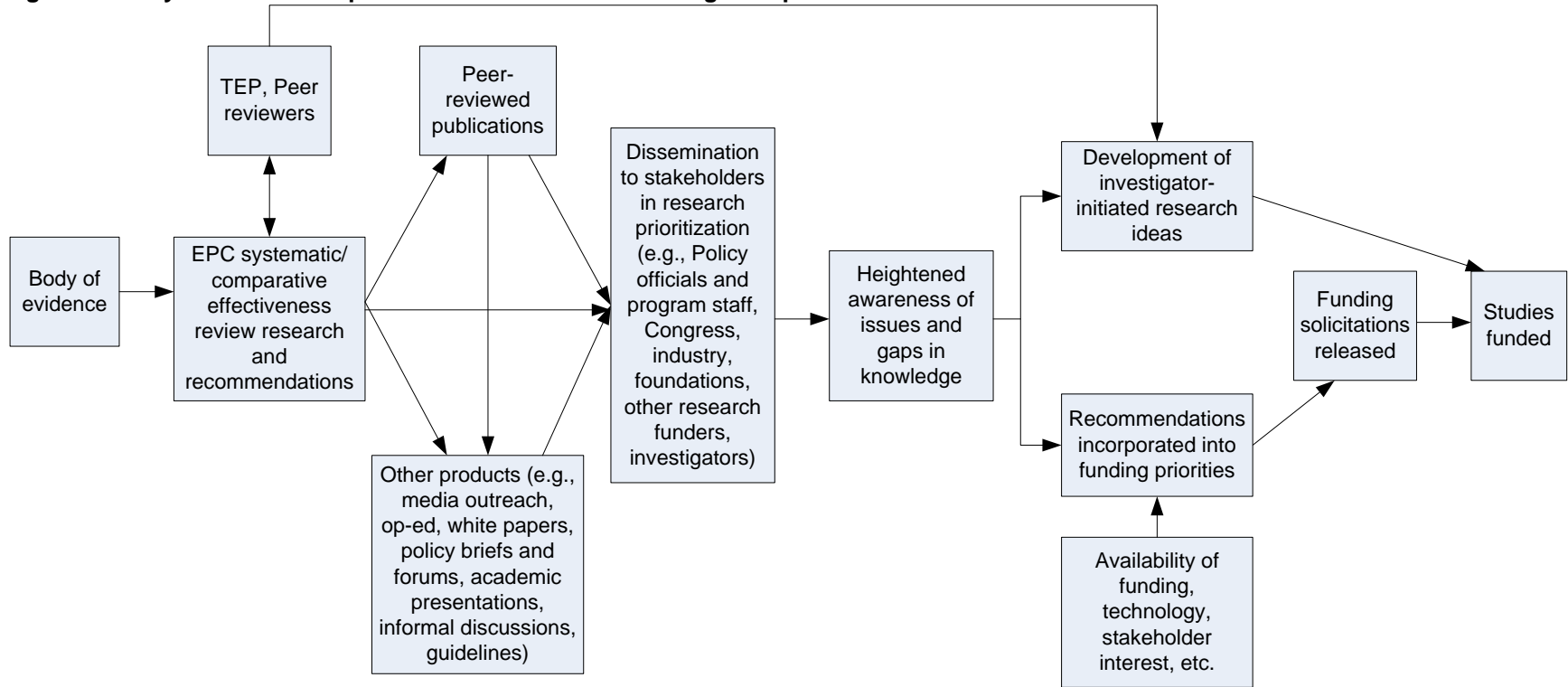
Based on conversations with key stakeholders in the EHC Program and EPC members, we developed and refined an analytic framework (Figure 1). The figure shows potential pathways by which we hypothesize that EPC reviews can influence future research. A body of evidence is the starting point for EPC comparative effectiveness or systematic reviews that then provide research recommendations. Members of Technical Expert Panels (TEPs) and peer reviewers may influence these research recommendations and may be influenced by the report to generate new research ideas. These reviews may be disseminated to stakeholders that set priorities for research (e.g., Agency and NIH program and policy officials, Congress, industry, foundations, other research funders) either directly or via peer-reviewed publications or other products (e.g., media outreach, journal editorials, media op-eds, white papers, policy briefs and forums, academic presentations, informal discussions). Dissemination of this information leads to a heightened awareness of issues and gaps in knowledge and incorporation of research recommendations into funding priorities. Availability of funding, technology, and stakeholder interest, among other factors, influences the process of developing funding priorities.

Determination of funding priorities leads to the release of funding solicitations and, then, to studies being funded. Completion of these investigations (and, usually, publication of the results) eventually adds to the body of evidence, and may prompt updates of the review. Of course, many factors outside this logic model may affect research funding decisions, such as activities by advocacy groups, advances in basic science, changes in organization structure, or legislative changes such as the recent passage of the Patient Protection and Affordable Care Act.

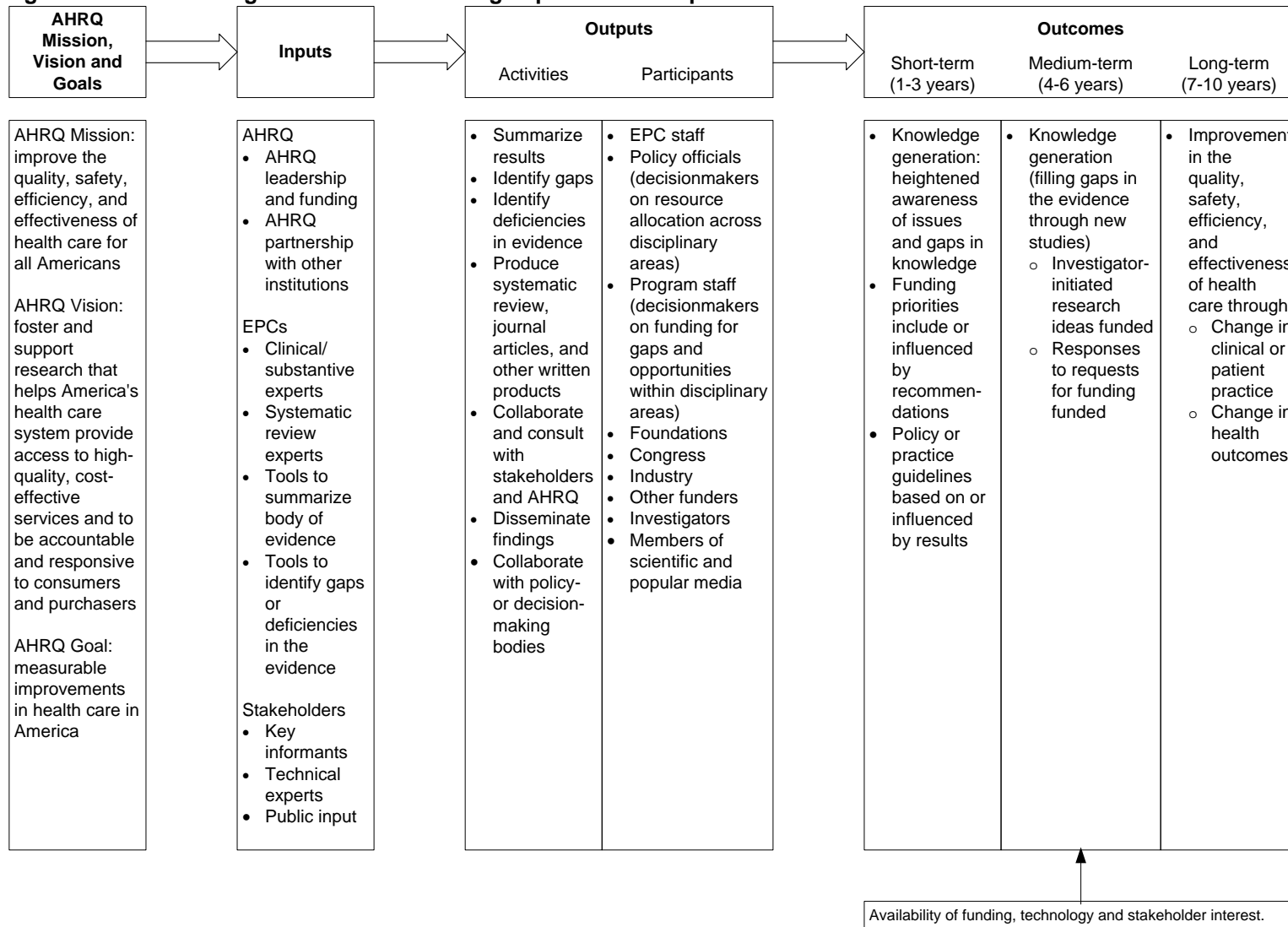
Based on this analytic framework, we developed an evaluation logic model (Figure 2), using the standard evaluation framework that identifies inputs, outputs, and outcomes. Impact refers to both outputs and outcomes.<sup>8</sup> In this scheme,

- inputs are resources, contributions, investments that go into the program;
- outputs are activities, services, events, and products that reach people who participate or who are targeted; and
- outcomes are results or changes for individuals, groups, communities, organizations, or systems.

**Figure 1. Analytic framework: processes and activities leading to impact of EPC reviews on future research**



**Figure 2. Evaluation logic model for evaluating impact of EPC reports on research outcomes**



Specific challenges for empirical measurement of the effect that EPC reports might have on the funding and framing of new research include fluctuations in the external funding environment, the time lag between publication of the EPC report and release of solicitations for research applications, and the lack of visibility of planning processes within funding agencies to outsiders.

## Key Questions

Based on our objectives, analytic framework, and the logic model, we ask the following key questions (KQs):

**Key Question 1. What is the impact of future research sections from EPC reports on solicited or funded research?**

**Key Question 2. What best practices or elements of the future research sections are likely to increase the impact of future research sections in EPC reports on future research?**

In addressing KQ 1, we acknowledge that the effects of EPC reports might occur directly through direct dissemination of the reports and subsequent filling of evidence gaps that the future research needs sections of the reports identify; they could also occur indirectly through other pathways, which we will seek to elucidate. As suggested by the logic model, we anticipate that EPC reports can have impact in the short term through both heightened awareness of issues and gaps in knowledge and influence on funding priorities and policy or practice guidelines. In the medium term, we anticipate that EPC reports can have effects through the commissioning of new research that fills specific, EPC-identified gaps. In the long term, EPC reports can influence improvements in the quality, safety, efficiency, and effectiveness of health care that then lead to new areas of research.

In answering KQ 1, we will seek information on barriers and facilitators of the pathways for impact. Examining these barriers and facilitators will help us to answer KQ 2. In answering KQ 2, we will focus on the impact of the reports on future research; although changes to elements of the report may improve the overall impact of the report, the focus of KQ 2 is the impact of the project on future research.

## Selected Case Studies

We selected two systematic reviews as case studies for this analysis: the 2004 report on literacy and health outcomes<sup>9</sup> and the 2004 reports on omega-3 and cardiovascular disease (CVD).<sup>10,11</sup> The methods chapter of this report provides further details on the selection of these case studies.

**Literacy and health outcomes.** The Berkman et al. 2004 report on literacy and health outcomes examined (1) whether literacy skills were related to use of health care services, health outcomes, costs of health care, and disparities in health outcomes or health care service use according to race, ethnicity, culture, or age, and (2) for individuals with low literacy skills, what were effective interventions to improve use of health care services, improve health outcomes and/or health care service use overall and among different racial, ethnic, cultural, or age groups, and affect the costs of health care.<sup>9</sup>

The report concluded that “low literacy is associated with several adverse health outcomes, including low health knowledge, increased incidence of chronic illness, poorer intermediate disease markers, and less than optimal use of preventive health services. Interventions to mitigate the effects of low literacy have been studied, and some have shown promise for improving patient health and receipt of health care services” (Berkman et al. 2004, p. vi).<sup>9</sup>

Berkman and colleagues offered the following research recommendations:<sup>9</sup>

- Conduct research on factors that mediate the relationship between literacy and important health outcomes. For instance, one question is whether poor reading ability causes adverse health outcomes or is a marker for other problems, such as low socioeconomic status, poor self-efficacy, low trust in medical providers, or impaired access to care.
- Perform more prospective cohort studies that measure changes in outcomes and literacy over time. The aim was to provide a greater understanding of the relationships among literacy, age, and health outcomes and the extent to which changes in health status actually affect literacy.
- Further develop measurement techniques for low-literacy populations.
- Test whether measuring or stratifying outcomes by numeracy provides additional predictive ability for health outcomes versus measuring and stratifying outcomes by literacy alone.
- Conduct studies linking short-term knowledge changes to important health outcomes.
- Carry out analyses to isolate the individual effect of elements of multicomponent interventions.
- Document the importance of low patient literacy in chronic illness programs.
- Study the extent to which interventions designed to allay the effects of low literacy are effective compared to the effects of other interventions in improving health outcomes.
- Stratify results of intervention studies by literacy level.
- Mount studies on provider-patient communication interventions that go beyond written materials.
- Evaluate further the concept of health literacy and its role beyond reading ability (or scores on reading ability).

**Omega-3 and cardiovascular disease.** The Tufts EPC produced a three-part report on omega-3 fatty acids and cardiovascular risk.<sup>10-12</sup> For the purposes of this review, we included the two reports that focused on outcomes and risk factors in humans;<sup>10,11</sup> we excluded the omega-3 report that focuses on arrhythmogenic mechanisms in animals and isolated organ/cell cultures.<sup>12</sup>

The Wang et al. report was the first of the three-part report on this topic and assessed the benefits of omega-3 fatty acid supplements or fish consumption on various CVD outcomes and the adverse events associated with intake of omega-3 fatty acid supplements.<sup>13</sup> The report concluded that “consumption of omega-3 fatty acids from fish or from supplements of fish oil reduces all cause mortality and various CVD outcomes. The evidence for ALA [alpha-linolenic acid] supplements is sparse and inconclusive. The adverse events due to consumption of fish oil or ALA supplements appear to be minor” (Wang et al., 2004, p. vi).<sup>14</sup>

Wang et al. offered the following research recommendations (pp. 99-100):

- “In general, future studies of omega-3 fatty acids should include the following:
  - Omega-6/omega-3 ratio should always be estimated and reported.



- Attempts should be made to determine the effect of higher fish intake on the consumption of other foods in the diet, specifically meat and cheese (sources of saturated fat).
- Future prospective cohort studies and diet trials on fish consumption should place special emphasis on collecting data on fish consumed, type of fish, and method of preparation.
- Well-designed, multicenter RCTs [randomized controlled trials] are needed to assess the effect of omega-3 fatty acid consumption on CVD outcomes in primary and secondary prevention settings. The trial design should include a period of long-term followup for 3 to 5 years so that long-term effects of omega-3 fatty acids can be monitored.
- Additional research should address questions about the effect of omega-3 fatty acid consumption on CVD outcomes in specific populations, including patients with diabetes and other chronic diseases.
- The potential effect of ALA is unknown. Current data sets are of poor quality and are too limited for adequate assessment. More trials are needed to confirm or report the effect of ALA, separate from fish or fish oil, on CVD outcomes. We need to know more about the potential interaction of ALA with EPA+DHA [eicosapentaenoic acid and docosahexaenoic acid].
- The relative effect of ALA versus fish oil is not well defined. Comparative trials between these two supplements should be conducted. Given the abundance of soybean and canola oils relative to fish in the diet, it would be useful to understand the economic and ecological impact of increased fish intake, and the potential to initiate change in US dietary patterns.”

The Balk et al. report assessed the consumption of omega-3 fatty acids on various CVD risk factors and intermediate markers of CVD in healthy people and people with dyslipidemia, diabetes, or known CVD. The report noted that “a large, consistent beneficial effect of omega-3 fatty acids was found only for triglyceride levels. Little or no effect of omega-3 fatty acids was found for a variety of other cardiovascular risk factors and markers of cardiovascular disease. The benefits of omega-3 fatty acids on reducing cardiovascular disease are not well explained by the fatty acids’ effects on the cardiovascular risk factors we examined. A strong, linear association was found across studies between omega-3 fatty acid intake and tissue levels” (Balk et al., 2004, p. vi).<sup>13</sup>

Balk et al. identified the following research recommendations (p. 116):

- “Future studies on CVD risk factors and intermediate markers of CVD should address the question of possible differences in the effect of omega-3 fatty acids in different subpopulations and as related to different covariates, including dose and duration of intake.
- The potential effect of ALA (18:3 n-3) is unknown. More multicenter trials are needed to assess the effect of ALA, separate from the effect of EPA+DHA, on CVD risk factors.
- Additional research is needed to clarify the effect of omega-3 fatty acids on markers of glucose tolerance. Specifically, sufficiently large trials are needed that perform appropriate sub-analyses to determine the cause of heterogeneity in effect across studies.
- The total dietary omega-6 to omega-3 fatty acid ratio should be estimated, reported, and analyzed in terms of its effect on outcomes and its association with any effect of omega-3 fatty acid treatment.

- Future research should attempt to determine the effect of higher fish intake on the consumption of other foods in the diet, specifically sources of saturated fat such as meat and cheese.
- Future prospective cohort studies and diet trials on fish consumption should place special emphasis to collecting data regarding the quantity and type of fish consumed and the method of preparation.”

## **Organization of the Remainder of the Report**

Chapter 2 describes the methodological constraints and approaches to evaluating the impact of research; it gives our specific indicators and measures and describes our methods to describe each outcome. Chapter 3 first presents the findings on KQ 1, that is, the impact of future research sections from EPC reports on solicited or funded research. It then compiles evidence on KQ 2, that is, factors likely to alter the impact of future research sections in EPC reports. Chapter 4 discusses the implications of the findings on likely pathways that influence the use of the recommendations of the report in future research.

## Methods

This chapter describes the methodological factors we considered in evaluating the impact of systematic reviews on future research and highlights their implications for the methodological approaches selected.

### Methodological Considerations and Approaches

Methodological concerns in identifying the effects of EPC reviews on research (opportunities, priorities, studies begun, and/or studies completed) include the following:

1. attributing impact to the EPC report itself, given that other factors may influence policy decisions or changes in research directions or opportunities;
2. accounting for the time lag between the report and the change in research funding priorities or actual investigations; and
3. taking into consideration what might have occurred in the absence of the EPC report.<sup>6,15</sup>

These three issues are interrelated. For example, for EPC reports to have any influence or effect will take time, the duration of which will be variable and somewhat unpredictable. Such impacts will take even more time to detect, but the further in time that they occur from the release of the report, the more difficult it is to attribute effect to the individual report. That is to say, exogenous variables could have influenced the impact.

Another challenge is over-attributing impact to the EPC report because of the multiple pathways through which such outcomes could have occurred. Additionally, trying to attribute credit to a particular report assumes that downstream consumers (funders and investigators) can parse the effect of an individual report on their overall thought processes.<sup>6</sup> In fact, one study found that policymakers were more likely to be informed by a body of research rather than a specific finding.<sup>16</sup> As a result of these concerns, evaluators focus on contribution, rather than attribution, and they lay out a clear logic model to understand the possible pathways for contribution.<sup>6</sup>

A time lag that is too long will result in impacts that may have already occurred and are difficult to attribute to the EPC report. With too short a time lag, the effects may simply not have had sufficient time to occur. Evaluators suggest that a time lag of 5 to 10 years following the completion of the research is needed for discernible effects to develop, but they caution that a 2-year time lag may be more appropriate for “hot” topics<sup>16</sup> or those in which the policy change is relatively simple.

An experimental design, i.e., a comparison of outcomes with and without the EPC report is, of course, neither plausible nor feasible in this context. At a minimum, addressing the counterfactual question—what if the report had not been published?—requires collection of baseline information and context.<sup>6</sup>

Two basic approaches can be used to answer questions of research impact: historical tracing or forward tracing.<sup>17</sup> With historical tracing (as with the classic Comroe and Dripps study<sup>18</sup>), evaluators first identify key advances and then determine the bodies of evidence that influenced the key advances. This particular approach relies heavily on bibliometric techniques (e.g., weight and interconnectedness of citations). Forward tracing starts with specific research and can use a variety of methods such as case studies, interviews, questionnaires, and bibliometric techniques to identify both the effects and the pathways for those effects. The former technique requires a comprehensive bibliographic source, without which results are likely to be biased. The latter

technique, through its narrower focus on the specific report for which effects are to be determined, uses a more targeted bibliographic search than historical tracing but may be particularly susceptible to biases relating to attribution. An additional concern with case study analyses that are often used in forward tracing is that of selection bias in identifying the cases, which may lead to focusing excessively on positive rather than negative findings or conclusions.

## **Implications of Methodological Constraints on Project Methods**

We attempted to answer the two key questions using forward tracing for two case studies. We used a combination of methods: key informant interviews, web searches, and bibliometric techniques for citation analysis. These methods are consistent with the most commonly used approach in assessing research impact, the “payback” framework.<sup>19,20</sup> The payback framework describes the sequence of activities in the research process, from needs assessment to dissemination, and it identifies a range of benefits or “paybacks” from the research.<sup>20</sup>

In addressing the two key questions and accounting for potential biases, we took the following tasks to be critical: (1) developing an analytic framework to depict and separate, when possible, the pathways for attribution of impact directly to the systematic review as contrasted with its contribution to a larger set of factors that impact future research; (2) stating the considerations weighed in selecting case studies; and (3) carrying out some assessment of funding priorities before and after the publication of the report to avoid a focus on overly positive findings.

**Development and revision of the analytic framework and logic model.** Chapter 1 presents our initial analytic framework (Figure 1), which we developed to illustrate the pathways of influence for an individual report. The logic model (Figure 2) represents anticipated outcomes at a broader level, for the AHRQ program. The programmatic considerations illustrated in the logic model are a means of specifying and differentiating among proximal and distal outcomes. In other words, the logic model serves as a heuristic to lay out a temporal sequence for events that lead to impact on future research. The logic model may not always translate directly for specific reports because the implied temporal sequence in it may not always hold true. For instance, “medium-term” impacts on knowledge generation may occur contemporaneously with “long-term” impacts on clinical practice.

The analytic framework, together with the logic model, guided our choice of outcomes, measures, and indicators for impact (Table 1). We explicitly asked each key informant for feedback on the analytic framework and used their input to revise our hypothesized pathways for impact. Their contributions served an important role in clarifying and validating the depicted pathways for impact. In addition, we used other sources to inform the revised version of the analytic frameworks (presented in Chapter 4).

**Table 1. Indicators of research outcomes and impact from future research sections in EPC reports**

Type of Outcome	Specific Outcome	Indicators	Methods
Short term (1-3 years)	Knowledge generation: heightened awareness of issues and gaps in knowledge	<ul style="list-style-type: none"> <li>- Heavy citation of the relevant papers or widespread use of a tool arising from the research</li> <li>- Public interest in the work from media</li> <li>- Downloaded requests for relevant AHRQ publications</li> <li>- Requests to EPC investigators to consult with or collaborate with funders, policymakers, or other investigators on research gaps identified by systematic review</li> </ul>	<ul style="list-style-type: none"> <li>- Bibliometric analysis</li> <li>- Web searches</li> <li>- Downloaded data (from AHRQ)</li> <li>- Qualitative data from interviews with EPC investigators</li> <li>- Orders from the AHRQ publication clearinghouse</li> </ul>
	Funding priorities included or influenced by systematic review recommendations	<ul style="list-style-type: none"> <li>- Citation of relevant papers in requests for funding or in funding prioritization documents</li> </ul>	<ul style="list-style-type: none"> <li>- Bibliometric analysis</li> <li>- Web searches</li> <li>- Qualitative data from interviews with EPC investigators and funders</li> </ul>
	Policy or practice guidelines based on or influenced by results	<ul style="list-style-type: none"> <li>- Citation of relevant papers in policy or practice guidelines</li> </ul>	<ul style="list-style-type: none"> <li>- Bibliometric analysis</li> <li>- Web searches</li> <li>- Qualitative data from interviews with EPC investigators and policy/practice guideline developers</li> </ul>
Medium term (4-6 years)	Knowledge generation (filling gaps in the evidence through new studies) <ul style="list-style-type: none"> <li>- Investigator-initiated research ideas funded</li> <li>- Responses to requests for proposals</li> </ul>	<ul style="list-style-type: none"> <li>- Citation of relevant papers in successful grant applications</li> </ul>	<ul style="list-style-type: none"> <li>- Bibliometric analysis</li> <li>- Qualitative data from interviews with EPC investigators and funders</li> </ul>
Long term (7-10 years)	Improvement in the quality, safety, efficiency, and effectiveness of health care	<ul style="list-style-type: none"> <li>- Change in clinical or patient practice</li> <li>- Change in health outcomes</li> </ul>	<ul style="list-style-type: none"> <li>- Qualitative data from interviews with EPC investigators and AHRQ staff</li> </ul>

**Selection of case studies.** We sought nominations for case studies from EPC directors to identify EPC reports known to have had impact. We identified 16 potential case studies. In evaluating each nomination, we considered and flagged concerns regarding measurement or attribution of impact and the likelihood for potential conflict of interest (Appendix A). In narrowing the selection further from this list, we consulted with senior AHRQ staff, specifically Stephanie Chang and Yen-Pin Chiang.

Two important additional considerations influenced the final selection of the topics: ongoing update activities and variation in the topic. The 2004 report on literacy and health outcomes<sup>9</sup> and the 2004 reports on omega-3 and cardiovascular issues<sup>10,11</sup> were in the process of updates, either formally or as part of a methods project. In addition, each of these projects represented very different types of topics. Health literacy is a broad topic that influences many different substantive areas; omega-3, by contrast, is a much more focused topic. The variation in topics

presented an opportunity to explore different pathways for impact. The choice of these relatively early-generation reports, although suitable for the evaluation of medium- and long-term outcomes, risks the production of insights or conclusions that are no longer relevant in light of changes in the EPC program.

**Assessment of funding priorities before and after the systematic reviews.** We addressed this issue through reviews of federal requests for applications and program announcements from 1993 to 2010 (a period that includes 11 years of funding before release of the reports and 6 years thereafter). We also asked funders who offered anecdotal evidence of changes in funding priorities to describe the contribution of the AHRQ report to these changes.

## **Data Sources for Bibliometric Analysis**

Our study, to the best of our knowledge, is the first to examine the impact of systematic reviews on future research. No guidance exists for how to select among sources of data and how to analyze citations. We drew, therefore, on established social-science approaches for program evaluations.

We began our searches by attempting to confirm the feasibility of the historical tracing approach rather than forward tracing. Our searches on health literacy used terms such as “literacy” or “health literacy,” depending on the source; when possible, we used date limits from 2003 to 2010. These searches yielded more than 4,000 hits; we interpreted these results to suggest that a forward-tracing approach would be more feasible than historical tracing.

In the absence of guidance on the best source of data, we planned to test the use of multiple sources of data. Specifically, we conducted searches in multiple funding databases to identify funding publications associated with EPC reports and solicitations that cited the selected EPC reports or associated publications. To identify the most appropriate data sources for citation analysis for the two case studies, we undertook an exploratory search for one specific EPC systematic review (*Community-based Participatory Research: Assessing the Evidence*)<sup>21</sup> that we knew from personal communications with investigators and funders to have had an impact on knowledge generation, i.e., on the development of federal requests for proposals and applications. We conducted an exhaustive search and found that numerous data sources did not yield any results. Appendix B presents the full search results for all data sources.

We used the results of this exploratory work to inform the choice of data sources for this task (Table 2). We describe methods for each source below.

**Table 2. Data sources for bibliometric analysis**

Type of Literature	Source	Ease of Use*	Import Function	Dates of Coverage
<b>Published literature</b>	ISI Web of Science	Satisfactory	Yes	Science Citation Index Expanded (SCI-EXPANDED)—1955-present Social Sciences Citation Index (SSCI)—1956-present Arts & Humanities Citation Index (A&HCI)—1975-present
	MEDLINE® via PubMed	Satisfactory	Yes	1950-present
<b>Ongoing studies</b>	ClinicalTrials.gov	Satisfactory	No	Unavailable Updated continuously
	NIH RePORTER (previously CRISP)	Difficult	No	1986-present
<b>Solicitations</b>	National Institutes of Health [NIH] Guide for Grants and Contracts	Difficult Phrase searching unavailable	No	1993-present Historical files available 1970-1992

\*We rated ease of use as “Satisfactory” or “Difficult.” Sources with a “Satisfactory” rating recognized phrase searching and Boolean connectors, or they provided other helpful search instructions. Sources with a “Difficult” rating did not recognize phrase searching and/or Boolean connectors, and/or they gave no search instructions, and/or the search results did not contain the search terms.

Note: CRISP = Computer Retrieval of Information on Scientific Projects.

**Published literature.** We used information provided by our key informants to obtain a list of “first-generation” references; those are publications derived directly from the report (i.e., peer-reviewed publications drawing upon the reports) (Table 3). We then used ISI Web of Science and PubMed Central citation listings in MEDLINE for each reference to obtain information on the weight and interconnectedness of citations. We ran searches in these sources for each of the original citations and first-generation citations to obtain the list of “second-generation” citations.

**Table 3. AHRQ systematic review and related citations**

Systematic Review	Original Citation	First-Generation Citations
<b>Report on literacy and health outcomes</b>	<ul style="list-style-type: none"> <li>Berkman ND, DeWalt DA, Pignone MP, Sheridan SL, Lohr KN, Lux L, Sutton SF, Swinson T, Bonito AJ: Literacy and health outcomes, summary, evidence report. Rockville, MD, Agency for Healthcare Research and Quality, 2004 (Tech. Assessment no. 87)</li> </ul>	<ul style="list-style-type: none"> <li>DeWalt DA, Berkman ND, Sheridan S, Lohr KN &amp; Pignone MP. Literacy and health outcomes: A systematic review of the literature. <i>J Gen Intern Med.</i> 2004;19:1228–1239.</li> <li>Pignone M, DeWalt DA, Sheridan S, Berkman N, Lohr KN. Interventions to improve health outcomes for patients with low literacy. A systematic review. <i>J Gen Intern Med.</i> 2005;20:185–92.</li> </ul>
<b>Omega-3 reports</b>	<ul style="list-style-type: none"> <li>Wang C, Chung M, Lichtenstein A, et al. Effects of omega-3 fatty acids on cardiovascular disease. Evidence Report/Technology Assessment No. 94 (Prepared by Tufts-New England Medical Center Evidence-based Practice Center, under Contract No. 290-02-0022). AHRQ Publication No. 04-E009-2. Rockville, MD: Agency for Healthcare Research and Quality 2004.</li> <li>Balk E, Chung M, Lichtenstein A, et al. Effects of omega-3 fatty acids on cardiovascular risk factors and intermediate markers of cardiovascular disease. Evidence Report/Technology Assessment No. 93 (Prepared by Tufts-New England Medical Center Evidence-based Practice Center under Contract No. 290-02-0022). AHRQ Publication No. 04-E010-2. Rockville, MD: Agency for Healthcare Research and Quality 2004.</li> </ul>	<ul style="list-style-type: none"> <li>Wang C, Harris WS, Chung M, et al. n-3 Fatty acids from fish or fish-oil supplements, but not alpha-linolenic acid, benefit cardiovascular disease outcomes in primary- and secondary-prevention studies: a systematic review. <i>Am J Clin Nutr.</i> 2006 Jul;84(1):5-17.</li> <li>Balk EM, Lichtenstein AH, Chung M, et al. Effects of omega-3 fatty acids on coronary restenosis, intima-media thickness, and exercise tolerance: a systematic review. <i>Atherosclerosis.</i> 2006 Feb;184(2):237-46.</li> <li>Balk EM, Lichtenstein AH, Chung M, et al. Effects of omega-3 fatty acids on serum markers of cardiovascular disease risk: a systematic review. <i>Atherosclerosis.</i> 2006 Nov;189(1):19-30.</li> <li>Balk EM, Horsley TA, Newberry SJ, et al. A collaborative effort to apply the evidence-based review process to the field of nutrition: challenges, benefits, and lessons learned. <i>Am J Clin Nutr.</i> 2007 Jun;85(6):1448-56.</li> </ul>

**Ongoing studies.** We searched two sources for ongoing studies and found little usable information. NIH RePORTER does not allow downloads of abstracts when searches yield more than 100 abstracts. Abstracts, when downloadable, lack sufficient information to judge whether the AHRQ reports and their derivative products influenced these studies. We do not use these results in the analysis.

**Solicitations.** We searched the National Institutes of Health [NIH] Guide for Grants and Contracts Web site for “health literacy” and “omega 3,” respectively. The Web site is limited in its search functionality: if users request inactive solicitations, they cannot set date limits. The yield included 92 requests for applications (RFAs) and program announcements since 1993 for health literacy and 34 for omega-3 (Appendix C).



## Update Searches

As noted earlier, one of the methodological limitations of the forward-tracing approach is its focus on positive results. Searches for studies in ISI Web of Science or MEDLINE<sup>®</sup> provide information on weight and interconnectedness of citations, but they cannot provide information on the *extent* to which the systematic review and its byproducts influenced future research. To understand the extent to which systematic reviews have had impact, we needed a denominator, which is effectively the (number of) studies that could potentially have cited the systematic review. As noted earlier, we selected both these case studies because they were being updated at the time (early 2010), and thus we were able to obtain updated search results for both of them.

The health literacy report conducted a full update of the literature and identified 177 new citations from 2003 to 2010 that met inclusion criteria.<sup>22</sup> The update search for omega-3 was an abbreviated search for the Balk et al. report on cardiovascular risk factors and intermediate markers and was conducted primarily to understand signals for whether the reports were ready to be updated.<sup>13</sup> These searches were conducted only in key journals and yielded 66 new citations that met inclusion criteria.

The availability of the results of these update searches considerably simplified the effort of identifying the denominator. We did not undertake this effort for the Wang et al. report on cardiovascular disease<sup>14</sup> because the search for updated literature would have been beyond the scope of this project.

We obtained full-text articles for each citation and reviewed each article for evidence of having cited the systematic review or associated articles (Appendix D). We abstracted data showing how each article cited the systematic review or associated articles. We reviewed each article and abstraction dually and recorded the context and purpose of the citation.

## Selection and Interviews of Key Informants

We planned to conduct key informant interviews with no more than nine EPC investigators and other key informants such as practice guideline developers, funders, other investigators, or AHRQ staff for each of the two selected EPC reports. We used snowball recruitment to identify and recruit key informants. We intended to interview at least two investigators of the original report, two funders, and two external experts. We began our interviews with the investigators of the reports and were guided by their input in the selection of subsequent key informants. A total of six key informants for the literacy and health outcomes case study and seven for the omega-3 and cardiovascular disease case study were able to provide us input within the timeframe of this report (Appendix E).

The chief purposes of the interviews were to locate (1) relevant funding solicitations and investigator-initiated funding and to identify (2) barriers and facilitators to the use of past reports for developing funding agendas or solicitations (Table 4). In addition to the questions listed in Table 4, we requested that the EPC investigators review and add to the list of citations (reports, journal articles, book chapters) that we had identified as being associated with their report. We also requested information on related ancillary materials produced by the EPC or AHRQ such as editorials, op-ed articles, policy briefs, presentations to academic and policy gatherings, continuing medical education materials, and clinical practice guidelines.

**Table 4. Questions for key informants**

<b>Indicator</b>	<b>Question</b>
Public interest in the work from media	Have you or others on the team been asked to speak with members of the media?  [If yes] Can you describe your experience?
Requests to EPC investigators to consult with or collaborate with funders, policymakers, or other investigators on research gaps identified by systematic review	Have you or others on the team been asked to consult with or collaborate with funders on research gaps identified by systematic review? Policymakers? Guideline developers? Other investigators? Other stakeholders?  [If yes] What was the nature of the collaboration? What factors contributed to collaboration?  What do you perceive as barriers to collaboration? How can these barriers be addressed?
Citation of relevant papers in requests for funding or in funding prioritization documents	To your knowledge, has [the report and/or its ancillary products] influenced requests for funding or in funding prioritization documents?  Has [the report and/or ancillary products] been cited in requests for funding or in funding prioritization documents? What factors contributed to its use?  [If yes] Can you share these materials?  What do you perceive as barriers to the use of the report? How can these barriers be addressed?
Policy or practice guidelines based on or influenced by results	To your knowledge, has [the report and/or its ancillary products] influenced policy or practice guidelines?  Has [the report and/or ancillary products] been cited in policy or practice guidelines?  [If yes] Can you share these materials?
Citation of relevant papers in successful grant applications	To your knowledge, has [the report and/or its ancillary products] influenced investigator-initiated funding?  Has [the report and/or ancillary products] been cited in successful grant applications? What factors contributed to its use?  [If yes] Can you share these materials?  What do you perceive as barriers to the use of the report? How can these barriers be addressed?
Change in clinical or patient practice	To your knowledge, has [the report and/or its ancillary products] resulted in changes in clinical or patient practice?  [If yes] What sources support evidence of such change? What factors contributed to its impact?  What do you perceive as barriers to the use of the report? How can these barriers be addressed?
Change in health outcomes	To your knowledge, has [the report and/or its ancillary products] resulted in changes in clinical or patient practice?  [If yes] What sources support evidence of such change? What factors contributed to its impact?  What do you perceive as barriers to the use of the report? How can these barriers be addressed?

## **Analysis of Key Informant Interviews**

We used QSR International's NVivo 9 qualitative data analysis software to analyze the data. The Principal Investigator (PI) conducted all the interviews. Two other investigators generated the transcripts from the interviews, and the PI reviewed all the transcripts for accuracy. One staff member coded all the interviews in NVivo. To do this, he used the analytic framework and logic model as a primary structure for coding the interview questions that related directly to short-, medium-, and long-term impact of the report; he then used the grounded theory approach for open-ended questions relating to the barriers and facilitators of impact.

## **Other Sources of Information**

We obtained information from AHRQ on the numbers of downloads from the AHRQ Web site and orders from the AHRQ clearinghouse. These data reveal trends in dissemination and use of the reports rather than information on the extent of impact.

We reviewed AHRQ's list of "articles of interest" (<http://www.ahrq.gov/news/articles.htm>) and compared its entries with the results from the updated article searches. We found very little overlap (two studies for health literacy and none for omega-3). The AHRQ "articles of interest" search is designed to be broad rather than focused. It identifies studies that cite AHRQ-funded research or contracts, either within the body of the text or in references. Not all the articles that cite AHRQ-funded research would be relevant to an update of the systematic review. We do not include these results in the body of this report.

# Results

## Organization of Results

The results chapter presents results for KQ 1 first, followed by results for KQ 2. KQ 1 asks about the impact of EPC reports on future research. We present results for the literacy and health outcomes case study first, followed by the case study on omega-3 and CVD. As noted earlier, the latter case study includes two reports, but we do not provide completely parallel results for both reports: update search results were available only for the Balk et al. report.<sup>14</sup> In keeping with our logic model, we distinguish among inputs, outputs, short-term outcomes, medium-term, and long-term outcomes to answer KQ 1 for each case study. For each type of outcome, we summarize the evidence on specific outcomes, using a variety of indicators and data sources (as detailed in Table 1). Our results for KQ 2 draw on qualitative evidence on barriers and facilitators to impact. KQ 2 summarizes themes across case studies and different lengths of outcomes to identify facilitators and barriers associated with the EPC reports that may modify their impact on future research.

## Impact of EPC Reports (KQ 1): The Literacy and Health Outcomes Case Study

**Inputs.** The American Medical Association (AMA) requested a report on literacy and health outcomes; AHRQ funded it. Principal authors included systematic review expert Nancy Berkman, Ph.D., of RTI International, and substantive experts Darren DeWalt, M.D., M.P.H., and Michael Pignone, M.D., M.P.H. of UNC.

**Outputs.** In January 2004, AHRQ released the report on literacy and health outcomes. The report prompted production of two journal articles that appeared in 2004 and 2005,<sup>23,24</sup> the first authors were DeWalt and Pignone, respectively. DeWalt and Pignone also published editorials, including “Reading is Fundamental: the Relationship between Literacy and Health” in the 2005 *Archives of Internal Medicine*<sup>25</sup> and “Literacy and Health Outcomes: Is Adherence the Missing Link?” in the 2006 *Journal of General Internal Medicine*.<sup>26</sup>

**Short-term impact: Increased awareness of issues.** Our analysis of the short-term impact of this report comes from several sources: evidence of citation of the report through searches from the updated reports, ISI Web of Science, and PubMed Central; dissemination through downloads and orders of the AHRQ report; qualitative reports of media interest; and heightened collaboration in the field.

*Citation of the report.* Our analysis of the literature from the health literacy update report suggests widespread citation of the 2004 report (Appendix D). Of 177 articles identified through the update search, nine had been published before the report and, therefore, could not have been influenced by the report. More than one-third (60 of 168) of the remaining new articles cited the 2004 report or its derived articles. Twenty-two articles cited the report in more than one context. Most commonly, articles cited the report to support the problem statement in the article, to illustrate the state of the science, or to place the findings in context (Table 5).

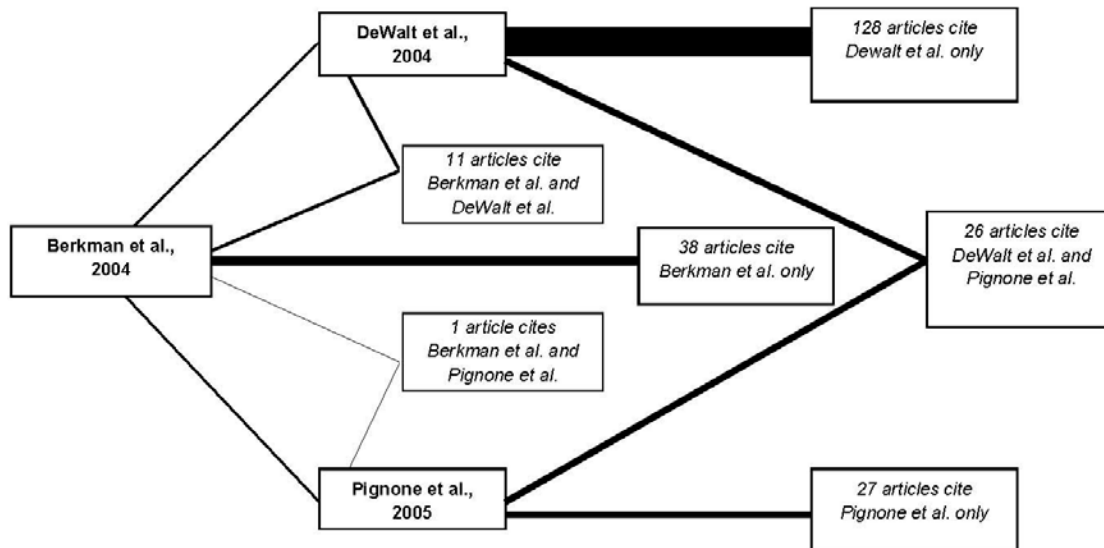
**Table 5. Citations from the updated health literacy report: Reasons for citing the 2004 AHRQ report**

Reason for citation	Number of articles citing the report
Citation supports problem statement	22
Citation illustrates state of the science	19
Citation places findings in context	19
Citation shows how study fills gaps	13
Citation helps to justify use of measure	8
Citation supports research recommendations of the study	3
Citation shapes hypotheses	1
Total number of articles citing the report or derived articles	60*

\* 22 articles cite the report more than once, so total reasons for citing the AHRQ report exceed the number of articles.

The most commonly cited reference was the DeWalt et al. article.<sup>23</sup> Our analysis of published literature from ISI Web of Science and PubMed Central also supports the finding that the DeWalt article was the most heavily cited source (Figure 3). The weight of the citation is reflected in the arrow.

**Figure 3. Weight and interconnectedness of health literacy citations to the AHRQ report and derived articles\***

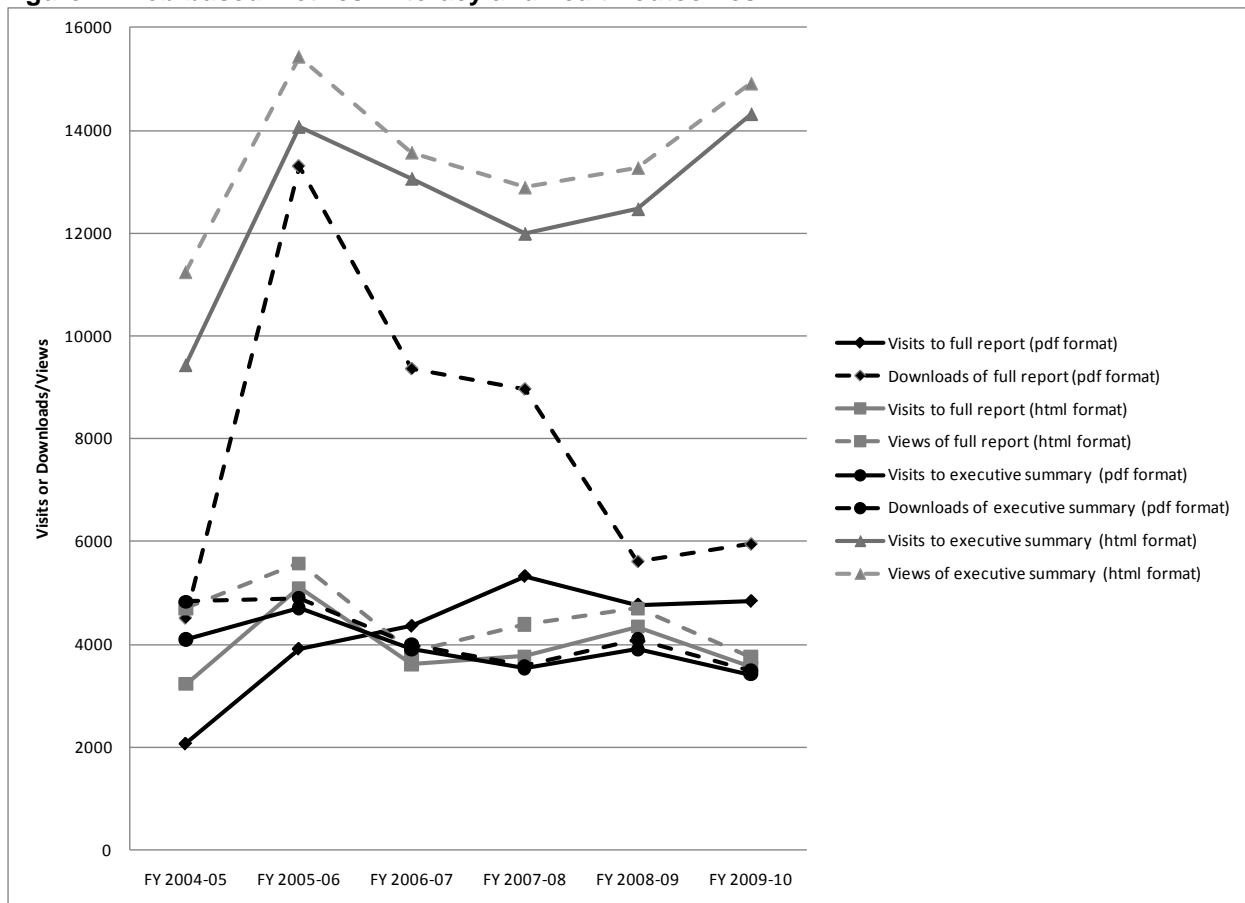


*Media coverage.* The EPC’s literacy and health report generated some media interest. EPC investigators, along with authors of a report from a committee of the Institute of Medicine (IOM) on health literacy (*Health Literacy: A Prescription to End Confusion*), presented their findings to the National Press Club in Washington, D.C., on April 8, 2004. Carolyn Clancy, the AHRQ Director, introduced the reports. However, beyond the Press Club appearance, key informants familiar with the EPC report’s release did not remember significant media coverage. One key informant noted that even the Press Club publicity was somewhat stifled by testimony given by the then-Secretary of State Condoleezza Rice before the U.S. Congress that same day. One stakeholder remembered that the AMA (the report’s sponsor) used its newsletters, weekly newspaper, and Web site to disseminate results.

*Dissemination through downloads and requests for the AHRQ report.* AHRQ maintains a record of downloads through HTML and PDF formats since the publication of the report. Over time,

interest in the executive summary in both PDF and HTML formats continues to be quite high (Figure 4) (2004 through October 2010). The only product for which demand has declined over time is the PDF format of the full report. AHRQ's Clearinghouse processed 613 orders for a total of 1,196 copies through the same period.

**Figure 4. Web-based metrics: Literacy and health outcomes**



**Notes:** Visits: a series of actions that begins when a visitor views the first page from the server and ends when the visitor leaves the site; these are a good indication of traffic to a site in terms of users. Page views: access to any file classified as an HTML page. The page and its embedded files count as a single page view; these are a good indication of usage of content. Download: access to any file type that is not an HTML page, such as PDF, PowerPoint, and multimedia files; these are a good indication of commitment to those file types for use.

*Collaboration.* EPC investigators were able, despite some constraints, to collaborate to fill research gaps following publication of the report. Some key informants believed that the EPC investigators were not funded either to disseminate the reports more broadly or to maintain systematic contact with policymakers or key stakeholders; this problem made it difficult for them to build on report findings.

However, several of the EPC investigators were in a position, as a result of their prominence in the field independent of the report, to collaborate on future health literacy research. Both Drs. DeWalt and Pignone were involved with health literacy before the EPC report and continued their work in the field after completion of the report. Their participation in the EPC report, while only one of many qualifications, did prove helpful in procuring future work. For example, AHRQ awarded a team led by Dr. DeWalt with a project to develop a Universal Precautions Care Toolkit. One respondent noted that although Dr. DeWalt's clinical research may have been

a more crucial factor in the AHRQ decision, participation with writing the EPC report was also likely to have been influential.

The EPC report, along with several other seminal developments such as the IOM report, ushered in new interest in health literacy that opened pathways for consultation and collaboration. “[T]he report helped to create a climate that created interest in the area [of health literacy].” One key informant noted that “the 2004 report helped on some level to push things in this direction so that AHRQ starts funding things like this [AHRQ-funded Universal Precautions] toolkit.”

One key informant noted that the topic of health literacy had been present for some time (it was a part of Healthy People 2010), but that the EPC report (together with the IOM report) pushed the topic to new visibility. The AHRQ and IOM reports led to reassessments of the topic; for example, two internal meetings with AHRQ leadership in 2005 changed the course of AHRQ involvement in health literacy. The EPC and the IOM reports helped convince the AHRQ leadership of the need to create an action plan for moving forward with research on the issue.

The ascendancy of health literacy as a topic also resulted in more and bigger health literacy conferences. For example, the AHRQ Health Literacy Annual Research Conference has been established and has built interest in the field. The gaps in evidence highlighted by the EPC report illustrated that the field of research was “not going to take care of itself without some nurturing.” One key informant from AHRQ noted the direct correlation between the report and the conference:

“[The conference] is very much trying to build the field, [to recruit] a cadre of researchers capable and interested in health literacy. One of the findings of the report was that there is not enough research to form an evidence base, and one of the ways to get more research is to support the development of young researchers who go into this area.”

**Short-term impact: Influence on funding priorities.** Of the 92 Requests for Applications (RFAs) and Program Announcements (PAs) identified through our searches, 17 (funded by a variety of agencies within NIH and AHRQ) preceded the release of the report. This tally suggests that the funders were pursuing active support of this field even before the release of the systematic review. Of the remaining 75 RFAs and PAs, four cite the AHRQ report.

According to key informants, the release of a NIH PA titled *Understanding and Promoting Health Literacy* (RO1 and RO3) in 2004 was a major development for the field of health literacy. The announcement, made jointly by NIH and AHRQ, has been reissued: the R03 mechanism in 2004, 2006, and 2010 and the R01 in 2010. An R21 mechanism was first issued in 2006 and reissued in 2010. Of the total of eight such PAs, the first four do not cite the EPC’s report on literacy and outcomes. The lack of citation to the EPC report is not compelling evidence of lack of impact: one funder noted that “the report influenced my thinking when it came out but that was 6 years ago. I didn’t specifically pull it off the shelf [when commissioning new work] and look at it because it had already become part of the way I think.” The remaining four PAs cite both the EPC report and the IOM report.

According to our key informants, the PA is important to health literacy researchers because it lets them know that “there is a place that they can apply for research funding.” One key informant noted that, along with the IOM report, the EPC report provided a foundation on which a PA and subsequent funding could be based.

Another key informant suggested that the EPC report was important for AHRQ internally. In this view, without the strong evidence base provided by the report, it would be hard for AHRQ to make the case that health literacy was an area that deserved research funding.

Although key informants believed that the EPC report had a role in increasing funding for health literacy, generally they were unable to identify many specific requests for funding or funding prioritization documents that referred to the report. They provided several explanations for this situation.

First, report findings were not compatible with future research. *“The findings from the first 2004 AHRQ report said [that] there is not a lot of evidence to know what to do, so it was a null finding. It is hard to know what to do with a null finding.”*

Second, the very nature of the topic is difficult to translate into funded research. Health literacy is relevant across the entire health care continuum, but it is not specific to any particular clinical area. Several key informants stated that funding and interest tend to cluster around diseases; researchers or research funders taking this traditional approach may not be able to connect the importance of health literacy to their field of study. Projects tailored to specific topic areas defined by condition (e.g., diabetes or HIV/AIDS) might be needed to capture interest and funding from outside the health literacy community.

Third, dissemination could have been planned better and targeted to end users. Much of the dissemination occurred through the leadership of the content experts on the project rather than through a planned formal process. Respondents noted citing the report routinely in the numerous presentations that they make on health literacy.

Finally, the report itself could have been easier to use. One key informant described it as long and difficult to digest completely. Another suggested that the future research needs section could have been clearer and more thoughtfully produced.

**Short-term impact: Influence on policy or practice guidelines.** Some organizations have developed policies about health literacy since 2004, but key informants noted the difficulty of directly attributing those developments to the EPC report. Key informants noted that the report’s failure to change policy and practice guidelines in any substantial way may be more the result of the state of research and literature on health literacy than the shortcoming of the report. At the time of the 2004 report on literacy and health outcomes, the field was still in nascent stages of development; the report made it clear that *“there was not enough clear data in any one field to make a guideline about anything.”* This finding made it impossible for policy or guideline developers to distill definitive principles related to health literacy.

Although we did not identify any direct changes in policy or practice guidelines as a result of the report, key informants thought that the EPC report, in conjunction with simultaneous developments in the field, has pushed health literacy research to a level at which policy or practice guidelines are inevitable. One key informant said that organizations like the AMA, the American College of Physicians, and the Joint Commission have all taken note of developments in health literacy and are likely to institute guidelines once the evidence base proves sufficient.

**Medium-term impact: Knowledge generation.** Key informants repeatedly referred to the AHRQ EPC report as a foundational document. They mentioned that it is frequently referenced (the report and its subsequent articles) in health-literacy-related, peer-reviewed articles. Several key informants referred to it as a *“basic citation,”* used to demonstrate that health literacy is a problem that needs to be addressed. As noted earlier, our analysis of the health literacy update



articles supports the notion that the 2004 report is cited primarily as a means of establishing the extent and nature of the problem.

In addition, 13 of 60 citations referred to the 2004 report as means of illustrating that their research addressed a gap identified by the report. An additional three studies referred to the AHRQ report and its products to support their own conclusions for future research.

In addition to the impact on other investigators, the report had an impact on the future research of the EPC investigators who wrote it. Independent of the EPC report, the EPC content experts were pursuing research in health literacy. However, their involvement in the report had two impacts. First, it helped to clarify for them the status of health literacy research and the gaps that needed to be filled. Second, it was one of many reports that provided them with a strong reputation for health literacy research. They were able to parlay their experience into future work and prominence in the field: serving on review panels, writing editorials, and presenting and planning major conferences. Without writing the report, that prominence and influence may have taken longer to achieve; *“there is no doubt that had we not done that [EPC Health Literacy] report, in my mind, there is no way that we would have gotten the prominence that we did so early.”* The fact that they were a part of the review helps to keep the document alive through their experiences and visibility throughout the health literacy community; for example, one of the key informants is often asked to give presentations on health literacy at conferences and usually includes a slide on the evidence review as background.

Although the report did influence future research, several key informants judged that the report could have done a better job of reaching important audiences. One key informant commented that the report dissemination was overly focused on clinical researchers already in the field rather than methodologists. These researchers may be more interested in clinical interventions than activities such as scale development, which has not been sufficiently pursued even though the 2004 report identified this work as an important gap. This key informant suggested that the report should be presented to different audiences, for example methodologists, that may not have thought of health literacy as an area for research but that may include individuals who may be more qualified or interested in filling some of the methodological research gaps. Another key informant was concerned that the report could have been more widely cited and utilized in subsequent research but offered a different explanation: namely, perhaps the report was not used as much as it could have been because the people who wrote it were not sufficiently steeped in health literacy research and the front lines of health literacy work.

**Long-term impact: Changes in clinical or patient practice.** In general, key informants felt that the report’s impact on clinical and patient practice was tangential at best. The report *“helped to coalesce the field and bring things together”* and *“create a climate that created interest in the area,”* but most key informants saw the report as several steps removed from changes at the clinical or patient practice level. Some of the reasons that the report has not changed clinical or patient practice can be attributed to the report itself. Several key informants noted that the report was not written for clinicians; the comprehensive review of literature is helpful for researchers but unwieldy for clinicians. One key informant suggested the creation of complementary documents created specifically with clinicians in mind. Another noted that the report does not work back from what needs to be done at the level of the clinician; as a result, the analysis and gaps feel disconnected from health literacy in the practical context.

One key informant discussed the strides made by AMA in training physicians and other health professionals on health literacy topics with a “Train-the-Trainer” program. This person mentioned that the videotapes and training materials had reached thousands of physicians and other interested parties. Initial feedback indicated the trained individuals had at least partially incorporated some methods to improve their patient communication skills. The EPC report was not the inciting factor behind the training, but the AMA was well aware of the report’s conclusions when they set out to create the training. Another key informant noted that important organizations are starting to incorporate health literacy into their work; the respondent thought that some credit can be given to the report for advancing the field far enough to get these kind of results in a short period of time: “*Big institutions like IHI [Institute for Healthcare Improvement] are starting to integrate health literacy. Whether they were influenced by the 2004 report is a stretch, but a lot of this might have moved faster because of the report.*”

In short, respondents felt that the EPC report, along with other developments in the field, created the environment in which the AMA, IHI, and other influential organizations are putting resources into health literacy improvements.

**Long-term impact: Changes in health outcomes.** The key informants generally agreed that if the report had any effect on health outcomes it was indirect, for many of the same reasons already discussed. They noted that the report is meant for researchers and that the bulk and content of the report make it hard to read; “*these reports do not support adoption and spread; they are hard to get the gist of.*” One key informant suggested that it takes significant amounts of time to translate research into health outcomes and concluded that sufficient time had not passed to judge the 2004 report.

## **Impact of EPC Reports (KQ 1): The Omega-3 and Cardiovascular Disease Case Study**

**Inputs.** The omega-3 reports on CVD were part of a series of reports requested and funded by the Office of Dietary Supplements (ODS), National Institutes of Health. The first authors of the three-part series on CVD were Ethan Balk, M.D., M.P.H., (CVD),<sup>13</sup> Chenchen Wang, M.D., M.Sc. (CVD risk factors),<sup>10</sup> and Harmon Jordan, Sc.D., (animal and other studies).<sup>12</sup> As noted earlier, this methods project used the two reports focusing on outcomes in humans, with the exception of one indicator for short-term impact (citation of the report or articles) and for medium-term impact (knowledge generation). For these two indicators, we derive information from an ongoing update of the literature by Balk and colleagues for the Balk et al. 2004 report. No similar resource was available for the Wang et al. report; conducting an update of the literature for the Wang et al. report would have been outside the scope of this methods project.

**Outputs.** In March 2004, AHRQ released both omega-3 reports on CVD and on CVD risk factors. The CVD risk factors report resulted in two journal articles, for which Dr. Balk was the first author.<sup>27,28</sup> Dr. Balk also published a methods paper on systematic reviews of nutrition topics based on several omega-3 reports.<sup>29</sup> The CVD report prompted a journal article for which Dr. Wang was the first author.<sup>30</sup> After the release of the EPC reports, the ODS (the report funder) and the National Heart, Lung, and Blood Institute (NHLBI) organized two workshops to discuss priorities for future funding.

**Short-term impact: Increased awareness of issues.** Our analysis of the short-term impact of both reports, unless otherwise stated, comes from several sources: evidence of citation of the report through searches from the updated report (for Balk et al. alone), ISI Web of Science, and PubMed Central; dissemination through downloads and orders of the AHRQ report; qualitative reports of media interest; and heightened collaboration in the field.

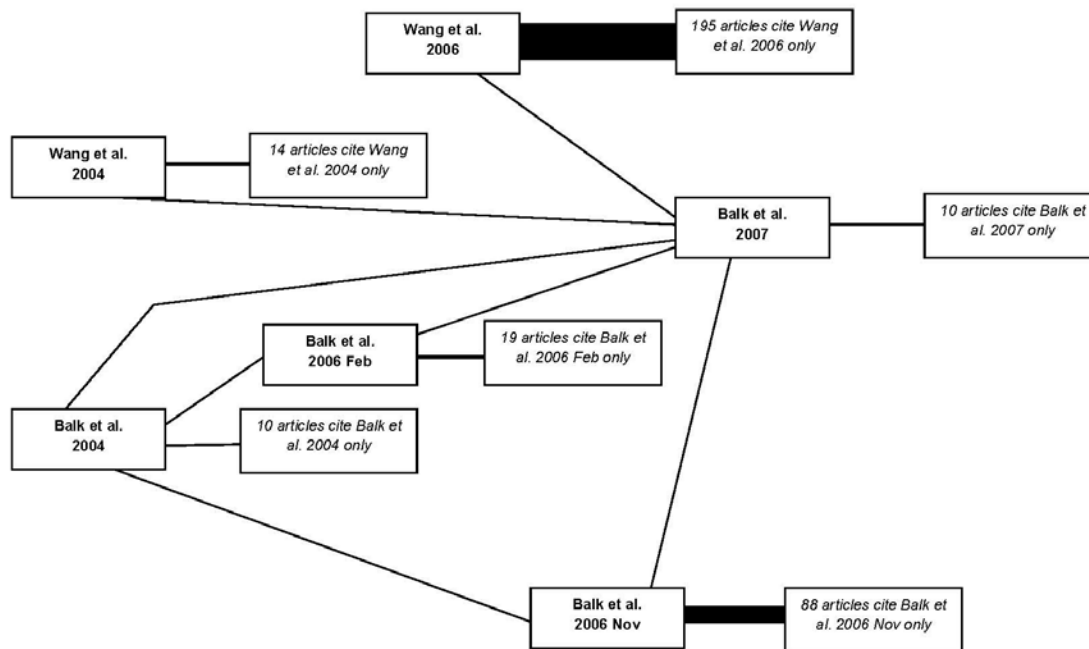
*Citation of the report.* Our analysis of the literature from the omega-3 update search suggests some citation of the 2004 report (Appendix D). Seventeen of 66 articles identified in the update search were published before the release of the report and/or articles and could not, therefore, have been influenced by the report. Of the remaining 49 articles, seven cite the omega-3 report or subsequent journal articles (Table 6). Most articles cite the report and articles to place their findings in context or to establish the state of the science. This finding is echoed in key informant interviews: one stakeholder noted her perception that the report was cited in the body of evidence primarily as a supporting document.

**Table 6. Citations from the updated omega-3 and cardiovascular risk factors and intermediate markers report: Reasons for citing the 2004 AHRQ report**

Reason for citation	Number of articles citing the report
Citation places findings in context	4
Citation shows how study fills gaps	2
Citation illustrates state of the science	1
Total number of articles citing the report or derived articles	7

Figure 5 illustrates the weight and interconnectedness of the 336 citations from the two 2004 omega-3 reports that cited a single AHRQ report or journal article (an additional 34 articles cited more than one AHRQ report and/or journal article). The reports resulted in three journal articles that summarized the reports and one that addressed broader concerns about systematically reviewing the literature in nutrition. Two of the journal articles were heavily cited (Figure 5).

**Figure 5. Weight and interconnectedness of omega-3 citations to the AHRQ report and derived articles\***

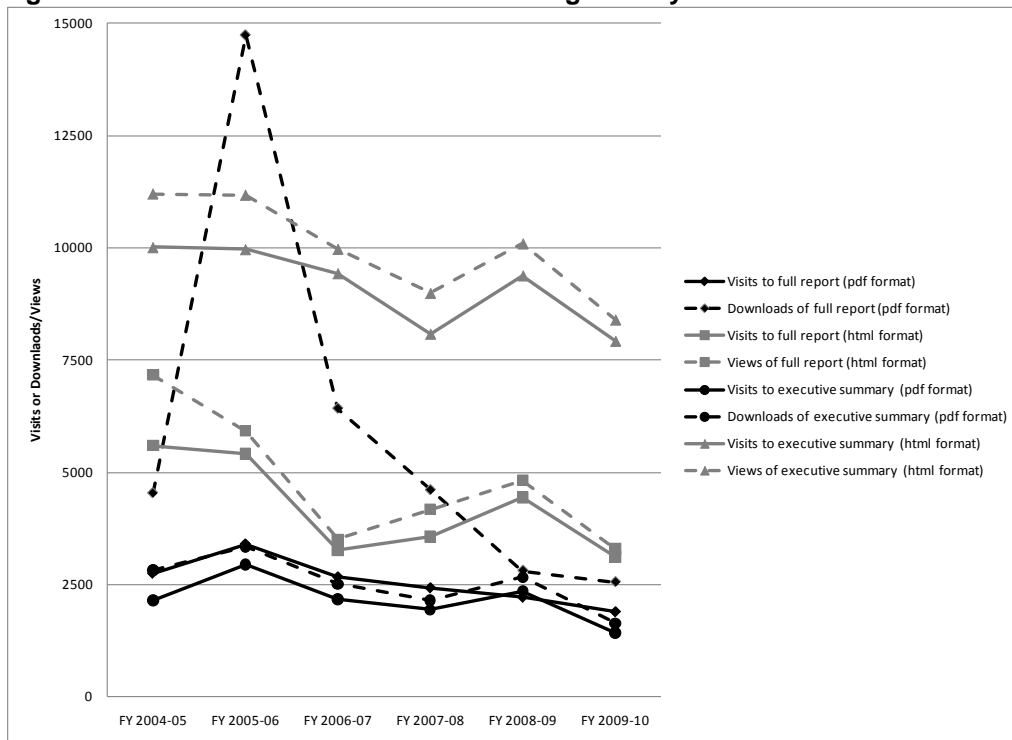


\*This figure illustrates forward tracing for the following citations: Wang et al., 2004,<sup>10</sup> Balk et al., 2004,<sup>11</sup> Wang et al., 2006,<sup>31</sup> Balk et al., 2006,<sup>27</sup> Balk et al., 2006,<sup>28</sup> and Balk et al., 2007.<sup>29</sup>

*Media coverage.* AHRQ and ODS orchestrated the press release, and it received some media publicity. Several key informants noted coverage from popular media as well as scientific media. Key informants also noted that omega-3 fatty acids have received substantial coverage overall on their positive effects.

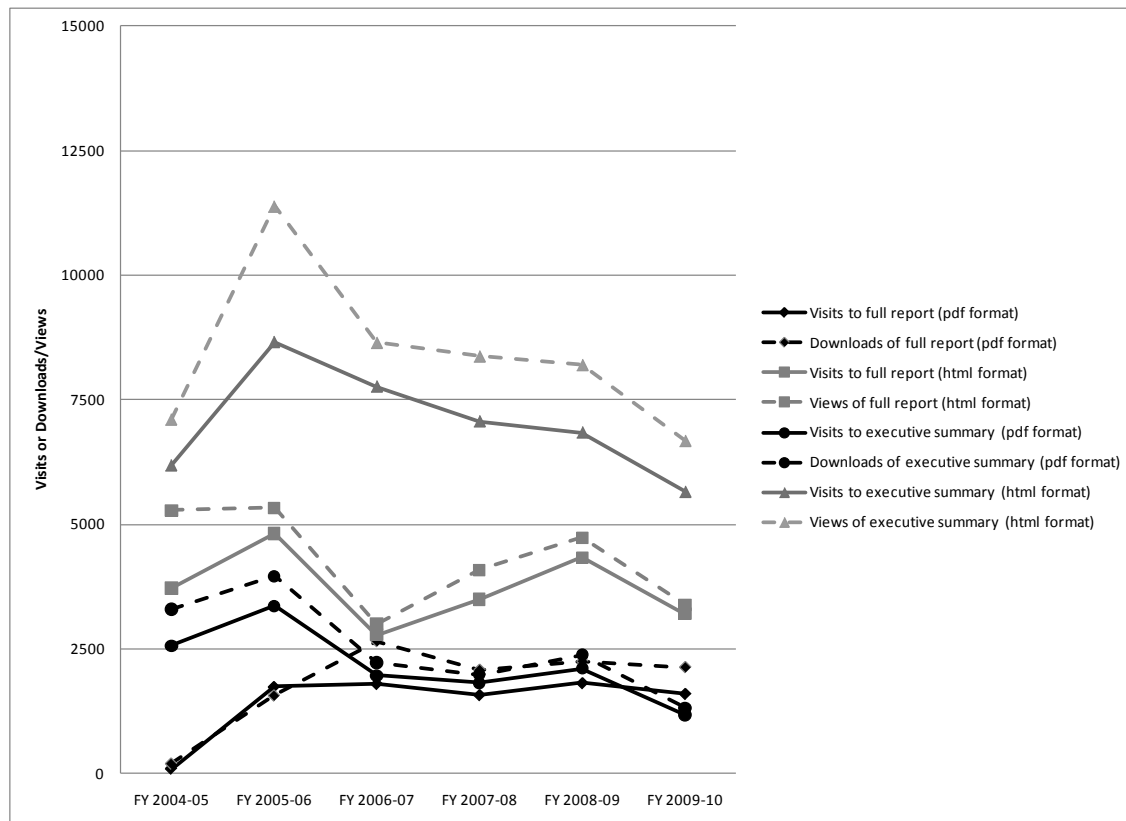
*Dissemination through downloads and orders of the AHRQ report.* AHRQ’s record of downloads through HTML and PDF formats since the publication of the reports through October 2010 show a peak of interest in the year following the report (downloads of the full report); interest leveled off after that point (Figures 6 and 7). For both reports, the executive summary remains the most consistently sought-after product (visits and views in the HTML format). AHRQ’s clearinghouse processed 103 orders for a total of 132 copies of the Balk et al. CVD report and 123 orders for a total of 175 copies of the Wang et al. risk factor report.

**Figure 6. Web-based metrics: Effects of omega-3 fatty acids on cardiovascular disease**



**Notes:** Visits: a series of actions that begins when a visitor views the first page from the server and ends when the visitor leaves the site; these are a good indication of traffic to a site in terms of users. Page views: access to any file classified as an HTML page. The page and its embedded files count as a single page view; these are a good indication of usage of content. Download: access to any file type that is not an HTML page, such as PDF, PowerPoint, and multimedia files; these are a good indication of commitment to those file types for use.

**Figure 7. Web-based metrics: Effects of omega-3 fatty acids on cardiovascular risk factors and intermediate markers of cardiovascular disease**



**Notes:** Visits: a series of actions that begins when a visitor views the first page from the server and ends when the visitor leaves the site; these are a good indication of traffic to a site in terms of users. Page views: access to any file classified as an HTML page. The page and its embedded files count as a single page view; these are a good indication of usage of content. Download: access to any file type that is not an HTML page, such as PDF, PowerPoint, and multimedia files; these are a good indication of commitment to those file types for use.

*Collaboration.* The co-investigators on this topic who were content experts had substantial expertise before their involvement in the report; thus, the report did not serve as a mechanism to create opportunities for collaboration with their peers on the topic. Nonetheless, participation did play a valuable role. As one key informant noted, “*Was the report the single most important factor [in helping to obtain additional funding]? No, but it was a contributing factor that helped us figure out what our research questions would be. Maybe it didn’t stimulate an initial collaboration, but it certainly contributed in a lot of different ways.*”

Co-investigators who were methodologists (i.e., EPC investigators) did not pursue additional work in this content area, so they did not seek opportunities for collaboration on this specific topic. They did, however, make connections with nutrition experts at Tufts as a result of this work and so expanded their capacity to do nutrition-related reviews.

**Short-term impact: Influence on funding priorities.** We found 9 RFAs and 25 PAs that cited the term “omega-3,” “fish oil,” “n-3 fatty acids,” or “omega-3 fatty acids.” Four RFAs and two PAs preceded the release of the report. None cited the EPC reports or articles. The low yield of

RFAs and PAs was validated by key informants who cited the importance of investigator-initiated research in this field.

As for influence of the report on funding solicitations, as noted earlier, NHLBI and ODS collaborated on two workshops. NHLBI's first workshop proposed a large clinical trial, but the lack of funding support prevented further evolution of the proposal. The second workshop resulted in a peer-reviewed journal article that was cited by three articles in the update search for the Balk et al. 2004 report and was reported by key informants to be influential in investigator-initiated funding ideas. Our review of citations using ISI Web of Science and PubMed Central found that 39 studies cited the article from the NHLBI workshop.<sup>32</sup> In addition, the workshop served as means of convening experts in the field, who then went on to submit investigator-initiated awards. As one key informant noted, "*Many of the successful applicants are in fact individuals who participated in our workgroups. Once they understood and recognized that it was unlikely for dollars to be set aside to support a specific funding opportunity in this area they submitted their applications and thoughts as an investigator-initiated application.*"

ODS recently conducted an assessment of the effect of EPC omega-3 reports on their grant portfolio and found that only one of 20 grants cited the AHRQ report. One possible reason for the citation could be that the sole investigator who cited the AHRQ report was involved in the workshop and knew about the reports beforehand.

Key informants noted that the reports lacked specificity, particularly when compared to other reports (e.g., from the IOM) that separate "major" knowledge gaps from noncritical research gaps. One key informant suggested that the lack of specificity was "*probably reflective of the panel makeup-maybe some of the AHRQ reports did not have the quorum of nutrition scientists that they needed to phrase the research questions.*"

**Short-term impact: Influence on policy or practice guidelines.** Key informants generally did not believe that the EPC reports had impact on policy and practice guidelines for several reasons. First, the AHA guidelines on eating oily fish preceded the reports; the AHA did not change their guidelines based on the reports. Second, no translation of the AHRQ report to clinical recommendations exists. A third explanation is that the evidence base is not compelling to guideline developers. Finally, one key informant noted that guideline developers may not always be driven by evidence.

When systematic reviews follow the publication of guidelines (e.g., the Food and Drug Administration's decision letter on the qualified health claim for food labeling on omega-3 fatty acids and cardiovascular health)<sup>33</sup> and do not contradict them, the reviews have only a limited scope for influencing later iterations of these practice guidelines.

**Medium-term impact: Knowledge generation.** Two sets of authors cited one of the AHRQ report<sup>13</sup> and two journal articles<sup>28,30</sup> to illustrate how their studies filled gaps identified by the AHRQ review.

Investigators on the EPC team expanded their portfolio of research in the area of systematic reviews of nutrition topics. Content experts became more involved in systematic review work and related activities, serving on a Technical Expert Panel and on guideline committees. Additionally, the methodological challenges of conducting systematic reviews in the nutrition field spurred the Tufts team to seek additional funding on methods from NIH.

External constraints include funding, the state of current patient practice, and the existing knowledge base among funders and reviewers. Regarding funding, one key informant noted that

some of the omega-3 gaps require studies that may be long-term and expensive and, therefore, be less likely to be funded. The high prevalence of omega-3 supplementation was cited as a constraint; the implication of such high prevalence is that studies may have trouble recruiting new users to meet their sample size. One key informant believed that EPC reports were unlikely to have attributable impact because of the existing knowledge base among funders and investigators. *“It’s hard to imagine that the gaps identified in that paper would not already be apparent to another investigator in this field. They already know it’s a gap without reading the AHRQ report.”*

**Long-term impact: Changes clinical or patient practice.** Key informants noted a substantial change in clinical practice and cited the commonplace use of omega-3 supplements. They noted however, that this change is attributable not to single report, but to a body of evidence, with a slow accumulation of data on benefits from 1985 onward (when the *New England Journal of Medicine* published three studies on omega-3) and limited evidence of harms. *“More and more people are getting the message that it’s good for you. Medical advertisers get out there and promote it. Obviously the EPC [report] was just one wave in the ocean.”*

**Long-term impact: Changes in health outcomes.** Key informants uniformly agreed that they could not make a judgment on whether the EPC report has had an impact on health outcomes. They cited the difficulty of attribution of effect to the EPC report in particular.

## **Factors Influencing the Impact of EPC Reports (KQ 2)**

Key informants discussed a number of benefits that resulted from the EPC reports. Among these were steps such as providing a foundation for the research community to build on, heightening awareness of the gaps in knowledge, increasing the quality of research, and sparking new directions of research. However, the degree to which these reports were influential and well received hinged on several factors including marketing efforts, the very nature of the reports, and factors external to the EPC domain. The following comments, which identify several barriers to effectiveness and offer recommendations for overcoming those problems, are drawn from both sets of key informants (i.e., on the literacy report and the omega-3 reports) unless otherwise noted.

**Dissemination.** First, dissemination (or lack thereof) was an important barrier and facilitator to the impact of these reports. Many key informants commented that the reports were not well known in the field because of lack of dissemination of the findings and little name recognition for AHRQ. They felt that more effort should be paid to dissemination activities. Simply posting the report to a Web site or relying on word of mouth was deemed inadequate. As one key informant noted: *“...if we don’t engage in promotional activity it’ll just be one more government report on a shelf.”* Improving dissemination in multiple venues and media. Our respondents suggested several improvements for dissemination of such reports in the future. One key informant drew on her experience in a different context and suggested a variety of dissemination activities for future reports, such as presenting them at conferences, conducting webinars, and posting them to social networking sites such as Twitter. Another key informant suggested that authors should publish targeted findings in peer-reviewed journals, thereby increasing exposure of the work to researchers using traditional routes of literature searches.



*Identifying “champions.”* Other key informants suggested that, for work of this sort, a champion was needed to spur interest among the research community and to promote a collaborative environment in which funders and researchers could align their interests. A champion could help to ensure that such reports were disseminated in appropriate forms to appeal to the intended audiences. Champions could be AHRQ staff, the staff of other agencies nominating or sponsoring the work, report authors, or other stakeholders interested in furthering the field.

*Presence of a committed partner.* A related issue to having a champion is the presence of a committed partner. One key informant cited the “model” partnership between ODS and AHRQ, where ODS served a critical role before and after the project by being able to identify areas that need to be informed by evidence.

**Nature of the reviews and target audiences.** A second set of barriers and facilitators to effective use of these reports was related to the nature of the reports themselves. Two authors commented that the reports were dense and were not easy to read, but they were challenged as to how to make the findings more accessible to the intended audience.

*“You try hard to make it user-friendly, but it is still a very large report. How do you get through that lengthy report? Who gets through it? How do you make it something that people can use?”*

One key informant viewed *“the papers published in peer-reviewed journals [as] most helpful. Perhaps because peer-reviewed publications are much more targeted which makes it easier, plus people are more used to citing and going to those kinds of sources.”*

The reports were also viewed as catering to a narrow audience of researchers. They were not seen as suitable for practitioners because they lacked specific guidelines that clinicians could put into practice and because practitioners do not have the time to wade through a thick report to find the relevance for how they could improve their programs. None of the three reports was written for or aimed at patient or advocacy groups.

*Expanding the intended reach of reports.* Broadening the targeted audience to include consumers and practitioners would increase awareness and promote change. One key informant highlighted this point as follows: *“...marketing to a patient audience might be as effective as anything—then have the patients advocate for change.”*

However, to be effective with a broader set of audiences, the reports would need to be sensitive to the needs of different types of readers. One key informant suggested that separate reports could be developed for each intended audience to better address their particular needs and interests. Marketing shorter, action-oriented digests of information to consumers and practitioners would be better received while more detailed reports focusing on gaps in the literature and methods could be developed for researchers and practitioners to help them best use the findings. Another key informant suggested that because the field of health literacy cuts across a wide range of topic areas, the findings of that review could be generalized to appeal to a wider audience.

*Improving recommendations.* How recommendations were presented was also criticized. Key informants thought that they were too broad, or unclear, or not feasible to implement (or some combination of these problems). One key informant suggested that the report team making the

recommendations lacked the knowledge and experience in the subject area needed to understand what it takes to parlay the recommendations into research.

To address these report critiques, suggestions to strengthen the usefulness of the recommendations included the following:

- Seek input from key stakeholders to identify research gaps and develop recommendations: *“We could have been clearer in describing the research needs... seeking more feedback would have led to a stronger section.”*
- Clearly state the direction that the research should take to fill major gaps in knowledge and advance the field: *“More direction on how urgent some of the recommendations may be. Something that indicates urgency. There might be low hanging fruit that people can get a hold of, but if it is not going to fill in major gaps, the field is just going to inch along.”*
- Clearly articulate the recommendations and be specific with regard to the type of research needed.

*Building on strengths of the systematic review approach.* Despite the critiques cited above, key informants mentioned that the methodology the EPC teams used gave credence to their findings. One stakeholder noted that the involvement of methodologists with no preconceived ideas or biases helped to generate a high regard for the reports: they were considered high quality and very accurate. These views suggest that EPCs should build on the core methods used to produce such reports, while collaborating with AHRQ and other stakeholders (e.g., nominators of topics; other agency sponsors) to improve dissemination, readability, and similar aspects of the broader EPC agenda.

**External factors.** The third set of barriers and facilitators was related to factors external to AHRQ and the nature of the reports; they are less “actionable” to address within AHRQ’s sphere of influence. Several key informants tied to the 2004 report on literacy and health outcomes discussed barriers inherent to a relatively new field of study that have hindered the usability of the report.

*Lack of evidence supporting a clear direction for future research.* Two key informants noted that the lack of available evidence in favor of a clear direction for future research in the 2004 report was problematic. Study design flaws and small sample sizes prevented the authors from specifying meaningful recommendations about research. Moreover, interventions that were known to have design flaws continued to be funded in subsequent studies because of mandates or *“they already had things in the works.”*

*Lack of research in basic science.* Key informants representing both the health literacy and omega-3 reports discussed the lack of basic science to support the growth of each field. As one key informant noted,

*“ the challenge has been to get down to the basic science of health literacy. I think the issue is conceptual; people really don’t know what health literacy is. The literature and our writing about it has not been clear enough on what we are measuring in terms of exposure.”*

Similarly, another key informant noted the lack of external support from funding agencies to conduct the necessary research.

*“Some more basic science that needs to be done [on nutrients and supplements] is not as highly sought as hypothesis-driven research, new and novel idea research.”*

*Size of the field.* Another key informant commented that because of the newness of the field, a relatively small cadre of researchers has been involved in health literacy. Thus, awareness of health literacy as an evolving field is generally lacking among individuals, communities, researchers, and practitioners. Conversely, the literature about the benefits of omega-3 fatty acids (and supplements) has become commonplace; in fact, it might be said to have led to difficulties because more individuals are taking these supplements, thereby complicating potential study designs and creating an obstacle to future research.

*Lack of funding.* Another external barrier that can affect future research is simply the lack of funding. One key informant (in discussing omega-3 supplements and CVD or risk factors) discussed the difficulty of getting research funded for which *“there is really no hypotheses that would support the belief that these agents are anti-arrhythmic.”* Moreover, the expense and time needed to conduct needed animal studies can be prohibitive and they are less likely to be funded.

*Convergence of findings.* Another key informant highlighted the need for researchers to pay more attention to findings and recommendations when data that speak to the same topic do converge, as was the case with the 2004 report on literacy and health outcomes and the IOM report. This observation suggests that timing of the release of report findings could be a factor in how much of an impact the report could have, especially if it follows on the heels of (or immediately precedes) a widely published study or report in the same topic area.

## Discussion

### Impact of EPC Reports on Future Research Funding (KQ 1)

The impact of EPC reports on future research funding can be conceptualized narrowly, as being limited to knowledge generation, that is, new studies inspired by the gaps that a systematic review identifies. A more comprehensive framework, and one that key informants reinforced, includes pathways for impact that include other outcomes such as increased awareness or changes in policy and practice that may then spur new research.

The impact of the selected EPC case studies is demonstrably greater on short-term outcomes, that is, greater awareness of the issues, than on medium-term (such as the generation of new knowledge) or long-term outcomes (such as changes in patient practice or health outcomes). The articles identified in the relevant updates of the literature searches cited reports and articles from both case studies in high numbers. As noted earlier, as many as 60 of 168 articles (36 percent) that were included in an update of the health literacy report cited the report and/or articles from the 2004 report. Similarly, 7 of 49 articles (14 percent) identified for an update of the Balk et al. report cited the 2004 report and associated articles. Such citations were intended primarily to support the problem statement, illustrate the state of the science, or place findings in context. A smaller number of included articles from the update searches used the citation to the AHRQ reports and associated articles to explain how their work filled gaps that the report identified (16 of 168, in the case of health literacy and 2 of 49 studies, in the case of omega-3).

We did not uncover evidence of impact of EPC reports on long-term outcomes. We emphasize, however, that important constraints related to timing and attribution imply that the absence of evidence cannot be interpreted as absence of impact. Long-term effects may take longer than the 6 years that have elapsed since the publication of the reports used for the two case studies. Attributing impact related to long-term outcomes back to the EPC reports may be poorly documented: the feedback from our respondents suggests that the longer a report is in existence, the more it is likely to be part of the “received wisdom” or common knowledge and the less likely it is to be cited.

In addition to the question of the type of impact (short-, medium-, or long-term), questions arise regarding the extent of impact, i.e., the degree to which impact can be attributed directly or specifically to the AHRQ reports. Our evaluation suggests that the extent of impact of an EPC report will vary, based on factors such as the nature of the topic and the timing of the report relative to the development of the field. Systematic reviews that cover a broad scope will likely be cited more frequently than more narrowly specified topics. Reports that summarize findings for an emerging field serve as foundational material for subsequent work.

The degree to which the new research can be directly attributed to the AHRQ reports remains unclear. Neither the literacy report nor the omega-3 reports directly resulted in allocation of dedicated funds for future research for that topic. In the case of health literacy, for example, the initial program announcements did not cite the AHRQ report until the second round of funding.

Nevertheless, the reports did influence the way that the EPC investigators, other investigators, and funders approached the topics. They also led to more research through tangential routes: in the case of omega-3, the involvement in the reports led the Tufts EPC to seek funding and specialize in reviews relating to nutrition. Similarly, involvement in the health literacy report spurred EPC investigators to seek funding for those gaps.

Our interviews with key informants, and the observations they made about barriers or ways to overcome those barriers, led us to revise the analytic framework for each case study (Figures 8 and 9). In our revised analytic frameworks, we added boxes and links to illustrate the role of experts, stakeholders, and funders before the commissioning of the report and their continued involvement (often entirely independent of the EPC report) that may significantly advance the field through the creation of other products, development of investigator-initiated research, and active championing and leveraging of funding opportunities.

Depending on the topic, the pathways for research may vary. For instance, a funding solicitation from the National Institute of Health for health literacy led to several funded studies. For omega-3, no funding solicitation was issued; investigator-initiated funding resulted in new studies.

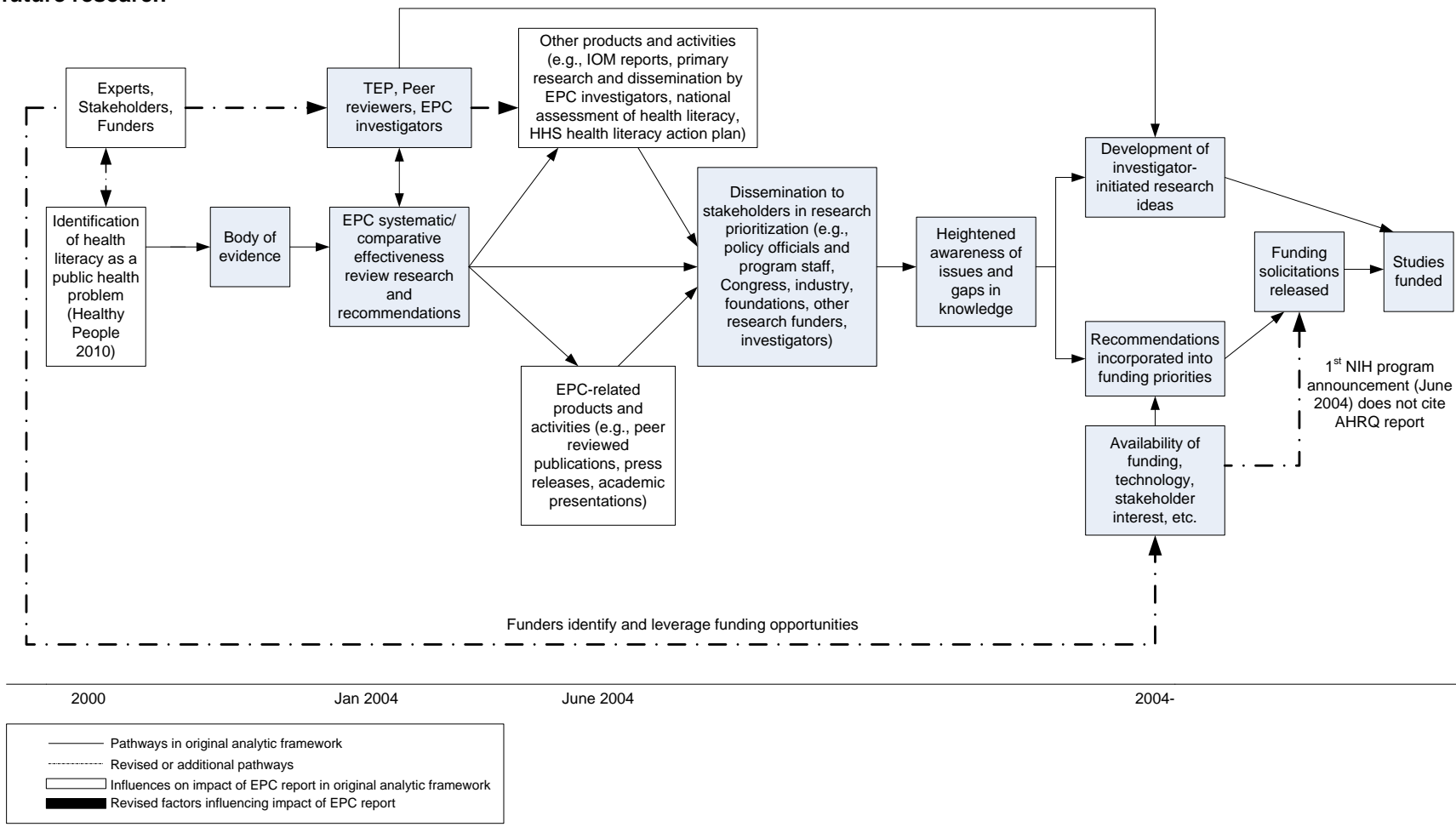
## Elements That Contribute to the Impact of EPC Reports (KQ 2)

Our interviews with key informants suggest that factors that contribute to or detract from the impact of EPC report are associated with the report itself, its dissemination, and the environment into which it is issued. AHRQ has already identified some of these challenges and has instituted (or is in the process of implementing) several specific solutions. Some appear in the new round of funding for future research documents; others are steps that EPCs can take by following revised methods for systematic reviews and comparative effectiveness reviews (Table 7).<sup>34</sup>

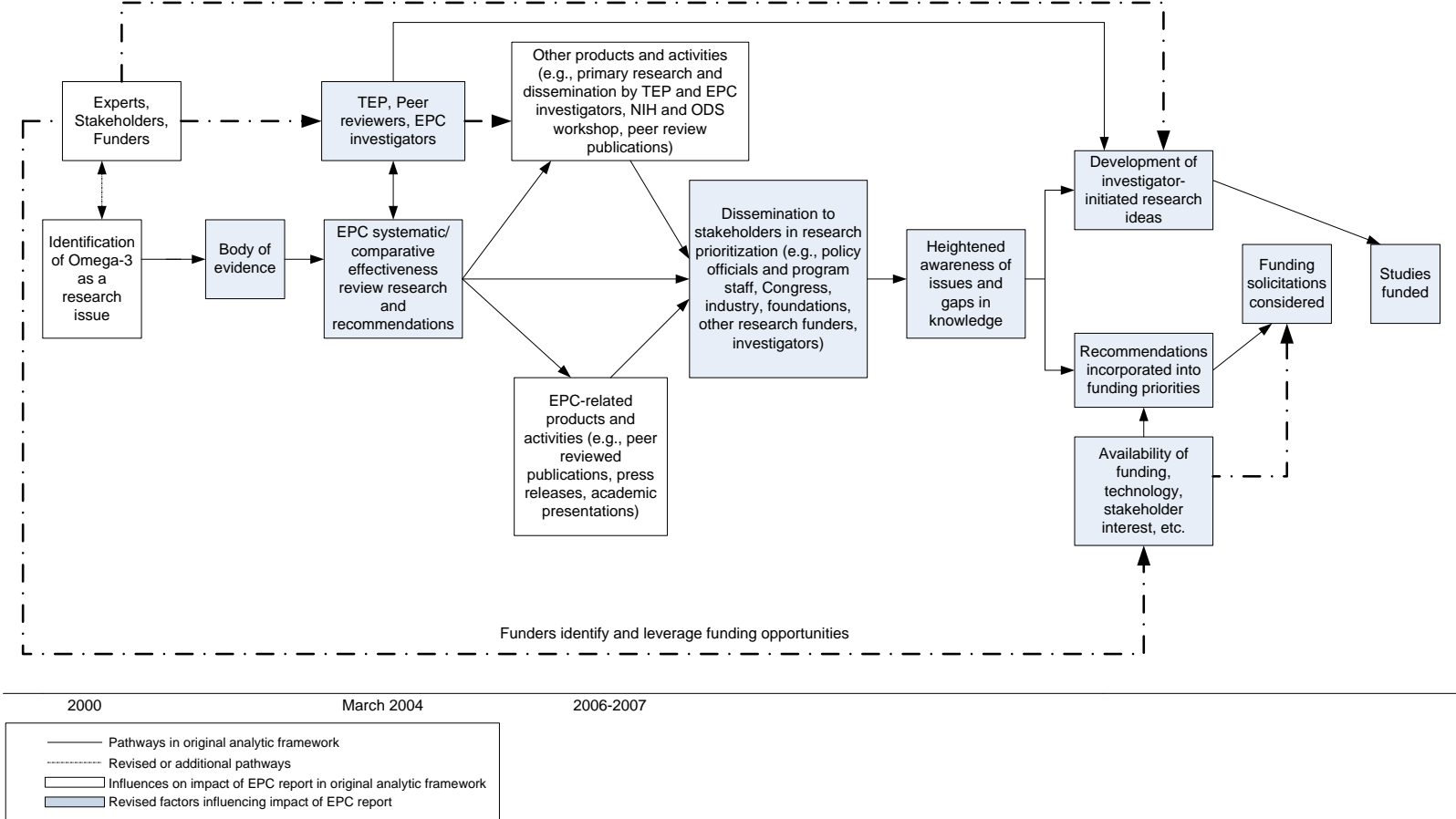
**Table 7. Ongoing and newly proposed changes to future research sections of systematic reviews**

<b>Ongoing changes</b>
• Greater specificity in future research needs (including providing a sense of relative urgency about specific recommendations)
• Greater involvement of funders and stakeholders in the research recommendations
• Improvements in readability of the systematic review
• Greater specificity in future research needs (including providing a sense of relative urgency about specific recommendations)
<b>Additional changes suggested by key informants and results of the report</b>
• Newly proposed changes
• Dissemination plan that involves EPC investigators and a “champion” funder
• Careful consideration of likely audience and impact when scoping the topic
• Balanced investigative team
• Targeted dissemination to funders and investigators
• Outreach to other funding agencies
• Greater funding support of journal articles (the most widely cited source of AHRQ-support research)

**Figure 8. Analytic framework of the processes and activities leading to impact of the 2004 report on literacy and health outcomes on future research**



**Figure 9. Analytic framework of the processes and activities leading to impact of the omega-3 and cardiovascular disease reports on future research**



Abbreviations:  
 AHRQ: Agency for Healthcare Research and Quality  
 EPC: Evidence-based Practice Center  
 HHS: Health and Human Services  
 IOM: Institute of Medicine  
 NIH: National Institutes of Health  
 ODS: Office of Dietary Supplements  
 TEP: Technical Expert Panel

## **Development of a Dissemination Plan**

In early years of the EPC program, investigators were asked to develop a dissemination plan for the report. A return to such an approach in the design phase (during topic refinement) will allow EPC investigators, AHRQ, and other stakeholders to specify and plan for a wide but appropriate set of methods of dissemination. Such advance planning can, take target audiences into account, and identify a “champion” funder or funders. The enhanced role of the peer and public comment in the Effective Health Care Program may be channeled for improved dissemination. For example, the technical expert panels (TEP), peer reviewers, and the public can be routinely asked whether and how they plan to disseminate AHRQ reports.

## **Consideration of Audience and Impact When Scoping the Topic**

The heightened involvement of EPCs in recent months in topic nomination development and topic refinement provides an opportunity for shaping the topic to achieve greater impact on future research. An important consideration for AHRQ, the nominators, and the EPC is how to balance breadth of review topics (i.e., scope of the review and its key questions) with specificity in those topics. The balance of these two perspectives may involve a tradeoff when impact on future research is balanced against impacts on clinical practice and patient outcomes.

Narrowly framed topics allow for a focused summary of clinical issues and a clearly specified target audience, but they may not have as wide-ranging implications for future research. Broadly framed topics have wider applicability and, therefore, could potentially offer wider implications for future research. In addition, broadly framed topics may generate cross-fertilization across disciplines. The potential benefits from broadly framed topics may not be realized when research gaps lack adequate specificity or when such topics suffer from lack of leadership or ownership in the topic and, thus, lack of dedicated funding. A closer examination of these issues during topic refinement will allow AHRQ and EPCs to involve the appropriate stakeholders in dissemination of the report.

## **Balanced Investigative Team**

Key informants noted the high regard for EPC reports, driven in part by the involvement of methodologists with no preconceived biases. At the same time, key informants for both case reports cited the lack of specificity of research recommendations; they suggested that a possible reason was lack of involvement of authors in the front lines of the research. EPCs may need to shift the balance of the investigative team over time to include more content experts in developing research recommendations.

## **Targeted Dissemination to Funders and Investigators**

A related concern is the development of short, practical guides or one-page fact sheets for funders and investigators about future research needs after the report is completed. These would complement ongoing products for practitioners and consumers.

Our findings clearly demonstrate that journal articles far outweigh other types of products in influencing future research. Targeted dissemination to other investigators requires the support of journal article preparation and participation in venues, such as the omega-3 case NHLBI workshops.



## **Outreach to Other Funding Agencies**

AHRQ will need to garner external support from other agencies and organizations to raise awareness of the topic and to fund recommended research. Early outreach may require engaging appropriate staff from sister agencies (or foundations, or industry, as appropriate) as the report is being put into final form.. Their continued involvement through the future research needs projects could enhance the likelihood of impact of EPC reports.

## **Limitations**

The two case reports selected for this methods project represent different types of content areas and, therefore, provide some variation in understanding how EPC reports may have impact on future research. Nonetheless, they are limited in applicability to other reports in the EPC program.

The impact from EPC reports on future research may occur within a few months or years after the release of the report, as a consequence of improved knowledge about gaps in the research and recommendations for future research. The methods used in this report are best suited to identifying impacts through short-term and medium-term pathways. Our analytic framework anticipated that EPC reports could have long-term impacts on health outcomes and changes in clinical practice that could then result in additional research, but we found no evidence of long-term impacts through EPC reports.

The logic model in this report is one of several potential approaches to framing potential research impacts. Another method of conceptualizing impact could start with the intended audience and then identify pathways that lead to potential impact. As one reviewer noted, three groups, which intersect but are not completely overlapping, may be of particular interest. One group sets “macro” research policy (e.g., those who must make decisions about research resources and allocations across a spectrum of research disciplinary areas, maintaining balance across competing claims for those resources); another is a group that might be said to focus more on “micro” research policy (e.g., decisionmakers about beginning or continuing funding within a given topical or disciplinary area); and finally, a third group comprises those in the research community who actually undertake the research and contribute to the knowledge base for whom technical challenges in the current state of science (as contrasted with resources per se) may be the guiding concern. Adopting one specific approach over other approaches, for repeated evaluations of impact, requires considered input from ARHQ and the EPCs.

One question that arises is how best to frame an operational definition of impact on future research in the long term. Our metrics, methods, and timeframe may have influenced our ability to find evidence of long-term impacts. Other metrics might include the intensity of knowledge translation as a whole; this idea involves building more efficiently on what is already known. Intensity may include both the pace and volume of new research, programs, and research capacity. A key consideration in interpreting these metrics will continue to be that of separating attribution from contribution.

In the physical and biological sciences, failed trials may lead to new ways of thinking to that may lead to breakthroughs in subsequent rounds of research. Similarly, systematic reviews that are unable to come to conclusions because of insufficient evidence may spur new research in topics that have major clinical uncertainties but may never be cited. Identifying appropriate metrics to account for both intended and unintended pathways of impact will continue to be challenging. Finally, during the design of this project, we were not aware of other reports that

sought to understand the impact of EPC reports on future research. We were limited by available data and indicators. Future monitoring and evaluation of impact would benefit from a routine, robust, and relatively low-effort assessment, such as citation analysis of included articles in updates of EPC reports, to understand whether and how EPC reports are being used to shape the field.

## **Conclusions**

The case studies of literacy and health outcomes and omega-3 fatty acid supplements illustrate the multiple and often nonlinear pathways by which EPC reports can have short- to long-term impact on future research. Although these pathways are not entirely predictable, common themes emerged from our work along several dimensions: the importance of the breadth, specificity, and “readiness” of the topic for more research; ongoing developments in the field; availability of funding; and the active engagement of champions. AHRQ and the EPCs may be able to improve the likelihood of impact by creating more targeted products, planning for and expanding dissemination activities, improving the readability and other attributes of the reports themselves, and actively involving funders early on and throughout the process of creating and publishing the reviews.

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# Appendix A. Case Study Identification

## Identification of Potential Case Studies

We sent each EPC director a memo from us asking for nominations. Specifically, we asked for nominations of systematic reviews from EPC-II and EPC-III known to have had impact on future research. We offered some examples:

The report was commissioned by a research agency for the express purpose of identifying future research needs.

The report, although not commissioned for the purpose, influenced the development of RFAs and RFPs.

The report influenced the field through its results and gaps analysis and was the catalyst for investigator-initiated funding.

The report influenced the development of guidelines or policy, which in turn, resulted in future research funding.

We received responses from 7 of 14 EPC directors after two reminders. Two EPC directors could not identify EPC reviews that had impact. A third identified an instance of reverse impact, that is, the EPC review was commissioned as a result of ongoing work for another agency. The remaining four EPCs nominated a total of 16 reviews, ranging from 1 to 7. Table A1 presents all nominations provided by EPC directors.

Entries in the table appear in reverse chronological order; the most recent reports are listed first. We evaluated each nomination for concerns regarding measurement or attribution of impact and the likelihood for potential conflict of interest (Notes column in Table A1). Under-attribution of impact is a risk for more recent reports. Overattribution is a likely risk of for older reports that are often routinely cited in ongoing research as background material. Key informants may have recall issues as well. Other external factors include the volume of other ongoing research and sharp increases in funding: in these instances, a likely risk is over-attribution of impact. We also identify the RTI-UNC EPC reports clearly because evaluating these reports may present a conflict of interest for this investigator (MV is first author on 2 of 7 RTI-UNC EPC reports in the list below). Reports that we judged to be the best choices for case study are shown in bold. We identify four likely choices other than the RTI-UNC reports: two reports that influenced external funding (soy and omega-3 fatty acids) by the Tufts EPC and two reports that led to clinical practice guidelines (surgical treatment of obesity and breastfeeding) by the RAND (Southern California) and Tufts EPCs, respectively.

**Table A1. Nominations for potential case studies**

<b>Nominator EPC</b>	<b>Topic</b>	<b>Date of publication</b>	<b>Type of impact</b>	<b>Cited impact</b>	<b>Notes</b>
Tufts	Vitamin D <sup>35</sup>	2009	Practice guidelines	Institute of Medicine Dietary Reference Intake revision on vitamin D	Likely too recent to be able to measure impact
Tufts	Breastfeeding <sup>36</sup>	2007	Practice guidelines	Office of Women's Health recommendations	
RTI-UNC	Second-generation antidepressants <sup>37</sup>	2007	Investigator-initiated research and external funding	Additional studies funded by DERP, AHRQ, and others	Attribution likely difficult: part of ongoing research debate; RTI-UNC review

**Table A1. Nominations for potential case studies (continued)**

<b>Nominator EPC</b>	<b>Topic</b>	<b>Date of publication</b>	<b>Type of impact</b>	<b>Cited impact</b>	<b>Notes</b>
RAND	Health information technology <sup>38</sup>	2006	Investigator-initiated funding	Additional work by David Blumenthal and the ONC, HIE federal policies	Research volume influenced by stimulus funding
Tufts	Soy <sup>39</sup>	2005	External funding	National Center for Complementary and Alternative Medicine/NIH Office of Dietary Supplements future research	
RTI-UNC	Episiotomy <sup>40</sup>	2005	Practice guidelines	American College of Obstetrics and Gynecology guidelines	RTI-UNC review
RAND	Surgical treatment of obesity <sup>41</sup>	2004	Practice guidelines	Clinical practice guidelines by the American College of Physicians	
Tufts	Omega-3 fatty acids <sup>10,11</sup>	2004	External funding	National Heart, Lung and Blood Institute future research	
RTI-UNC	Community-based participatory research <sup>21</sup>	2004	Investigator-initiated research and external funding	Cited in requests for applications and proposals	Research methods, atypical of EPC reviews; part of ongoing research methods development; RTI-UNC review
RTI-UNC	Health literacy <sup>9</sup>	2004	Investigator-initiated research, practice guidelines	IOM report, additional funding for investigators, cited in RFAs	RTI-UNC review
RAND	Ephedra <sup>42</sup>	2003	Change in policy	Used at the justification to withdraw ephedra from the market	EPC 1: attribution issues
Tufts	Neonatal hyperbilirubinemia <sup>43</sup>	2003	Practice guidelines	American Academy of Pediatrics guidelines	EPC 1: attribution issues
McMaster	Dissemination of cancer control interventions <sup>44</sup>	2003	NR	NR	EPC 1, attribution issues
RTI-UNC	Systems to rate the strength of evidence <sup>45</sup>	2002	Investigator-initiated research?	Cited in numerous methodological papers	EPC 1; attribution issues; part of ongoing methods development; RTI-UNC review
RTI-UNC	Prostate cancer screening <sup>46,47</sup>	2002	External funding	CDC funding on communication of PSA messages	EPC 1: attribution issues; RTI-UNC review
RTI-UNC	Preterm labor <sup>48</sup>	2000	External funding	Follow-on report funded by AHRQ	EPC 1: attribution issues; RTI-UNC review



## Appendix B. Sources Searched for Assessment of Impact of an EPC Report

Table B1. Sources Searched for Assessment of Impact of an EPC Report

Source	URL	Date of Last Search	Yield	Ease of Use*	Import Function?	Search Strategy	Dates of Coverage
<b>FOR PUBLISHED LITERATURE</b>							
CINAHL	<a href="http://www.ebscohost.com/cinahl/">http://www.ebscohost.com/cinahl/</a>	2/9/2010	209	Satisfactory	Yes	"community-based participatory research" OR CBPR, limited to publication years 2004-2010; 85 were duplicates with other databases, 124 were unique and imported.	1982-present
Cochrane Library	<a href="http://www.cochrane.org/">http://www.cochrane.org/</a>	2/9/2010	4	Satisfactory	Yes	"community-based participatory research" OR CBPR, limited to publication years 2004-2010; 3 duplicates, 1 imported.	varies
Google Scholar	<a href="http://scholar.google.com/">http://scholar.google.com/</a>	5-Feb-10	187	Satisfactory	Yes/1 at a time	Viswanathan "Community-Based Participatory Research: Assessing the Evidence"	Not available
ISI Web of Science	<a href="http://apps.isiknowledge.com/">http://apps.isiknowledge.com/</a>	2/9/2010	404	Satisfactory	Yes	"community-based participatory research" OR CBPR; 25 were duplicates with PubMed/ final total 379	Science Citation Index Expanded (SCI-EXPANDED)--1955-present Social Sciences Citation Index (SSCI)--1956-present Arts & Humanities Citation Index (A&HCI)--1975-present
PubMed/Medline	<a href="http://www.ncbi.nlm.nih.gov/pubmed/">http://www.ncbi.nlm.nih.gov/pubmed/</a>	2/5/2010	597	Satisfactory	Yes	"Related Articles" link to the Viswanathan report in PubMed	1950-present

**Table B1. Sources Searched for Assessment of Impact of an EPC Report (continued)**

Source	URL	Date of Last Search	Yield	Ease of Use*	Import Function?	Search Strategy	Dates of Coverage
<b>FOR ONGOING STUDIES</b>							
AHRQ grants database	<a href="http://www.gold.ahrq.gov/">http://www.gold.ahrq.gov/</a>	2/9/2010	5	Difficult/No Boolean searching	No	"community-based participatory research"; CBPR	1998-present
ClinicalTrials.gov	<a href="http://clinicaltrials.gov">http://clinicaltrials.gov</a>	2/9/2010	10	Satisfactory	No	"community-based participatory research" OR CBPR	Unavailable/Updated continuously
CMS Web site	<a href="http://www.cms.hhs.gov/">http://www.cms.hhs.gov/</a>	2/9/2010	0	Satisfactory	No	"community-based participatory research" OR CBPR	Unavailable
CMS Active Projects Report	<a href="http://www.cms.hhs.gov/ActiveProjectReports/">http://www.cms.hhs.gov/ActiveProjectReports/</a>	2/9/1010	0	Satisfactory	No	"community-based participatory research" OR CBPR	Fiscal Year 2009
Commonwealth Fund	<a href="http://www.commonwealthfund.org/Grants-and-Programs/Search-Grants.aspx">http://www.commonwealthfund.org/Grants-and-Programs/Search-Grants.aspx</a>	2/10/2010	0	Satisfactory	No	"community-based participatory research" OR CBPR	1995-2010
Department of Veterans Affairs	<a href="http://www.va.gov/">http://www.va.gov/</a>	2/9/1010	1	Satisfactory	No	"community-based participatory research" OR CBPR	Unavailable
The Foundation Directory Platinum Online (UNC has subscription)	<a href="http://fconline.foundationcenter.org/">http://fconline.foundationcenter.org/</a>	2/11/2010	18	Satisfactory	No	"community-based participatory research" OR CBPR	2003-present
HRSA grants	<a href="http://www.hrsa.gov/grants/">http://www.hrsa.gov/grants/</a>	2/10/2010	0	Difficult	No	"community-based participatory research" OR CBPR	2010
HSRProj	<a href="http://wwwcf.nlm.nih.gov/hsr_project/home_proj.cfm">http://wwwcf.nlm.nih.gov/hsr_project/home_proj.cfm</a>	2/10/2010	86	Satisfactory	Yes	"community-based participatory research" OR CBPR	Projects are listed until 4 years after each project's end date
Kaiser Family Foundation	<a href="http://www.kaisernetwork.org/gsa/kfadvanced.jsp">http://www.kaisernetwork.org/gsa/kfadvanced.jsp</a>	2/10/2010	0	Satisfactory	No	"community-based participatory research" as a phrase, OR CBPR	

**Table B1. Sources Searched for Assessment of Impact of an EPC Report (continued)**

Source	URL	Date of Last Search	Yield	Ease of Use*	Import Function?	Search Strategy	Dates of Coverage
NIH RePORTER (previously CRISP)	<a href="http://projectreporter.nih.gov/reporter.cfm">http://projectreporter.nih.gov/reporter.cfm</a>	2/10/1010	189	Difficult	No	"Community-Based Participatory Research" "Assessing the Evidence" OR CBPR - limited to Fiscal Years: Active projects	1986-present
Rural Health Research Gateway	<a href="http://www.ruralhealthresearch.org/">http://www.ruralhealthresearch.org/</a>	2/10/2010	0	Satisfactory	No	"community-based participatory research" OR CBPR	2006-present
RWJF grants database online	<a href="http://www.rwjf.org/grants/pg.jsp">http://www.rwjf.org/grants/pg.jsp</a>	2/10/2010	49	Satisfactory	No	"Community-Based Participatory Research" OR CBPR	Within the last 5 years
SPIN (InfoEd International) (UNC has subscription)	<a href="http://www.infoed.org/new_spin/spinmain.asp">http://www.infoed.org/new_spin/spinmain.asp</a>	2/10/2010	19	Satisfactory	No	phrase search: community-based participatory research (32); CBPR (6). There may be overlap	Unavailable/Updated continuously
<b>FOR SOLICITATIONS</b>							
FedBizOpps (Federal Business Opportunities) (click "Find Opportunities")	<a href="https://www.fbo.gov">https://www.fbo.gov</a>	2/9/1010	0	Difficult	No	"community-based participatory research" OR CBPR	Past year
Grants.gov	<a href="http://www.grants.gov">http://www.grants.gov</a>	5-Feb-10	0	Difficult/Phrase searching unavailable	No	"community-based participatory research" OR CBPR	Unavailable
HHS Grants Forecast	<a href="https://extranet.acf.hhs.gov/hhsgrantsforecast/">https://extranet.acf.hhs.gov/hhsgrantsforecast/</a>	10-Feb-10	0	Difficult	No	"community-based participatory research" OR CBPR	2009-September 2011 (estimated posting)
<b>INPUT</b>							
National Institutes of Health [NIH] Guide for Grants and Contracts	<a href="http://grants.nih.gov/grants/guide/">http://grants.nih.gov/grants/guide/</a>	10-Feb-10	32	Difficult/Phrase searching unavailable	No	Community-Based Participatory Research (20); CBPR (12) some overlap; 5 copied, 1 cited the Viswanathan report.	1993-present (Historical files available 1970-1992)

**Table B1. Sources Searched for Assessment of Impact of an EPC Report (continued)**

Source	URL	Date of Last Search	Yield	Ease of Use*	Import Function?	Search Strategy	Dates of Coverage
<b>FOR BOTH ONGOING STUDIES AND SOLICITATIONS</b>							
Google, limited to .gov sites	http://www.google.com	5-Feb-10	12+	Satisfactory	No	Viswanathan "Community-Based Participatory Research: Assessing the Evidence"	Not applicable

\* Ease of Use is rated as Satisfactory or Difficult. Sources with a Satisfactory rating recognized phrase searching and Boolean connectors, or other helpful search instructions were provided. In addition, the search "worked," providing results containing the search terms. Those sources with a Difficult rating did not recognize phrase searching and/or Boolean connectors, and/or there were no search instructions, and/or the search results did not contain the search terms.

## Appendix C. Potentially Relevant National Institutes of Health (NIH) Requests for Applications and Program Announcements

**Table C1. Requests for Applications (RFAs) and Program Announcements since 1993 for “health literacy”**

Announcement Number	Related Announc.	Issuing Organization	Release Date	Opening Date (SF424 Only)	Expiration Date	Activity Code(s)	Title
PAR-11-023	See Related	AHRQ	11/09/2010	01/16/2011	01/08/2014	R21	Patient Safety and Medical Liability Reform Planning Projects (R21)
PAR-11-024	See Related	AHRQ	11/09/2010	12/25/2010	01/08/2014	R18	Advances in Patient Safety through Simulation Research (R18)
PAR-11-025	See Related	AHRQ	11/09/2010	12/25/2010	01/08/2014	R18	Patient Safety and Medical Liability Reform Demonstration Projects (R18)
RFA-HS-11-002	See Related	AHRQ	11/08/2010	n/a	02/16/2011	U18	Infrastructure for Maintaining Primary Care Transformation (IMPACT) Support for Models of Multi-sector, State-level Excellence (U18)
RFA-DK-10-009	See Related	NIDDK	08/24/2010	n/a	11/18/2010	P30	NIDDK Centers for Diabetes Translation Research (P30)
RFA-LM-10-001	See Related	NLM	05/13/2010	06/14/2010	07/15/2010	G08	NLM Information Resource Grants to Reduce Health Disparities (G08)
PAR-10-168	See Related	AHRQ	04/15/2010	05/16/2010	03/17/2014	R03	AHRQ Small Research Grant Program (R03)
RFA-EB-10-002	See Related	NIBIB	03/19/2010	04/20/2010	01/08/2011	R43,R44	Development and Translation of Medical Technologies that Reduce Health Disparities (SBIR [R43/R44])
PA-10-100	See Related	NIAAA	03/17/2010	05/05/2010	05/08/2013	R01	Alcohol Use Disorders: Treatment, Services Research, and Recovery (R01)
PA-10-101	See Related	NIAAA	03/17/2010	05/16/2010	05/08/2013	R03	Alcohol Use Disorders: Treatment, Services Research, and Recovery (R03)

**Table C1. Requests for Applications (RFAs) and Program Announcements since 1993 for “health literacy” (continued)**

<b>Announcement Number</b>	<b>Related Announc.</b>	<b>Issuing Organization</b>	<b>Release Date</b>	<b>Opening Date (SF424 Only)</b>	<b>Expiration Date</b>	<b>Activity Code(s)</b>	<b>Title</b>
PA-10-102	See Related	NIAAA	03/17/2010	05/16/2010	05/08/2013	R21	Alcohol Use Disorders: Treatment, Services Research, and Recovery (R21)
PAR-10-133	See Related	OBSSR	03/12/2010	05/05/2010	05/08/2013	R01	Understanding and Promoting Health Literacy (R01)
PAR-10-134	See Related	OBSSR	03/12/2010	05/16/2010	05/08/2013	R03	Understanding and Promoting Health Literacy (R03)
PAR-10-135	See Related	OBSSR	03/12/2010	05/16/2010	05/08/2013	R21	Understanding and Promoting Health Literacy (R21)
RFA-MD-10-005	See Related	NCMHD	03/12/2010	04/17/2010	05/18/2010	R01	NCMHD Advances in Health Disparities Research on Social Determinants of Health (R01)
RFA-HS-10-010	See Related	AHRQ	02/19/2010	02/28/2010	03/30/2010	R01	ARRA OS Recovery Act 2009 Limited Competition: Enhanced State Data for Analysis and Tracking of Comparative Effectiveness Impact: Improved Clinical Content and Race-Ethnicity Data (R01)
RFA-HS-10-013	See Related	AHRQ	02/19/2010	02/23/2010	04/08/2010	R18	ARRA OS Recovery Act 2009 Limited Competition: Comparative Effectiveness Delivery System Demonstration Grants (R18)
RFA-HS-10-012	See Related	AHRQ	02/12/2010	02/18/2010	04/01/2010	R01	ARRA OS Recovery Act 2009 Limited Competition: Comparative Effectiveness Delivery System Evaluation Grants (R01)

**Table C1. Requests for Applications (RFAs) and Program Announcements since 1993 for “health literacy” (continued)**

Announcement Number	Related Announc.	Issuing Organization	Release Date	Opening Date (SF424 Only)	Expiration Date	Activity Code(s)	Title
RFA-HS-10-014	See Related	AHRQ	02/05/2010	02/24/2010	03/25/2010	R18	ARRA OS: Recovery Act 2009 Limited Competition: Accelerating Implementation of Comparative Effectiveness Findings on Clinical and Delivery System Interventions by Leveraging AHRQ Networks (R18)
PA-10-089	See Related	AHRQ	01/21/2010	03/01/2010	01/08/2013	R18	Prevention and Management of Healthcare Associated Infections (R18)
RFA-HS-10-015	See Related	AHRQ	01/21/2010	02/10/2010	03/11/2010	R01	ARRA OS: Recovery Act 2009 Limited Competition: Scalable Distributed Research Networks for Comparative Effectiveness Research (R01)
RFA-HS-10-018	See Related	AHRQ	01/21/2010	02/26/2010	06/22/2010	R18	Improving Patient Safety through Simulation Research (R18)
RFA-HS-10-020	See Related	AHRQ	01/21/2010	02/28/2010	03/30/2010	R01	ARRA OS Recovery Act 2009 Limited Competition: Enhanced Registries for Quality Improvement and Comparative Effectiveness Research (R01)
RFA-HS-10-001	See Related	AHRQ	12/22/2009	n/a	01/21/2010	R24	Recovery Act 2009 Limited Competition: Expansion of Research Capability to Study Comparative Effectiveness in Complex Patients (R24)

**Table C1. Requests for Applications (RFAs) and Program Announcements since 1993 for “health literacy” (continued)**

Announcement Number	Related Announc.	Issuing Organization	Release Date	Opening Date (SF424 Only)	Expiration Date	Activity Code(s)	Title
RFA-HS-10-009	See Related	AHRQ	12/17/2009	12/20/2009	01/21/2010	R21	Recovery Act 2009 Limited Competition OS ARRA: Comparative Effectiveness Research to Optimize Prevention and Healthcare Management for the Complex Patient (R21)
RFA-HS-10-016	See Related	AHRQ	12/17/2009	n/a	03/26/2010	P50	Active Aging: Supporting Individuals and Enhancing Community-based Care through Health Information Technology (HIT) (P50)
PA-10-008	See Related	NINR	10/05/2009	01/16/2010	01/08/2013	R03	Mechanisms, Models, Measurement, and Management in Pain Research (R03)
RFA-CA-09-032	See Related	NCI	10/02/2009	n/a	12/16/2009	U54	Community Networks Program (CNP) Centers for Reducing Cancer Disparities through Outreach, Research and Training (U54)
RFA-HD-09-010	See Related	NICHD	07/24/2009	09/28/2009	12/01/2009	R03	Limited Competition: Addressing Health Disparities in Maternal and Child Health through Community-Based Participatory Research (R03)
RFA-MD-09-007	See Related	NCMHD	05/12/2009	n/a	07/02/2009	P20	Recovery Act Limited Competition: NCMHD Exploratory Centers of Excellence (P20)
RFA-MD-09-005	See Related	NCMHD	04/14/2009	n/a	06/20/2009	P20	NCMHD Exploratory Centers of Excellence (P20)
RFA-HS-09-001	See Related	AHRQ	02/20/2009	n/a	04/22/2009	R24	AHRQ Research Infrastructure Program: Phase II Limited Competition (R24)



**Table C1. Requests for Applications (RFAs) and Program Announcements since 1993 for “health literacy” (continued)**

Announcement Number	Related Announc.	Issuing Organization	Release Date	Opening Date (SF424 Only)	Expiration Date	Activity Code(s)	Title
PAR-09-092	See Related	NICHD	01/30/2009	03/01/2009	03/03/2011	U13	Academic-Community Partnership Conference Series (U13)
PAR-09-085	See Related	AHRQ	01/23/2009	02/09/2009	01/08/2012	K08	Mentored Clinical Scientist Research Career Development Award (K08)
PAR-09-086	See Related	AHRQ	01/23/2009	02/09/2009	01/08/2012	K02	Independent Scientist Award (K02)
PAR-09-087	See Related	AHRQ	01/23/2009	02/09/2009	01/08/2012	K01	Mentored Research Scientist Research Career Development Award (K01)
PA-09-070	See Related	AHRQ	01/02/2009	01/05/2009	01/08/2012	R01	AHRQ Health Services Research Projects (R01)
PA-09-071	See Related	AHRQ	01/02/2009	02/09/2009	01/08/2012	R18	AHRQ Health Services Research Demonstration and Dissemination Grants (R18)
RFA-ES-09-001	See Related	NIEHS	12/23/2008	03/01/2009	04/02/2009	R21	Research to Action: Assessing and Addressing Community Exposures to Environmental Contaminants (R21)
RFA-EB-09-001	See Related	NIBIB	12/16/2008	01/20/2009	01/08/2010	R43,R44	Development and Translation of Medical Technologies that Reduce Health Disparities (SBIR [R43/R44])
PAR-08-261	See Related	NICHD	09/08/2008	12/15/2008	09/16/2010	R01	Research on Emergency Medical Services for Children (R01)
RFA-MD-08-004	See Related	NCMHD	05/29/2008	n/a	08/01/2008	P20	NCMHD Exploratory Centers of Excellence (P20)
RFA-MD-08-005	See Related	NCMHD	05/28/2008	n/a	08/30/2008	P60	NCMHD Comprehensive Centers of Excellence (P60)
RFA-DE-08-009	See Related	NIDCR	12/26/2007	01/22/2008	11/15/2008	R21	Developing Complex Models of Oral Health Behavior (R21)

**Table C1. Requests for Applications (RFAs) and Program Announcements since 1993 for “health literacy” (continued)**

Announcement Number	Related Announc.	Issuing Organization	Release Date	Opening Date (SF424 Only)	Expiration Date	Activity Code(s)	Title
RFA-HS-08-002	See Related	AHRQ	11/16/2007	01/21/2008	02/22/2008	R18	Ambulatory Safety and Quality Program: Improving Management of Individuals with Complex Healthcare Needs through Health IT (R18)
RFA-CA-08-004	See Related	NCI	11/09/2007	n/a	02/23/2008	P50	Centers of Excellence in Cancer Communication Research II (CECCR II) (P50)
PA-07-391	See Related	NINR	06/29/2007	09/05/2007	09/08/2010	R21	Reducing Health Disparities Among Minority and Underserved Children (R21)
PA-07-392	See Related	NIH	06/29/2007	09/05/2007	09/08/2010	R01	Reducing Health Disparities Among Minority and Underserved Children (R01)
RFA-DE-08-008	See Related	NIDCR	05/03/2007	n/a	11/16/2007	U54	Centers for Research to Reduce Disparities in Oral Health (U54)
PA-07-282	See Related	NINR	01/08/2007	01/08/2007	01/08/2010	R01	Mechanisms, Models, Measurement, and Management in Pain Research (R01)
RFA-AI-07-004	See Related	NIAID	12/27/2006	n/a	03/14/2007	U01	Women’s Interagency HIV Study (WIHS) IV, Limited Competition (U01)
PA-07-169	See Related	NIDCR	12/14/2006	01/05/2007	01/08/2010	R01	Epidemiological and Behavioral Research in Oral Health (R01)
PA-07-151	See Related	NIDCR	12/12/2006	01/05/2007	01/08/2010	R01	Oral Health of Special Needs and Older Populations (R01)
RFA-HS-07-007	See Related	AHRQ	12/05/2006	01/15/2007	02/16/2007	R18	Ambulatory Safety and Quality: Enabling Patient-Centered Care through Health IT (R18)
PAR-07-020	See Related	OBSSR	11/20/2006	01/05/2007	01/26/2010	R01	Understanding and Promoting Health Literacy (R01)
PAR-07-018	See Related	OBSSR	10/27/2006	03/23/2007	01/26/2010	R21	Understanding and Promoting Health Literacy(R21)

**Table C1. Requests for Applications (RFAs) and Program Announcements since 1993 for “health literacy” (continued)**

Announcement Number	Related Announc.	Issuing Organization	Release Date	Opening Date (SF424 Only)	Expiration Date	Activity Code(s)	Title
PAR-07-019	See Related	OBSSR	10/27/2006	03/23/2007	01/26/2010	R03	Understanding and Promoting Health Literacy (R03)
RFA-AG-07-005	See Related	NIA	10/27/2006	n/a	01/09/2007	P30	Resource Centers and Coordinating Center for Minority Aging Research (RCMAR)
PA-06-542	See Related	NINR	08/31/2006	09/01/2006	01/08/2010	R21	Mechanisms, Models, Measurement, & Management in Pain Research (R21)
PA-06-543	See Related	NINR	08/31/2006	09/01/2006	01/08/2010	R03	Mechanisms, Models, Measurement, & Management in Pain Research (R03)
PA-06-544	See Related	NINR	08/31/2006	n/a	01/03/2007	R01	Mechanisms, Models, Measurement, & Management in Pain Research (R01)
RFA-DE-07-008	See Related	NIDCR	07/28/2006	11/19/2006	01/20/2007	R21	Health Promotion Research Directed to Improving the Oral Health of Women and Their Infants (R21)
PA-06-351	See Related	NCI	04/12/2006	05/02/2006	05/08/2009	R21	Exploratory Grants for Behavioral Research in Cancer Control (R21)
PAR-06-246	See Related	NIDCR	03/17/2006	05/02/2006	01/08/2008	R21	NIDCR Exploratory and Developmental Grants in Clinical Research (R21)
PAR-06-132	See Related	OBSSR	03/02/2006	05/02/2006	10/14/2006	R03	Understanding and Promoting Health Literacy (R03)
RFA-IP-06-008	See Related	NIP	02/22/2006	n/a	04/10/2006	U01	Racial/Ethnic Differences in Parental Factors Related to Children Missing Scheduled Immunization Visits
RFA-LM-06-001	See Related	NLM	01/12/2006	n/a	03/18/2006	T15	Institutional Grants for Research Training in Biomedical Informatics (T15)

**Table C1. Requests for Applications (RFAs) and Program Announcements since 1993 for “health literacy” (continued)**

Announcement Number	Related Announc.	Issuing Organization	Release Date	Opening Date (SF424 Only)	Expiration Date	Activity Code(s)	Title
RFA-DP-04-003	See Related	NCCDPHP	05/13/2005	n/a	06/16/2005	U48	Health Promotion and Disease Prevention Research Centers: Special Interest Project Competitive Supplements
RFA-CD-05-108	See Related	OPHR	05/02/2005	n/a	06/18/2005	P01	Centers of Excellence in Health Marketing and Health Communication
PAR-05-020	See Related	NIDCR	11/23/2004	n/a	05/02/2006	R21	NIDCR Exploratory and Developmental Grants in Clinical Research
PAR-04-116	See Related	OBSSR	06/22/2004	n/a	10/14/2006	R01	UNDERSTANDING AND PROMOTING HEALTH LITERACY (R01)
PAR-04-117	See Related	OBSSR	06/22/2004	n/a	03/02/2006	R03	UNDERSTANDING AND PROMOTING HEALTH LITERACY (R03)
RFA-ES-04-007	See Related	NIEHS	06/09/2004	n/a	01/08/2005	R25	ENVIRONMENTAL JUSTICE: PARTNERSHIPS FOR COMMUNICATION
RFA-CD-04-001	See Related	OPHR	04/22/2004	n/a	06/23/2004	K01	CDC PUBLIC HEALTH RESEARCH: HEALTH PROTECTION RESEARCH INITIATIVE MENTORED RESEARCH SCIENTIST DEVELOPMENT AWARD (K01)
RFA-CD-04-002	See Related	OPHR	04/22/2004	n/a	06/23/2004	R01	CDC PUBLIC HEALTH RESEARCH: HEALTH PROTECTION RESEARCH INITIATIVE INVESTIGATOR INITIATED RESEARCH (R01)
PA-04-031	See Related	NIDCR	12/08/2003	n/a	11/01/2006	R01	ORAL HEALTH OF SPECIAL NEEDS AND OLDER POPULATIONS

**Table C1. Requests for Applications (RFAs) and Program Announcements since 1993 for “health literacy” (continued)**

Announcement Number	Related Announc.	Issuing Organization	Release Date	Opening Date (SF424 Only)	Expiration Date	Activity Code(s)	Title
PA-04-022	See Related	NIDCR	11/14/2003	n/a	11/01/2006	R01, U01	EPIDEMIOLOGICAL AND BEHAVIORAL RESEARCH IN ORAL HEALTH
RFA-DE-04-009	See Related	NIDCR	11/14/2003	n/a	04/15/2004	R21	NIDCR EXPLORATORY AND DEVELOPMENTAL GRANTS IN CLINICAL RESEARCH
PAS-03-166	See Related	NINDS	08/28/2003	n/a	07/01/2006	R01	REDUCING STROKE DISPARITIES THROUGH RISK FACTOR SELF-MANAGEMENT
RFA-ES-03-007	See Related	NIEHS	04/22/2003	n/a	10/18/2003		ENVIRONMENTAL JUSTICE: PARTNERSHIPS FOR COMMUNICATION
RFA-ES-03-002	See Related	NIEHS	10/28/2002	n/a	01/15/2003		ENVIRONMENTAL JUSTICE: PARTNERSHIPS FOR COMMUNICATION
RFA-DE-02-004	See Related	NIDCR	01/11/2002	n/a	04/19/2002		PILOT GRANTS FOR RESEARCH TO PREVENT OR REDUCE ORAL HEALTH DISPARITIES
RFA-DE-02-005	See Related	NIDCR	01/11/2002	n/a	04/19/2002		PLANNING GRANTS FOR RESEARCH TO PREVENT OR REDUCE ORAL HEALTH DISPARITIES
RFA-GM-02-001	See Related	NIGMS	08/24/2001	n/a	12/13/2001		NATIVE AMERICAN RESEARCH CENTERS FOR HEALTH
RFA-DC-02-001	See Related	NIDCD	07/24/2001	n/a	10/11/2001		PROMOTION AND DISEASE PREVENTION: HEALTH COMMUNICATION, DEVELOPMENT, AND DISSEMINATION
RFA-GM-00-007	See Related	NIGMS	08/21/2000	n/a	12/13/2000		NATIVE AMERICAN RESEARCH CENTERS FOR HEALTH

**Table C1. Requests for Applications (RFAs) and Program Announcements since 1993 for “health literacy” (continued)**

<b>Announcement Number</b>	<b>Related Announc.</b>	<b>Issuing Organization</b>	<b>Release Date</b>	<b>Opening Date (SF424 Only)</b>	<b>Expiration Date</b>	<b>Activity Code(s)</b>	<b>Title</b>
RFA-DC-00-003	See Related	NIDCD	07/31/2000	n/a	10/12/2000		PROMOTION AND DISEASE PREVENTION: HEALTH COMMUNICATION, DEVELOPMENT, AND DISSEMINATION
RFA-HS-00-003	See Related	AHRQ	10/20/1999	n/a	01/22/2000		UNDERSTANDING AND ELIMINATING MINORITY HEALTH DISPARITIES
RFA-DE-99-003	See Related	NIDCR	09/30/1999	n/a	11/16/2000		CENTERS FOR RESEARCH TO REDUCE ORAL HEALTH DISPARITIES
RFA-ES-99-005	See Related	NIEHS	04/21/1999	n/a	07/15/1999		ENVIRONMENTAL JUSTICE: PARTNERSHIPS FOR COMMUNICATION
RFA-ES-96-002	See Related	NIEHS	09/22/1995	n/a	12/23/1995		ENVIRONMENTAL JUSTICE: PARTNERSHIPS FOR COMMUNICATION
RFA-ES-94-005	See Related	NIEHS	01/07/1994	n/a	04/02/1994		ENVIRONMENTAL EQUITY: PARTNERSHIPS FOR COMMUNICATION

**Table C2. Requests for Applications (RFAs) and Program Announcements since 1993 for “omega 3,” “fish oil,” “n-3 fatty acids,” and “omega-3 fatty acids”**

<b>Announcement Number</b>	<b>Related Announc.</b>	<b>Issuing Organization</b>	<b>Release Date</b>	<b>Opening Date (SF424 Only)</b>	<b>Expiration Date</b>	<b>Activity Code(s)</b>	<b>Title</b>
RFA-HD-12-105	See Related	NICHD	08/30/2010	11/21/2010	12/22/2010	R03	The Role of Human-Animal Interaction in Child Health and Development (R03)
PA-10-239	See Related	NIAAA	07/30/2010	09/05/2010	09/08/2013	R01	Nutrition and Alcohol-Related Health Outcomes (R01)
PA-10-240	See Related	NIAAA	07/30/2010	09/16/2010	09/08/2013	R03	Nutrition and Alcohol-Related Health Outcomes (R03)
PA-10-241	See Related	NIAAA	07/30/2010	09/16/2010	09/08/2013	R21	Nutrition and Alcohol-Related Health Outcomes (R21)
PA-10-088	See Related	NCI	03/17/2010	05/16/2010	05/08/2013	R21	Exploratory Cancer Prevention Studies Involving Molecular Targets for Bioactive Food Components (R21)
RFA-HD-10-008	See Related	NICHD	01/29/2010	n/a	06/02/2010	U10	Eunice Kennedy Shriver NICHD Maternal Fetal Medicine Units Network (U10)
RFA-HD-09-030	See Related	NICHD	08/11/2009	10/19/2009	11/20/2009	R03	The Role of Human-Animal Interaction in Child Health and Development (R03)

**Table C2. Requests for Applications (RFAs) and Program Announcements since 1993 for “omega 3,” “fish oil,” “n-3 fatty acids,” and “omega-3 fatty acids” (continued)**

<b>Announcement Number</b>	<b>Related Announc.</b>	<b>Issuing Organization</b>	<b>Release Date</b>	<b>Opening Date (SF424 Only)</b>	<b>Expiration Date</b>	<b>Activity Code(s)</b>	<b>Title</b>
RFA-HD-09-031	See Related	NICHD	08/11/2009	10/19/2009	11/20/2009	R01	The Role of Human-Animal Interaction in Child Health and Development (R01)
RFA-HL-10-001	See Related	NHLBI	10/30/2008	n/a	05/29/2009	P20	Cardiac Translational Research Implementation Program (C-TRIP) (P20)
PA-08-210	See Related	NCI	07/18/2008	09/05/2008	09/08/2011	R01	Diet-Induced Changes in Inflammation as Determinants of Colon Cancer (R01)
PA-08-211	See Related	NCI	07/18/2008	09/16/2008	09/08/2011	R21	Diet-Induced Changes in Inflammation as Determinants of Colon Cancer (R21)
PA-08-030	See Related	NCI	11/26/2007	01/05/2008	01/08/2011	R01	Exfoliated Cells, Bioactive Food Components, and Cancer (R01)
PA-08-031	See Related	NCI	11/26/2007	01/16/2008	01/08/2011	R21	Exfoliated Cells, Bioactive Food Components, and Cancer (R21)
PA-07-403	See Related	NIAAA	07/16/2007	09/05/2007	09/08/2010	R01	Nutrition and Alcohol-Related Health Outcomes (R01)



**Table C2. Requests for Applications (RFAs) and Program Announcements since 1993 for “omega 3,” “fish oil,” “n-3 fatty acids,” and “omega-3 fatty acids” (continued)**

<b>Announcement Number</b>	<b>Related Announc.</b>	<b>Issuing Organization</b>	<b>Release Date</b>	<b>Opening Date (SF424 Only)</b>	<b>Expiration Date</b>	<b>Activity Code(s)</b>	<b>Title</b>
PA-07-404	See Related	NIAAA	07/16/2007	09/16/2007	09/08/2010	R03	Nutrition and Alcohol-Related Health Outcomes (R03)
PA-07-405	See Related	NIAAA	07/16/2007	09/16/2007	09/08/2010	R21	Nutrition and Alcohol-Related Health Outcomes (R21)
PA-07-362	See Related	NCI	04/23/2007	05/16/2007	03/17/2010	R21	Exploratory Cancer Prevention Studies Involving Molecular Targets for Bioactive Food Components (R21)
PA-07-207	See Related	NCI	12/19/2006	01/05/2007	01/08/2008	R01	Exfoliated Cells, Bioactive Food Components, and Cancer (R01)
PA-07-186	See Related	NCI	12/18/2006	01/05/2007	09/08/2008	R01	Diet-Induced Changes in Inflammation as Determinants of Colon Cancer (R01)
PA-07-120	See Related	NIDA	12/08/2006	01/05/2007	05/08/2008	R01	Complementary and Alternative Medicine for Substance and Alcohol Related Disorders (R01)

**Table C2. Requests for Applications (RFAs) and Program Announcements since 1993 for “omega 3,” “fish oil,” “n-3 fatty acids,” and “omega-3 fatty acids” (continued)**

<b>Announcement Number</b>	<b>Related Announc.</b>	<b>Issuing Organization</b>	<b>Release Date</b>	<b>Opening Date (SF424 Only)</b>	<b>Expiration Date</b>	<b>Activity Code(s)</b>	<b>Title</b>
PA-06-424	See Related	NIDA	05/19/2006	05/19/2006	05/08/2008	R03	Complementary and Alternative Medicine for Substance and Alcohol Related Disorders (R03)
PA-06-425	See Related	NIDA	05/19/2006	05/19/2006	05/08/2008	R21	Complementary and Alternative Medicine for Substance and Alcohol Related Disorders (R21)
PA-06-359	See Related	NCI	04/13/2006	05/02/2006	01/08/2008	R21	Exfoliated Cells, Bioactive Food Components, and Cancer (R21)
PA-06-360	See Related	NCI	04/13/2006	05/02/2006	01/08/2008	R03	Exfoliated Cells, Bioactive Food Components, and Cancer (R03)
PA-06-283	See Related	NCI	03/28/2006	05/02/2006	09/08/2008	R21	Diet-Induced Changes in Inflammation as Determinants of Colon Cancer (R21)
PA-05-125	See Related	NCI	06/20/2005	n/a	01/03/2007	R01, R21	Diet-Induced Changes in Inflammation as Determinants of Colon Cancer
PA-05-097	See Related	NIDA	04/26/2005	n/a	01/03/2007	R01, R03, R21	Complementary and Alternative Medicine for Substance and Alcohol Related Disorders

**Table C2. Requests for Applications (RFAs) and Program Announcements since 1993 for “omega 3,” “fish oil,” “n-3 fatty acids,” and “omega-3 fatty acids” (continued)**

<b>Announcement Number</b>	<b>Related Announc.</b>	<b>Issuing Organization</b>	<b>Release Date</b>	<b>Opening Date (SF424 Only)</b>	<b>Expiration Date</b>	<b>Activity Code(s)</b>	<b>Title</b>
PA-04-114	See Related	NCI	06/18/2004	n/a	01/03/2007	R01, R03, R21	Exfoliated Cells, Bioactive Food Components, and Cancer
RFA-CA-01-015	See Related	NCI	09/20/2000	n/a	02/15/2001		Planning Grant for Collaborations on Nutritional Modulation of Genetic Pathways Leading to Cancer
RFA-HL-98-005	See Related	NHLBI	12/05/1997	n/a	03/18/1998		Origins of Asthma in Early Life
RFA-CA-95-010	See Related	NCI	04/14/1995	n/a	07/13/1995		Human Metabolic Studies of Modification of Dietary Fatty Acid Intake for Prevention of Dietary Fatty Acid Intake for Prevention of Breast, Prostate, and Colon Cancer
RFA-HL-94-013	See Related	NHLBI	04/01/1994	n/a	09/16/1994		Specialized Centers of Research in Hemostatic and Thrombotic Disease
PA-93-103	See Related	NIDDK	08/20/1993	n/a	08/20/1996		Nutrition in Cystic Fibrosis
PA-93-065	See Related	NIDDK	03/19/1993	n/a	03/19/1996		Nutrient Antioxidants, Cellular Metabolism and Function

## Appendix D. Results of Update Search

Appendix D contains four tables: D1, D2, D3, and D4. Tables D2 and D4 record how studies published after the release of the AHRQ report use the report and related citations. Tables D1 and D3 serve as codes for Tables D2 and D4, respectively. Table D2 lists all the articles identified as being relevant for inclusion during an update of the *Literacy and Health Outcomes* report and provides the author, year, and title of the article. The column titled “References” lists whether or not the article cited the original AHRQ report, subsequent articles, or other work by the EPC investigators. If the article cited one or more of these references, the column entitled “Reference” also lists a numerical code (Table D1 provides the key to the code). The “Text” column provides the exact string of text that cites the AHRQ report, subsequent articles, or EPC investigators and includes either a numbered citation or the author’s last name. Because the entry in the “Text” column is a direct quote from the article, the format of the citations may appear in superscripts or brackets as numbered references or in parentheses with the author’s last name, with the full citation appearing in the reference list for each entry in the table. Due to the difficulty of reproducing the entire reference list from each article in the table, we highlighted the exact string of references to the original AHRQ report, subsequent articles, or other work by EPC investigators in bold in brackets..

Tables D3 and D4 serve similar functions as Tables D1 and D2. Table D4 lists all the articles identified as being relevant for inclusion during an update of the *Effects of Omega-3 Fatty Acids on Cardiovascular Risk Factors and Intermediate Markers of Cardiovascular Disease* report and provides the author, year, and title of the article. Table D3 serves as a key to understanding the codes in the column titled “References” in Table D4.

**Table D1. Key to review of update of health literacy**

	Citation
1	Berkman ND, DeWalt DA, Pignone MP, Sheridan SL, Lohr KN, Lux L, Sutton SF, Swinson T, Bonito AJ: <b>Literacy and health outcomes, summary, evidence report.</b> Rockville, MD, Agency for Healthcare Research and Quality, 2004 (Tech. Assessment no. 87)
2	DeWalt, D.A., Berkman, N.D., Sheridan, S., Lohr, K.N., & Pignone, M.P. (2004). <b>Literacy and health outcomes: A systematic review of the literature.</b> <i>Journal of General Internal Medicine</i> , 19, 1228–1239.
3	DeWalt DA, Boone RS, Pignone MP. <b>Literacy and its relationship with self-efficacy, trust, and participation in medical decision making.</b> <i>Am J Health Behav.</i> 2007;31 Suppl 1:S27-35. [PMID: 17931133]
4	DeWalt DA, Pignone MP. <b>Reading is fundamental: the relationship between literacy and health</b> [Editorial]. <i>Arch Intern Med.</i> 2005;165:1943-4. [PMID: 16186462]
5	Pignone MP, Dewalt D. <b>Literacy and health outcomes Is adherence the missing link?</b> <i>J Gen Intern Med.</i> 2006;21(8):896–7.
6	DeWalt, D. A., Pignone, M., Malone, R., Rawls, C., Kosnar, M. C., George, G., et al. (2004). <b>Development and pilot testing of a disease anagement program for low literacy patients with heart failure.</b> <i>Patient Education and Counseling</i> , 55(1), 78–86.
7	DeWalt DA, Malone RM, Bryant ME, et al. <b>A heart failure self-management program for patients of all literacy levels: a randomized, controlled trial</b> [ISRCTN11535170]. <i>BMC Health Serv Res.</i> March 13 2006;6:30.
8	DeWalt DA, Pignone M, Malone RM, Bryant B, Felix K, Corr K, et al. <b>Randomized controlled trial of a primary care-based heart failure disease management program for patients with low literacy.</b> <i>J Gen Intern Med</i> 2004;19(s1):203.
9	Pignone M, DeWalt DA, Sheridan S, Berkman N, Lohr KN. <b>Interventions to improve health outcomes for patients with low literacy. A systematic review.</b> <i>J Gen Intern Med.</i> 2005;20:185–92.
10	Dewalt DA, Pignone M. <b>Health literacy and health outcomes: overview of the literature.</b> In: Schwartzberg J, VanGeest J, Wang C, editors. <i>Understanding health literacy – implications for medicine and public health.</i> American Medical Association; 2005. p. 205–28.
11	DeWalt DA, Dilling MH, Rosenthal MS, Pignone MP. <b>Low parent literacy is associated with worse asthma care measures in children.</b> <i>Ambul Pediatr</i> 2007;7(January–February):25–31.
12	DeWalt DA, Boone RS, Pignone MP. <b>Literacy and its relationship with self-efficacy, trust, and participation in medical decision making.</b> <i>Am. J. Health Behav.</i> 2007; 31: S27–S35.

**Table D2. Purpose of citation for health literacy update search**

<b>First Author</b>	<b>Year</b>	<b>Title</b>	<b>References</b>	<b>Text</b>	<b>Purpose of citation</b>
Marteleteo L.	2008	Sexual behavior, pregnancy, and schooling among young people in urban South Africa	None		
Torres RY	2009	Relationships among health literacy, knowledge about hormone therapy, self-efficacy, and decision-making among postmenopausal health	None		
Kalichman SC	2008	Association between health literacy and HIV treatment adherence: further evidence from objectively measured medication adherence	None		
Grubbs V	2009	Health literacy and access to kidney transplantation	None		
Lincoln A	2008	Limited literacy and psychiatric disorders among users of an urban safety-net hospital's mental health outpatient clinic	1	The recent Agency for Healthcare Research and Quality evidence review, "Literacy and Health Outcomes: Evidence Report/Technology Assessment," cited 5 studies that evaluate the association between a marker of health literacy and a marker of mental illness (Berkman et al., 2004). Four of these studies reported statistically significant associations between limited literacy and higher prevalence of depression, but not all of the associations remained significant in adjusted analyses. For example, Gazmarian et al. (2000) found that 13% of new Medicare recipients met criteria for depression on the Geriatric Depression Scale.	Introduction: study fills gap

**Table D2. Purpose of citation for health literacy update search (continued)**

<b>First Author</b>	<b>Year</b>	<b>Title</b>	<b>References</b>	<b>Text</b>	<b>Purpose of citation</b>
Ginde AA	2008	Multicenter study of limited health literacy in emergency department patients	1	The Institute of Medicine and Agency for Healthcare Research and Quality have recently reported that 90 million adult Americans have difficulty comprehending and acting on medical information [1,2]. Patients with inadequate health literacy have limited knowledge of their chronic disease, poor medication adherence, and worse health outcomes.	Introduction: supports the problem statement
Drainoni ML	2008	Health literacy of HIV-positive individuals enrolled in an outreach intervention: results of a cross-site analysis.	None		
Waite KR	2008	Literacy, social stigma, and HIV medication adherence	5		
Greene J	2008	Comprehension and choice of a consumer-directed health plan: an experimental study	None		
Huizinga MM	2008	Low numeracy skills are associated with higher BMI	None		

**Table D2. Purpose of citation for health literacy update search (continued)**

<b>First Author</b>	<b>Year</b>	<b>Title</b>	<b>References</b>	<b>Text</b>	<b>Purpose of citation</b>
Wallace LS	2008	Relationship between health literacy and health-related quality of life among Tennesseans	1	<p>One factor of particular importance was health literacy, which does not always correlate strongly with health literacy [4]</p> <p>Poor health literacy has been linked to poor general health status [4], but general health status is just one component of HRQOL. However, most studies of HRQOL have examined health status in specific populations, such as those with chronic disease, or targeted groups such as the elderly and Medicaid enrollees. We could find no published research, however, that studied the association of health literacy with overall HRQOL in adults of varying ages. To address this gap, we studied the relationship between health literacy and HRQOL in a sample of Tennessee adults obtaining healthcare at a university-based family medicine clinic.</p>	Introduction: study fills gap



**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Cavanaugh K	2008	Association of numeracy and diabetes control	3, 4	<p>3: We did not find a statistically significant association between literacy or general numeracy and hemoglobin A1c, and other recent studies have also not found a significant correlation between literacy and hemoglobin A1c [19 –21]. One explanation may be that diabetes-related numeracy skills are more specific to diabetes self-management activities, and therefore are more strongly associated with hemoglobin A1c than are literacy or general numeracy.</p> <p>4: We chose not to include education, literacy, and general numeracy skill level in our models because of high colinearity between these variables and DNT score and because of the potential for overadjustment [34]. We evaluated for interaction between DNT score and covariates, and this was not statistically significant.</p>	
Juzych MS	2008	Functional health literacy in patients with glaucoma in urban settings	None		
Muir KW	2008	Health literacy and vision-related quality of life	None		
Wright AJ	2009	The impact of numeracy on reactions to different graphic risk presentation formats: an experimental analogue study	None		
Tang YH	2008	Health literacy, complication awareness, and diabetic control in patients with type 2 diabetes mellitus	None		

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Baker DW	2008	Health literacy, cognitive abilities, and mortality among elderly persons	None		
Cho YI	2008	Effects of health literacy on health status and health service utilization amongst the elderly	1	As <b>[Berkman et al. (2004)]</b> has cautioned, potential confounders may lie in the causal pathway between health literacy and health outcomes. However, prior research tended to examine the consequences of low health literacy in a singular fashion and did not consider the inter-relationships among the various health outcomes (Lee, Arozullah, & Cho, 2004). In this study, we explored four potential intermediate factors that may link health literacy and health status and utilization: (1) disease knowledge, (2) health behavior, (3) preventive care, and (4) compliance. The relevance of these potential intermediary variables is reviewed below.	Introduction: study fills gap
White S	2008	Relationship of preventive health practices and health literacy: a national study	None		
Wolf MS	2007	Patients' shame and attitudes toward discussing the results of literacy screening	6	The benefits of literacy screening are apparent, as it could lead to a proper allocation of health education and care management resources <b>[DeWalt et al., 2004]</b> . The risks are less clear however, identifying patients as having limited literacy may result in adverse consequences, such as concerns for social stigma and the avoidance of health services out of shame.	

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Nokes KM	2007	Health literacy and health outcomes in HIV seropositive persons	1, 2	<p>Introduction:</p> <p>In the Agency for Healthcare Research and Quality (AHRQ) evidence-based report on health literacy, <b>Berkman et al. [2004]</b> reviewed 44 articles published as of May 2003 to examine whether health literacy skills were related to health outcomes, use of healthcare services, costs of healthcare, and disparities in health outcomes or healthcare service use, according to race, ethnicity, culture, or age. Variables associated with health outcomes included knowledge or comprehension, health behaviors, adherence, biochemical and biometric health outcomes, measures of disease prevalence, incidence, morbidity (including depression), and global health status measures. The AHRQ reviewers found that health literacy was related to knowledge and comprehension, hospitalization, global measures of health, and some chronic diseases, but the evidence was mixed, and findings were often dependent upon the analytic methods used.</p> <p>Methods:</p> <p>Health literacy is usually treated as a categorical variable [<b>DeWalt, Berkman, Sheridan, Lohr, &amp; Pignone, 2004</b>].</p>	<p>Introduction: lays out the state of the science</p> <p>Methods: justifies use of measure</p>
von Wagner C	2007	Functional health literacy and health-promoting behaviour in a national sample of British adults	None		

**Table D2. Purpose of citation for health literacy update search (continued)**

<b>First Author</b>	<b>Year</b>	<b>Title</b>	<b>References</b>	<b>Text</b>	<b>Purpose of citation</b>
Peterson NB	2007	The influence of health literacy on colorectal cancer screening knowledge, beliefs and behavior	2	[Cited with the IOM report]  More than 90 million Americans have poor literacy skills, and studies have suggested that low health literacy can be associated with less knowledge about cancer screening in general, less screening participation and worse clinical outcomes [17-19]. Little is known about how health literacy affects knowledge, attitudes and behaviors regarding CRC testing.	Introduction: supports problem statement
Osborn CY	2007	Health literacy: an overlooked factor in understanding HIV health disparities		None	
Aggarwal A	2007	The role of numeracy on cancer screening among urban women	4	Low health literacy has been found to correlate with less health knowledge, worse self management skills, less use of preventative tactics, higher rates of hospitalization, and death [15,16]. Individuals with low literacy may find themselves unable to read prescription labels; health education materials; test results, appointment reminders; and other important, but basic, documents.	Introduction: state of the science

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Persell SD	2007	Limited health literacy is a barrier to medication reconciliation in ambulatory care	2	<p>Methods:            Patients are classified as having inadequate, marginal, or adequate health literacy skills. For this small study, we defined patients as having either inadequate health literacy or marginal/adequate health literacy. Although prior findings are mixed regarding associations between health outcomes and marginal health literacy, these individuals more often appear to be similar to those with adequate rather than inadequate literacy [16–18].</p> <p>Discussion:            Our finding that inadequate health literacy was associated with having two or more antihypertensive medications recorded in the medical record but not with the number of antihypertensive medications patients reported taking could indicate a relationship between inadequate health literacy and nonadherence in this population. Prior findings in HIV treatment found inconclusive results as to the relationship between health literacy and medication adherence. [10,13,18–20] . Yet HIV may differ from hypertension. Antiretroviral medications generally have a single manufacturer, and a prior study found that patients with limited literacy often rely on pill characteristics for identification</p>	<p>Methods: provides context for measure chosen</p> <p>Discussion: places findings in context</p>

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Jones M	2007	Oral health literacy among adult patients seeking dental care	2	<p>Introduction: Patients with a low literacy level generally are 1.5 to three times more likely to experience poor outcomes in areas such as knowledge, intermediate disease markers, morbidity, general health status and use of health resources[7]. Little research has been done on the role of literacy in oral health.</p> <p>Discussion: Although very little research has been undertaken in dentistry, ample justification exists for pursuing research in this area. Studies of medical care demonstrate the importance of health literacy in various health outcomes [1,7] and many peripheral studies show that those with low levels of education also tend to have poor dental behaviors and bad oral health outcomes [9].</p>	<p>Introduction: problem statement</p> <p>Discussion: study fills gap</p>
Walker D	2007	Patient education in rheumatoid arthritis: the effectiveness of the ARC booklet and the mind map	None		
Hibbard JH	2007	Consumer competencies and the use of comparative quality information: it isn't just about literacy	None		
Yin HS	2007	Association of low caregiver health literacy with reported use of nonstandardized dosing instruments and lack of knowledge of weight-based dosing	None		
Baker DW	2007	Health literacy and mortality among elderly persons	7		

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Laramée AS	2007	Relationship of literacy and heart failure in adults with diabetes	2, 4	Dewalt's systematic review concluded that people who read at low levels are 1.5 to 3 times more likely to have an adverse outcome compared to people who read at higher levels [17].	Introduction: supports problem statement
Wolf MS	2007	To err is human: patient misinterpretations of prescription drug label instructions		None	
Campbell MJ	2007	Developing a parsimonious model for predicting completion of advance directives	None		
Bennett IM	2007	Literacy and depressive symptomatology among pregnant Latinas with limited English proficiency. Am J Orthopsychiatry	1	The standard designations of inadequate and marginal literacy levels were selected for the current analysis because they have been associated with increased risk of poor health outcomes [Baker, Parker, Williams, & Clark, 1998; Berkman et al., 2004; Kalichman et al., 1999; Schillinger et al., 2002; Williams, Baker, Honig, Lee, & Nowlan, 1998; Williams, Baker, Parker, & Nurss, 1998]. Owing to ceiling effects, this instrument is used with ordered categorical rather than continuous outcomes for analyses.	Methods: justification of measure
Schillinger D	2008	Seeing in 3-D: examining the reach of diabetes self-management support strategies in a public health care system	7	Although efficacy studies have demonstrated the benefit of a range of SMS strategies— even among selected vulnerable populations [Dewalt et al., 2006; Philis-Tsimikas et al., 2004; Rothman et al., 2004]—there is little translational research on SMS implementation to guide health system planners and little research on the reach of such programs with respect to diverse clinics, providers, and populations in safety net systems (Eakin et al., 2002; Lemon, Zapka, Estabrook, & Benjamin, 2006).	

**Table D2. Purpose of citation for health literacy update search (continued)**

<b>First Author</b>	<b>Year</b>	<b>Title</b>	<b>References</b>	<b>Text</b>	<b>Purpose of citation</b>
Murray MD	2007	Pharmacist intervention to improve medication adherence in heart failure: a randomized trial	7	Although some programs involved a pharmacist [51–53], we are unaware of any that were managed from a pharmacy by a pharmacist who dispensed medications and provided other helpful functions.	
Mayben JK	2007	Predictors of delayed HIV diagnosis in a recently diagnosed cohort. AIDS Patient Care STDS	2, 4	According to the National Adult Literacy Survey of over 26,000 adults, approximately 40–44 million (21%–23%) adults in the United States were functionally illiterate, and an additional 50 million (25%–28%) adults were marginally literate [6]. Minorities, older adults, and those with less than a high school education tended to perform in the lower literacy levels [6]. Low literacy has been associated with poorer health outcomes [7]. Health literacy is a type of literacy that has been defined as “the degree to which individuals have the capacity to obtain, process and understand basic health information and services for appropriate health decisions” [8].	Introduction: supports problem statement
Peters E	2007	Less is more in presenting quality information to consumers	None		
Miller DP	2007	The effect of health literacy on knowledge and receipt of colorectal cancer screening: a survey study	None		
Mayhorn CB	2007	Refining teratogen warning symbols for diverse populations	None		



**Table D2. Purpose of citation for health literacy update search (continued)**

<b>First Author</b>	<b>Year</b>	<b>Title</b>	<b>References</b>	<b>Text</b>	<b>Purpose of citation</b>
Kripalai S	2007	Development of an illustrated medication schedule as a low-literacy patient education tool	2, 5	The effects of low health literacy extend to many other areas of healthcare, contributing to disparities in disease-related knowledge, self-care activities, and health outcomes [21, 22]. Low-literacy patients demonstrate greater utilization of acute care services, incur significantly higher health care costs, and have higher mortality rates [23–26].	Introduction: supports problem statement

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Powell CK	2007	The relationship between health literacy and diabetes knowledge and readiness to take health actions	2	<p>Methods: For each of the 3 models, the covariates chosen for analysis were those found to be significant at the .10 level in bivariable analyses or reported to be significantly associated with diabetes outcomes in previous published work on health literacy [3,13,20]. Most recent hemoglobin A1C level, chosen to represent the patient's current level of glycemic control, required log base 10 transformation to induce approximate normality.</p> <p>Results: Years with diabetes was initially considered for inclusion in the model based on prior research [3,13,20]; however, the model lost significance with the addition of the covariate (<math>P \square \square .06</math>), with no impact on fit (<math>R^2</math> remained 0.27).</p> <p>However, suspected that these patients would be less likely than the general population to be ready to care for their disease given the number of perceived barriers they must overcome to receive adequate medical care. Also, the recent systematic review from <b>DeWalt et al.</b> states that one of the key aspects to determining the true relationship between literacy and health is the analysis of confounders. If the appropriate confounders are not included in the model, the significance of the relationship may be inaccurate.</p>	<p>Methods: justification of measures</p> <p>Results: justification of measures</p> <p>Conclusions: places study findings in context</p>
Sanders LM	2007	Caregiver health literacy and the use of child health services	None		

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Wolf MS	2007	Health literacy and health risk behaviors among older adults	1, 2	<p>1: In 2004, the Agency for Healthcare Research and Quality released a systematic review of the literature on health literacy and its relationship to healthcare use and outcomes [13]. This report issued a call for further research to document more consistently the causal pathways through which health literacy affects individual health. One particular mechanism that has been previously proposed is through various health risk behaviors known to be linked to health status and outcomes, despite the lack of empirical evidence to support such a pathway</p> <p>2: One particular mechanism that has been previously proposed is through various health risk behaviors known to be linked to health status and outcomes, despite the lack of empirical evidence to support such a pathway [14,15] Although prior studies have documented an association between lower educational attainment and higher prevalence of health risk behaviors (i.e., cigarette smoking, alcohol consumption, physical activity, and body mass index [BMI]), [16–18].</p>	Introduction: study fills gap
Davis TC	2006	Literacy and misunderstanding prescription drug labels	None		

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Wolf MS	2007	Literacy, self-efficacy, and HIV medication adherence	2, 6	<p>Based on prior studies examining the relationship between literacy and health outcomes [22], and common proposed pathways for how literacy might impact HIV medication adherence [23], we hypothesized that limited literacy would directly influence both patients' knowledge of their treatment regimen and self-efficacy to properly manage medication schedules.</p> <p>Our research also supports previous speculations that the relationship between literacy and health outcomes, including medication adherence, is not linear [37–40]. Rather, there may be a threshold effect where low literacy, at the 6th grade level and below, poses a substantial problem on adherence to antiretroviral regimens.</p>	Introduction: basis for hypotheses
Gazmararian JA	2006	Factors associated with medication refill adherence in cardiovascular-related diseases: a focus on health literacy	9	<p>It would be expected that an adequate level of functional health literacy is essential for understanding and processing messages that generate the motivation, beliefs, and behaviors to achieve successful medication adherence [32]. It is likely that inadequate health literacy skills are related to impaired comprehension of medical care instructions, and as a consequence, reduced medication adherence [33]. The 3 published studies that have directly examined this relationship found inconsistent results. Kalichman et al. [27] noted an association between health literacy and self-reported adherence to antiretroviral agents, while Golin et al. [34].</p>	Introduction: state of the science

**Table D2. Purpose of citation for health literacy update search (continued)**

<b>First Author</b>	<b>Year</b>	<b>Title</b>	<b>References</b>	<b>Text</b>	<b>Purpose of citation</b>
Graham J	2007	Medication beliefs as mediators of the health literacy-antiretroviral adherence relationship in HIV-infected individuals	1	In general, patients with low literacy have less knowledge of the management and treatment of their own chronic diseases and have poorer disease outcomes [Berkman et al, 2004; Estrada, Martin-Hryniewicz, Peek, Collins, and Byrd, 2004; Hope, Wu, Tu, Young and Murray, 2004; Schillingger et al, 2002; Wilson, Tchetgen, and Speigelman, 2001].	Introduction: statement of problem

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Morrow D	2006	Correlates of health literacy in patients with chronic heart failure	2	<p>Approximately half of the adults in the United States have inadequate or marginal functional health-related literacy, which challenges their ability to navigate the health care system. Lower health literacy is associated with poorer health status, less health care knowledge, poorer self-care abilities (e.g., medication adherence), reduced use of preventive services, and increased hospitalization and health care costs [Ad Hoc Committee, 1999; <b>DeWalt, Berkman, Sheridan, Lohr, &amp; Pignone, 2004</b>; Nielsen-Bohlman, Panzer, &amp; Kindig, 2004]. Thus, it is important to identify people with less than adequate health literacy and determine the reasons why this is so. We investigated health literacy among middleaged and older adults with chronic heart failure (CHF)</p> <p>Such a model would help explain associations between health literacy and demographic variables such as age and race, which researchers have investigated because of their interest in health literacy as a mediator of differences in health care outcomes related to socioeconomic status [Ad Hoc Committee, 1999; <b>DeWalt et al., 2004</b>]. The model would also guide development of strategies for mitigating effects of low literacy on health behaviors and outcomes.</p> <p>We plan to investigate whether relationships between health literacy and adherence are mediated by differences in cognitive abilities and whether these relationships also mediate the impact of demographic variables on adherence and health outcomes. Such findings would be consistent with functional definitions that view health literacy in terms of how individuals' skills match the demands of specific</p>	Introduction: supports problem statement

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Rothman RL	2006	Patient understanding of food labels: the role of literacy and numeracy	2, 9	<p>Discussion:</p> <p>In multivariable analyses lower literacy status and numeracy status remained significantly associated with poorer understanding of nutrition labels even after adjusting for income, education, and other factors. Previous studies have demonstrated that patients with poor literacy skills have worse knowledge of their chronic illness and can have worse clinical outcomes [15,17,32].</p> <p>Providers need to be careful, for example, about asking a patient with heart failure or hypertension to limit their sodium intake to 2 g if the patient cannot accurately interpret food labels. Speaking clearly and concisely, avoiding jargon, setting realistic goals, and using low-literacy— oriented materials can aid patient comprehension [32, 35-42].</p>	Discussion: places findings in context  [DeWalt and Pignone peer reviewed]
Rutherford J	2006	Low literacy: a hidden problem in family planning clinics	None		
Vavrus F	2006	Girls' schooling in Tanzania: the key to HIV/AIDS prevention? AIDS Care	None		
Yates K	2006	Comprehension of discharge information for minor head injury: a randomised controlled trial in New Zealand	None		

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Morris NS	2006	Literacy and health outcomes: a cross-sectional study in 1002 adults with diabetes	2, 9	<p>Introduction: Evidence is beginning to accumulate about the prevalence of limited health literacy and its association with the use of health care services [5-7,10-13] and health outcomes [8,14-16].</p> <p>Discussion: Another possible explanation for our finding of a lack of a significant association between literacy and health outcomes is that optimal self-management of diabetes may not be solely dependent on reading ability. In addition to print literacy, health literacy includes numeracy, oral literacy, culture and context [2]. The published literature on "health literacy" typically reports measures of reading ability and rarely, if ever, addresses the broader domains of health communication [14,31,32]. While there may be great value in assessing health literacy to address communication barriers between patients and health care providers, we still do not know what aspects of health literacy</p>	<p>Introduction: state of the science</p> <p>Discussion: placing findings in context</p>
Sudore RL	2006	Use of a modified informed consent process among vulnerable patients: a descriptive study	None		
Sentell TL	2006	Importance of adult literacy in understanding health disparities	None		



**Table D2. Purpose of citation for health literacy update search (continued)**

<b>First Author</b>	<b>Year</b>	<b>Title</b>	<b>References</b>	<b>Text</b>	<b>Purpose of citation</b>
Howard DH	2006	Impact of health literacy on socioeconomic and racial differences in health in an elderly population	2	Despite the intuitive connection between low health literacy and disparities, a recent review of the literature on health literacy [2] found only 1 study [3] documenting the link statistically. In this study, we used one of the only large datasets containing measures of health literacy, demographic characteristics, and health outcomes to explore the impact of health literacy on differences in health status and vaccination by educational attainment and race.	Introduction: study fills gap
Fang MC	2020	Health literacy and anticoagulation-related outcomes among patients taking warfarin	2	Limited health literacy is prevalent in certain populations in the United States, such as the elderly,[2,3] and is associated with receiving fewer preventive services, difficulty following medication instructions, and in some studies, with poorer health outcomes [4–10]. Health literacy may be of particular importance under conditions that involve substantial patient-provider discussion of risks and benefits and in those requiring complex management. One such therapy is anticoagulation with warfarin.	Introduction: supports the problem statement

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Paasche-Orlow MK	2006	Health literacy, antiretroviral adherence, and HIV-RNA suppression: a longitudinal perspective	2	<p>Introduction: Health literacy has emerged as a cross-cutting priority to improve the quality of health and health care in America.1–4 Medical and public health literature highlight the high reading demands made on people who are often in need of important health information.5 In addition, there is a growing body of literature indicating that people with limited health literacy have worse health status [6,7].</p> <p>Discussion: Fourth, health literacy was defined by the 66-word REALM, which is merely a word pronunciation test. While the REALM is the most commonly used tool to measure literacy in the medical literature and correlates well with other established health literacy and basic literacy instruments (r=.84 to .97), a more comprehensive test of health literacy might have provided different results [4,7].</p>	<p>Introduction: supports problem statement</p> <p>Discussion: places findings in context</p>
Lindau ST	2006	Health literacy as a predictor of follow-up after an abnormal Pap smear: a prospective study	1	<p>This study adds to a growing number of investigations that implicate low literacy as a correlate of negative health behaviors 7,8 and a cause of poor health outcomes [9-10]. In the context of general medical care, it has been suggested that literacy testing should and can occur routinely in the clinic [11–13].</p>	<p>Discussion: places findings in context</p>

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Weiss BD	2006	Literacy education as treatment for depression in patients with limited literacy and depression: a randomized controlled trial	1	Research has demonstrated that limited literacy is associated with poorer health outcomes and lower health status [5–9]. But, as pointed out in a report on health literacy from the Agency for Healthcare Quality and Research [10], there is little evidence that improving literacy skills can improve an individual's health. Indeed, to our knowledge, no research in an industrialized nation has ever demonstrated that enhancing literacy skills can actually cause someone to “get better” from an illness or chronic condition. The study reported here is a preliminary investigation of whether improving literacy skills can improve a specific health outcome—severity of depression—in a cohort of depressed individuals with limited literacy skills in the United States.	Introduction: state of the science; study fills gap
Lincoln A	2006	Impact of health literacy on depressive symptoms and mental health-related: quality of life among adults with addiction	1,2	Introduction Approximately 90 million American adults have low health literacy and lack the basic literacy skills to function in society.1–3 A growing body of work exists linking low literacy with an array of negative outcomes [4]. These outcomes include more frequent hospitalization,5,6 higher rates of health services utilization, and worse prevention practices in people with diabetes,7,8 asthma,9,10 cancer,11–13 and other chronic illnesses.14,15  Discussion The recent AHRQ evidence review, “Literacy and Health Outcomes: Evidence Report/Technology Assessment ” [23] cites 5 studies that evaluate the association between a marker of health literacy and a marker of mental illness.	Introduction: state of the science  Discussion: places findings in context

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
				<p>Four of these studies report statistically significant associations between low literacy and higher prevalence of depression; however, not all of these associations remained significant in adjusted analyses. Each of these studies and more recent work by Wolf et al. [24] have relied on cross-sectional analyses, and thus do not allow for consideration of causal inferences. For example, Gazmarian et al. 2000 [25] found that 13% of new Medicare recipients had depression according to the geriatric depression scale. Subjects with low health literacy were 3 times more likely to have depression. However, after controlling for demographics, social support, health behavior, and health status, health literacy did not remain an independent risk factor for depressive symptoms.</p>	
Mancuso CA	2006	Impact of health literacy on longitudinal asthma outcomes	2, 4	<p>The term health literacy has been used to describe the ability to read and comprehend medical information [1]. Such skills may impact all aspects of medical care. In particular, multiple studies carried out in different countries provide evidence that patients with less health literacy have worse health outcomes [2,3]. Some of the main outcomes considered were resource utilization and markers of disease control [4,5].</p>	Introduction: supports problem statement

**Table D2. Purpose of citation for health literacy update search (continued)**

<b>First Author</b>	<b>Year</b>	<b>Title</b>	<b>References</b>	<b>Text</b>	<b>Purpose of citation</b>
Sudore RL	2006	Limited literacy and mortality in the elderly: the health, aging, and body composition study	7	Finally, given the mismatch between the high literacy demands of the health care system and the limited literacy capacities of many older individuals [50] limited literacy may impede access to health care and/or effective chronic disease management. Health care systems may be poorly designed to meet the needs of persons with limited literacy, thereby contributing to literacy-related disparities. Two trials that evaluated the effect of re-engineering health care delivery to lower literacy demands demonstrated improvements in outcomes among those with lower literacy [52,53].	
Muir KW	2006	Health literacy and adherence to glaucoma therapy	None		
Sudore RL	2006	Limited literacy in older people and disparities in health and healthcare access	7	Additional research should be conducted to identify creative and multidisciplinary interventions to help older people with limited health literacy access the healthcare system to obtain the services they need. Interventions will likely need to combine multidisciplinary case management approaches that have been successful in geriatric [47,48] and low-literacy populations [49,50].	
Haggstrom DA	2006	Black-white differences in risk perceptions of breast cancer survival and screening mammography benefit	None		

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Schillinger D	2006	Does literacy mediate the relationship between education and health outcomes? A study of a low-income population with diabetes	4, 8	4: “Health literacy” has been defined as a measure of an individuals’ ability to perform basic reading and numerical tasks required to optimally function in the health care environment,18 and more broadly as the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions.9,19 Current measures of health literacy are highly correlated with standard measures of general literacy [20-22].  8: A small body of evidence suggests that such approaches could reduce or even eliminate education- and literacy-related disparities in the chronic disease context [33,34,78,79].	
Raehl CL	2006	Screening tests for intended medication adherence among the elderly	None		

**Table D2. Purpose of citation for health literacy update search (continued)**

<b>First Author</b>	<b>Year</b>	<b>Title</b>	<b>References</b>	<b>Text</b>	<b>Purpose of citation</b>
Sarkar U	2006	Is self-efficacy associated with diabetes self-management across race/ethnicity and health literacy?	1	Within this patient population, individuals with limited health literacy may be especially vulnerable to these experiences. A growing body of research demonstrates that limited health literacy, a prevalent problem in vulnerable populations, is independently associated with poor self-rated health [23,24], higher utilization of services [25–28], fewer preventive services [29,30], and worse glycemic control and more diabetes complications [31]. Therefore, self-efficacy may be a relevant determinant of self management behaviors among populations with limited health literacy [32–35]. We sought to determine whether diabetes self-efficacy was associated with recommended self-management behaviors in an urban, diverse population with a high prevalence of limited health literacy.	Introduction: state of the science

**Table D2. Purpose of citation for health literacy update search (continued)**

<b>First Author</b>	<b>Year</b>	<b>Title</b>	<b>References</b>	<b>Text</b>	<b>Purpose of citation</b>
Mancuso CA	2006	Asthma patients' assessments of health care and medical decision making: the role of health literacy	2	<p>Introduction: Most recent investigations focusing on health literacy have considered its impact on knowledge of disease, outcomes of disease, and resource utilization [3-6]. Few studies have considered health literacy and patients' experiences with health care [7]. In addition, it is not known whether literacy affects patients' desires to be informed of their treatment options and to participate in making decisions about their care.</p> <p>Discussion: To our knowledge, this is the first study to assess the association between health literacy and medical decision making in asthma patients. This result provides additional incentive to physicians to find better ways to explain treatments to patients and to encourage them to collaborate in their care. These are critical issues for asthma because self-management is a determinant of outcome [6].</p>	Introduction: state of the science  Discussion: placing findings in context
Kalichman SC	2005	Nurse-delivered antiretroviral treatment adherence intervention for people with low literacy skills and living with HIV/AIDS	None		



**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Seligman HK	2005	Physician notification of their diabetes patients' limited health literacy. A randomized, controlled trial	1	<p>Both the Institute of Medicine<sup>1</sup> and the Agency for Healthcare Research and Quality [5] have recently released reports highlighting the clinical significance of limited HL. When compared to patients with adequate HL, patients with limited HL demonstrate lower knowledge of chronic disease prevention and management [6–12] worse health status<sup>7,13,14</sup> and higher utilization of hospital and emergency room services [15,16]. The relationship between limited HL and poorer health outcomes, particularly among patients with chronic disease, may be mediated by sub-optimal physician-patient communication and patient self-management skills [2,6,9,17,18].</p> <p>Discussion: The increased attention to HL<sup>1</sup>, [5] and the evolution of shorter screening instruments<sup>25,27,28</sup> has increased interest in developing screening programs in the clinical context. This trial suggests we exercise caution before implementing such programs.</p>	<p>Introduction: supports problem statement</p> <p>Discussion: places findings in context</p>
van Servellen G	2005	Effects of a treatment adherence enhancement program on health literacy, patient-provider relationships, and adherence to HAART among low-income HIV-positive Spanish-speaking Latinos	None		
Guerra CE	2005	Literacy and knowledge, attitudes, and behavior about colorectal cancer screening	None		

**Table D2. Purpose of citation for health literacy update search (continued)**

<b>First Author</b>	<b>Year</b>	<b>Title</b>	<b>References</b>	<b>Text</b>	<b>Purpose of citation</b>
Roth MT	2005	Self-reported medication use in community-residing older adults: A pilot study	None		

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Wolf MS	2005	Health literacy and functional health status among older adults	1, 2	<p>Introduction:            These cumulative findings have led to groundbreaking responses by national organizations and federal agencies [13,15-17]. The Agency for Healthcare Research and Quality, in a recently released report, calls for further research that more consistently and clearly documents the relationship between health literacy and health status and outcomes [17]. The Agency for Healthcare Research and Quality report raises important questions about the characterization of the relationship between literacy and personal health. Although the body of literature has grown considerably within the past several years, few research studies<sup>11,18</sup> have been published that directly link health literacy to the health status of individuals. The objective of this study was to investigate the relationship between health literacy and functional health status among a cohort of new Medicare managed care enrollees from 4 US cities.</p> <p>Discussion:            Our finding that inadequate health literacy is independently associated with worse health is consistent with the results of previous cross-sectional studies [11,18, 28, 29] of highly selected patient populations. Because our study was population based, it should be less subject to selection bias than previous studies that enrolled people at the time they were seeking medical care.</p>	<p>Introduction: study fills gap</p> <p>Discussion: places findings in context</p>

**Table D2. Purpose of citation for health literacy update search (continued)**

<b>First Author</b>	<b>Year</b>	<b>Title</b>	<b>References</b>	<b>Text</b>	<b>Purpose of citation</b>
Paasche-Orlow MK	2005	Tailored education may reduce health literacy disparities in asthma self-management	1, 2, 8	<p>Health literacy is “the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions” [1–4] and is most often measured by reading comprehension of health-related information [5–6]. Multiple studies indicate that inadequate health literacy is associated with worse health status and higher rates of hospitalization across a number of patient populations [4, 7, 8], including patients with diabetes mellitus, patients with HIV infection, and the elderly [9–12].</p> <p>In cross-sectional studies, inadequate health literacy has been linked to lower asthma-related knowledge [14, 15] and improper use of metered dose inhalers (MDIs) [14]. Although national asthma guidelines recommend patient education to improve patient–physician partnerships for care [16], no studies have evaluated the extent to which inadequate health literacy serves as a barrier for patients to learn and retain asthma self-management skills [17]. The objective of this study was to examine the relationship between inadequate health literacy and difficulties learning and retaining instructions about discharge medications and appropriate MDI technique.</p>	Introduction: state of the science; study fills gap
Johnston MV	2005	Health literacy, morbidity, and quality of life among individuals with spinal cord injury	None		



**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
				<p>Certain groups have an especially high prevalence of low literacy. They include people who have completed fewer years of education, persons of certain racial or ethnic groups, the elderly, and persons with lower cognitive ability [6].</p> <p>Discussion Previous studies have found that individuals with low health literacy are less likely than individuals with adequate literacy to know essential information about their health, [1–6] to have poorer health outcomes, and increased hospitalization rates [6, 17, 18].</p>	
Hwang SW	2005	The effect of illustrations on patient comprehension of medication instruction labels	None		

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Howard DH	2005	The impact of low health literacy on the medical costs of Medicare managed care enrollees	1	<p>Recently released reports by the Institute of Medicine and Agency for Healthcare Research and Quality conclude that the 90 million adults in our country with limited health literacy cannot fully benefit from medical care and the health care system [4,27]. The reports note various interventions that hold promise for improving health literacy in various clinical settings.</p> <p>We have elected to present the more conservative set of results based on models that include controls for education and comorbid conditions, but, as stated above, these may lead to estimates that are biased downwards. As noted by Berkman et al. [27], “One limitation of the knowledge base to date is lack of appropriate specification for analytic models when variables being considered as potential confounders actually mediate the effect of reading ability on important health outcomes.” With further refinements to the concept of “health literacy,” it may be possible to narrow down the list of potential confounders for future cost studies.</p>	Discussion: context for findings; support research recommendations
Guerra CE	2005	Literacy and knowledge, attitudes and behavior about mammography in Latinas	None		
Ferreira MR	2005	Health care provider-directed intervention to increase colorectal cancer screening among veterans: results of a randomized controlled trial	None		

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Garbers S	2004	Inadequate functional health literacy in Spanish as a barrier to cervical cancer screening among immigrant Latinas in New York City	1	Health literacy has been defined as “the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions” [1]. Improving health literacy has been added as a <i>Healthy People 2010</i> objective [2], and two recent reports by the Institute of Medicine and the Agency for Healthcare Research and Quality summarize the data regarding the prevalence of low health literacy and its relationship to health care quality, use, outcomes, and disparities [3, 4]. Despite these findings, health care providers are often unaware of the health literacy skills of their patients [5–7].	Introduction: state of the science; problem statement
Kim S	2004	Association of health literacy with self-management behavior in patients with diabetes	None (pre report)		
Wolf MS	2004	Health literacy and patient knowledge in a Southern US HIV clinic	None (pre report)		
Chew LD	2004	The impact of low health literacy on surgical practice	None (pre report)		
Estrada CA	2004	Literacy and numeracy skills and anticoagulation control	None (pre report)		
Rothman R	2004	The relationship between literacy and glycemic control in a diabetes disease-management program	None (pre report)		DeWalt is a coauthor
Davids SL	2004	Predictors of pessimistic breast cancer risk perceptions in a primary care population	None (pre report)		
Baker DW	2004	Health literacy and use of outpatient physician services by Medicare managed care enrollees	None (pre report)		



**Table D2. Purpose of citation for health literacy update search (continued)**

<b>First Author</b>	<b>Year</b>	<b>Title</b>	<b>References</b>	<b>Text</b>	<b>Purpose of citation</b>
Kleinpeter MA	2003	Health literacy affects peritoneal dialysis performance and outcomes	None (pre report)		
Endres LK	2004	Health literacy and pregnancy preparedness in pregestational diabetes	None (pre report)		
van Servellen G	2003	Program to enhance health literacy and treatment adherence in low-income HIV-infected Latino men and women	None (pre report)		
Smith JL	2003	Literacy in primary care populations: is it a problem?	None (pre report)		
Coyne CA	2003	Randomized, controlled trial of an easy-to-read informed consent statement for clinical trial participation: a study of the Eastern Cooperative Oncology Group	None (pre report)		
Sheridan SL	2002	Numeracy and the medical student's ability to interpret data	None (pre report)		
Schwartz LM	1997	The role of numeracy in understanding the benefit of screening mammography	None (pre report)		
Conwell LS	2003	Early adolescent smoking and a web of personal and social disadvantage	None (pre report)		
Sentell TL	2003	Low literacy and mental illness in a nationally representative sample	None (pre report)		
Campbell FA	2004	The effect of format modifications and reading comprehension on recall of informed consent information by low-income parents: a comparison of print, video, and computer-based presentations	None (pre report)		

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
DeWalt DA	2004	Development and pilot testing of a disease management program for low literacy patients with heart failure	None (pre report)		
Hope CJ	2004	Association of medication adherence, knowledge, and skills with emergency department visits by adults 50 years or older with congestive heart failure	None (pre report)		
LeVine RA	2004	Maternal literacy and health behavior: a Nepalese case study	None (pre report)		
Rothman RL	2004	Influence of patient literacy on the effectiveness of a primary care-based diabetes disease management program	1	No published studies have rigorously examined interventions that can mitigate literacy-related disparities in patients with diabetes [14]. We previously conducted a pilot study that suggested that a comprehensive intervention might improve glycemic control for patients with low literacy [15] but that study lacked a control group. To better examine this issue, we recently completed a randomized controlled trial of a comprehensive disease management program that included strategies to overcome clinician deficits and patient barriers, including low literacy, for patients with diabetes and poor glycemic control. This program successfully improved blood pressure and glycemic control [16]. This article examines how patient literacy influenced the effectiveness of this program.	Introduction: study fills gap Coauthored by DeWalt
Weiss BD	2004	Relationship between health care costs and very low literacy skills in a medically needy and indigent Medicaid population	None (pre report)		

**Table D2. Purpose of citation for health literacy update search (continued)**

<b>First Author</b>	<b>Year</b>	<b>Title</b>	<b>References</b>	<b>Text</b>	<b>Purpose of citation</b>
Bosworth HB	2005	Nurse administered telephone intervention for blood pressure control: a patient-tailored multifactorial intervention	None		

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Paasche-Orlow MK	2005	Educational attainment but not literacy is associated with HIV risk behavior among incarcerated women	2	<p>Introduction:                      Low educational attainment and low literacy have been linked to low levels of knowledge and worse health outcomes for such chronic diseases as diabetes, asthma, and HIV infection [30–35]. However, the relationship of educational attainment and literacy with HIV risk behavior has not been evaluated. We sought to examine the relationship between educational factors and HIV risk behavior among women in short-term incarceration. In addition, we sought to provide an estimate of the independent relationship of specific educational factors and HIV risk behavior in an adjusted analysis.</p> <p>Discussion:                      The mechanisms by which this association is elaborated are likely complex and include such factors as life course social stratification that clusters types of experiences over an individual's lifetime, biological factors that predispose people both to education and health advantages, and social dynamics that involve the broader cultural, economic, policy, and political environment [43]. Similar mechanisms have been evoked to explain the connection between literacy and health, [35,44] but specific delineation of risk factors and mechanisms for crucial health conditions, such as HIV, may help inform the development and implementation of successful interventions.</p>	<p>Introduction: study fills gap</p> <p>Discussion: placing findings in context</p>
Arozullah AM	2006	The roles of low literacy and social support in predicting the preventability of hospital admission	None		

**Table D2. Purpose of citation for health literacy update search (continued)**

<b>First Author</b>	<b>Year</b>	<b>Title</b>	<b>References</b>	<b>Text</b>	<b>Purpose of citation</b>
Bennett I	2006	Breaking it down': patient-clinician communication and prenatal care among African American women of low and higher literacy	1	We were surprised that literacy was not associated with prenatal care utilization. The adherence to medical care by patients with chronic diseases has been shown to vary by literacy [24]. The women in this sample all had very high rates of poor prenatal care, and it may be that the risk associated with low literacy is not distinguishable in that context. We were intrigued by the finding that communication with clinicians was an important theme for all of the participants in this study.	Discussion: placing findings in context
Carbone ET	2006	Testing the feasibility of an interactive learning styles measure for U.S. Latino adults with type 2 diabetes and low literacy	None		
DeWalt DA	2006	A heart failure self-management program for patients of all literacy levels: a randomized, controlled trial [ISRCTN11535170]	2, 6	Limited literacy skills are common among adults in the United States [1]. Low literacy is associated with increased risk of hospitalization and worse control of chronic diseases [1-4]. Heart failure is a common chronic illness requiring multiple medications and significant self-care. Heart failure is the leading cause of hospitalization in the Medicare population [5]. The complexity of care for heart failure puts people with low literacy at considerable risk for adverse outcomes including hospitalization, worse quality of life, and mortality.	Introduction: supports problem statement  DeWalt is a co-author
Ives TJ	2006	Predictors of opioid misuse in patients with chronic pain: a prospective cohort study	None		DeWalt was a co-author

**Table D2. Purpose of citation for health literacy update search (continued)**

<b>First Author</b>	<b>Year</b>	<b>Title</b>	<b>References</b>	<b>Text</b>	<b>Purpose of citation</b>
Kripalani S	2006	Predictors of medication self-management skill in a low-literacy population. J Gen Intern Med	4	Two alternate modeling strategies were also performed. In one, years of schooling was excluded from the list of potential predictors. Some note that education is causally associated with literacy and that controlling for education may therefore constitute over adjustment and falsely attenuate the observed effect between literacy and the outcome of interest [20]. The second alternate approach treated continuous covariates as such, to ensure that categorization of these predictors had no meaningful effect on the observed association between literacy and MMC.	
Wolf MS	2006	A critical review of FDA-approved Medication Guides	None		
Wolf MS	2006	Literacy, race, and PSA level among low-income men newly diagnosed with prostate cancer	None		
Brock TP	2007	Using digital videos displayed on personal digital assistants (PDAs) to enhance patient education in clinical settings	None		

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
DeWalt DA	2007	Literacy and its relationship with self-efficacy, trust, and participation in medical decision making	2, 9	<p>Research over the past decade has demonstrated an association between literacy and health-related knowledge, self-management behaviors, self-reported health, rates of hospitalization, and control of diabetes [1]. However, research to date has not elucidated the factors that mediate the relationship between low literacy and worse health outcomes [1,2] Finding a relationship between literacy and health implies that an inability to acquire and understand health related information is an important mediating factor for determining good outcomes. Thus, many interventions have sought to improve readability of written materials, use other media altogether, or enlist additional clinical personnel to educate patients [3].</p> <p>Further, no study demonstrates that enhancing the readability of health information alone improves health outcomes [3].</p>	<p>Introduction: state of the science</p> <p>DeWalt is co-author</p>
DeWalt DA	2007	Low parental literacy is associated with worse asthma care measures in children	2, 4	<p>Low literacy is associated with a range of adverse health outcomes in adults including self reported health status, diabetes control, HIV viral load, rate of all-cause hospitalization, and all-cause mortality [8, 9]. Additionally, low literacy is associated with several other markers of vulnerability including non-white race and low socioeconomic status (SES). 10 Many researchers have hypothesized that low literacy may be a contributing factor in disparities according to race or SES, although this research is just emerging [11–13].</p>	<p>Introduction: supports problem statement</p>
Hahn EA	2007	The impact of literacy on health-related quality of life	1, 2, 4	<p>2: Introduction:</p>	<p>Introduction: study fills gap</p>

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
		measurement and outcomes in cancer outpatients		<p>Evidence about the relationship between literacy and patient-reported outcomes such as HRQL and perceived health status is limited. A systematic review by DeWalt and colleagues identified only four high-quality studies that evaluated this relationship [15]. These were conducted with adult education students [16], patients with Type-2 diabetes [17], patients presenting to the emergency department or ambulatory clinic [18], and Medicare managed care patients [19]. Additional analyses were recently published for the Medicare patients [20]. Four studies found an association between poorer reading ability and poorer HRQL/perceived health status [16, 18–20], while the fifth did not [17]. Furthermore, two of these studies used only a single global health item and all used interviewers to gather self-report data. Research is needed to better clarify the relationship between literacy and patient-reported health outcomes. Prerequisites for this research are the development and validation of measurement techniques for low literacy populations, and validation of measures to ensure that differences in reported health between literacy groups do not reflect underlying measurement bias [15, 18]. The purpose of this study was to address all of these research needs.</p>	Discussion: places findings in context
				<p>1: Discussion: Recent studies have reported that low literacy is associated with health disparities such as reduced access to health information, poorer understanding of illness and treatment, less effective</p>	



**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
				disease management, less understanding and use of preventive services, poorer physiological health markers, lower medication adherence, increased hospitalizations and higher financial costs [18, 61, 64–68]. However, little has been known about the association between literacy and HRQL/health status. The results of this study suggest that low literacy is not an independent risk factor for poorer HRQL outcomes.	
Murray MD	2009	Factors associated with exacerbation of heart failure include treatment adherence and health literacy skills	2	However, until recently, socioeconomic and biomedical factors have seldom been simultaneously assessed [9,10]. In addition, assessments of treatment adherence and health literacy skills are rarely considered in any analysis, even though these patient abilities are essential for effective self-management of chronic illness and are important for improved health outcomes [11–13]. Guided by a framework that links the health system and patient characteristics to self-care and health outcomes [14], we measured a comprehensive set of variables in a cohort of 192 participants nested within a randomized controlled trial to ascertain patient characteristics and risk factors associated with clinical deterioration requiring emergency department visits or hospitalization.	Introduction: study fills gap
Kripalai S	2007	Low-literacy interventions to promote discussion of prostate cancer: a randomized controlled trial	None		
Sudore RL	2007	An advance directive redesigned to meet the literacy level of most adults: a randomized trial	None		

**Table D2. Purpose of citation for health literacy update search (continued)**

<b>First Author</b>	<b>Year</b>	<b>Title</b>	<b>References</b>	<b>Text</b>	<b>Purpose of citation</b>
Davis TC	2008	Provider and patient intervention to improve weight loss: a pilot study in a public hospital clinic	2	Health literacy in its simplest terms refers to one's ability to understand and act on health information [6]. Research suggests that an individual's general literacy skills will likely influence his or her health literacy abilities [6,11,12]. Recent studies of obese patients in a public hospital found that those with low literacy skills had significantly less knowledge about weight loss and its health implications, poorer attitudes, and more negative behaviors [13,14].	Introduction: state of the science
Kripalani S	2008	Clinical research in low-literacy populations: using teach-back to assess comprehension of informed consent and privacy information	None		

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Powers BJ	2008	Literacy and blood pressure--do healthcare systems influence this relationship? A cross-sectional study	2, 7	<p>Introduction: Over 90 million adult Americans lack the literacy skills to effectively function in the current healthcare environment [1] – a number that has not changed significantly in the past 10 years [2]. Low health literacy is found in many different healthcare settings [3,4] and is most common in older patients, those with lower education levels, immigrants, and racial minorities [5]. Prior research has supported the association between literacy and disease knowledge, utilization of preventative services, hospitalization, overall health status, chronic disease control, and mortality in elderly adults [6-8]. Due to a growing body of evidence regarding these associations, literacy has been deemed a national priority [1,9,10].</p> <p>Discussion: Although we adjusted for several patient variables that may be associated with systolic blood pressure, we did not include measures of patient knowledge, health beliefs, or health status, which have previously been associated with literacy and may differ between the two patient populations [6,7]. In addition to patient characteristics, we did not explore other variables that may mediate our findings such as type of health insurance coverage or more specific clinic site level differences in how care is delivered.</p>	<p>Introduction: state of the science</p> <p>Discussion: places findings in context</p>

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Robinson LD	2008	The impact of literacy enhancement on asthma-related outcomes among underserved children	2	Studies conducted in low-income urban populations have documented that low literacy is a predictor of poor health outcomes, even after other sociodemographic variables are considered [24-26]. Other studies have also reinforced the concept that literacy is vital to health-related outcomes [24,25,27-29]. To the best of our knowledge, there have not been any asthma-related interventions which have evaluated the relationship between literacy and health by improving both areas simultaneously.	Introduction: state of the science
Sudore RL	2008	Engagement in multiple steps of the advance care planning process: a descriptive study of diverse older adults	None		
Waldrop-Valverde D	2008	The effects of low literacy and cognitive impairment on medication adherence in HIV-positive injecting drug users	1,	Literacy. Readingability was assessed using the Wide Range Achievement Test _ 3 (WRAT-3: Wilkinson, 1993). This test requires pronunciation of increasingly complex vocabulary words. Results indicate level of Reading ability expressed as both a standard score and a grade level equivalent. This test can be useful for those persons in the lower ranges of verbal IQ (Johnstone et al., 1996). Since this study was not originally designed to test the effects of health literacy, measures such as the Test of Functional Health Literacy in Adults (TOFHLA) and the Rapid Estimate of Adult Literacy in Medicine (REALM) were not used. However, the WRAT-3 has been reported to be highly correlated with these other health literacy measures [Berkman et al., 2004].	Methods: justification for measure
Lee S-YD	2009	Health literacy, social support, and health status among older adults	None		

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Clarke C	2005	Emergency department discharge instructions comprehension and compliance study	None		
Bennett IM	2009	The contribution of health literacy to disparities in self-rated health status and preventive health behaviors in older adults	1, 7, 9	<p>Significant differences in health status and preventive care utilization among older adults are well documented [5-9]. Particularly troubling are disparities in the use and delivery of immunizations and cancer screening related to race/ethnicity and educational attainment [6-12]. It is commonly thought that health literacy (the ability to use health information from any source to make appropriate health decisions) is an important contributor to these disparities [13,14]. Despite calls for research in this area, there has been little effort to assess formally the contribution of health literacy to disparities in health [3,15,16]. The only study that has addressed this question directly was limited to members of a single regional insurance carrier.<sup>16</sup> In addition, limitations in the screening instruments widely used to estimate health literacy undermine the importance of previous findings. These brief instruments are convenient for large studies that primarily aim to assess health outcomes [17-20]. Rather than measuring health literacy skills directly, these instruments estimate reading skills in the health context [13,20,21]. That is, they have limited ability to assess the functional capacity of an adult to use printed and written health related materials to perform a range of health-related tasks, a critical component of health literacy [15,21,22].</p> <p>Methods:</p>	<p>Introduction: supports problem statement; state of the science</p> <p>Methods: justification of methods</p> <p>Discussions: supports future research based on current study</p> <p>Methods:</p>

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
				<p>Potentially confounding demographic variables were identified a priori through a review of the literature on literacy and health in older adults. Demographic variables were age, sex, income, nativity (US born), and marital status [7-12,13].</p> <p>9:</p> <p>Although these instruments have been crucial in building an evidence base for the link between literacy and health outcomes, additional research using more-rigorous measures of health literacy are needed to confirm previous studies and solidify this developing field [22-25].</p>	
Pandit AU	2009	Education, literacy, and health: Mediating effects on hypertension knowledge and control	None		
Hironaka LK	2009	Caregiver health literacy and adherence to a daily multi-vitamin with iron regimen in infants	10	<p>It has been hypothesized that the relationship between health literacy and medication adherence may mediate the effect on specific health outcomes. However, several adult studies assessing the relationship between health literacy and adherence have produced varied results [3-9]. Some studies suggest worse adherence among individuals with limited health literacy [9]; others report no association [7] or even better adherence [4].</p>	Introduction: state of the science
Kandula NR	2009	The relationship between health literacy and knowledge improvement after a multimedia type 2 diabetes education program	None		

**Table D2. Purpose of citation for health literacy update search (continued)**

<b>First Author</b>	<b>Year</b>	<b>Title</b>	<b>References</b>	<b>Text</b>	<b>Purpose of citation</b>
von Wagner C	2009	Health literacy and self-efficacy for participating in colorectal cancer screening: The role of information processing	2	The associations between health literacy and the outcome variables in this study therefore seem to contradict previous suggestions of a threshold effect where only low literacy (at the 6th grade level or below) poses a substantial problem for the enactment of health behaviors [13,29–32]. Instead, our findings may indicate that even subtle differences between adults with adequate health literacy may make an appreciable difference to important variables underpinning information processing, such as information-seeking and the effort involved in reading health education materials. As such, the findings support efforts to expand the focus of health literacy research beyond at-risk populations.	Discussion: places findings in context
Rudd RE	2009	A randomized controlled trial of an intervention to reduce low literacy barriers in inflammatory arthritis management	1	Health materials are complex and currently well over 800 peer-reviewed studies indicate a mismatch between the reading demands of these materials and the literacy skills of U.S. adults [5]. This mismatch between demands and skills has serious implications [6]. Poor literacy skills have been associated with unfavorable health outcomes for a number of chronic diseases such as diabetes, asthma, HIV, and heart disease [7]. Arthritis studies have contributed to this body of literature indicating, for example, that patients with rheumatoid arthritis who had not completed high school showed poorer clinical status than patients who had and that low formal education was a predictor of premature mortality for arthritis patients over a ten-year period [8,9].	Introduction: supports problem statement

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Bickmore TW	2009	Using computer agents to explain medical documents to patients with low health literacy	None		
Shone LP	2009	The role of parent health literacy among urban children with persistent asthma	11	Our results differ from those of DeWalt and Pignone, who found that limited parent HL was associated with worse asthma care and outcomes [8]. However this is likely explained by differences in the range of asthma severity in the two studies. DeWalt and Pignone included children with a broad range of severity, from mild to severe, whereas our study included only children with persistent asthma.	
Nitri DW	2009	Transformative learning intervention: effect on functional health literacy and diabetes knowledge in older African Americans	None		
Sheridan SL	2003	A randomized comparison of patients' understanding of number needed to treat and other common risk reduction formats	None		
Schillinger D	2009	Effects of self-management support on structure, process, and outcomes among vulnerable patients with diabetes: a three-arm practical clinical trial	None		
DeWalt DA	2009	Goal setting in diabetes self-management: Taking the baby steps to success	None		



**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Wallace AS	2009	Literacy-appropriate educational materials and brief counseling improve diabetes self-management	6	The results of our intervention are consistent with other studies suggesting that goal setting is feasible and effective in vulnerable populations [26–28], and that disease-related education can improve self-management for those with low-literacy [29,30]. In addition, the health-related psychological and behavioral changes resulting from our brief intervention are comparable to other interventions incorporating much more intensive strategies.	Co-authored by DeWalt
Bosworth HB	2009	Two self-management interventions to improve hypertension control: a randomized trial	2	Health literacy was evaluated as a dichotomous variable with low literacy defined as The Rapid Estimate of Adult Literacy in Medicine (REALM) [19] score 0–60 (<9th grade level) and adequate literacy defined as REALM score 61–66 (≥9th grade level) [20]. Body mass index were obtained from patients' medical records.	Methods: justification for measures
Kang EY	2009	Informed consent recall and comprehension in orthodontics: traditional vs improved readability and processability methods	None		
Bryant MD	2009	Multimedia version of a standard medical questionnaire improves patient understanding across all literacy levels	None		
Kim SH	2009	Health literacy and functional health status in Korean older adults	2	Introduction: As for the factors associated with health status in older adults, many researchers have identified problems associated with health literacy. Health literacy is defined as 'the cognitive and social skills, which determine the motivation and ability of individuals to gain access to, understand and use information in ways that	Introduction: state of the science

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
				<p>promote and maintain good health' (World Health Organization 2004). In research conducted mostly in the US, limited health literacy has been reported to have an adverse effect on health outcomes, such as the use of preventive services (Davis et al. 2001, Scott et al. 2002), adherence to medical instructions [Dewalt et al. 2004, Wolf et al. 2007] and self-management skills (Schillinger et al. 2002).</p>	<p>Methods: justifies analysis</p>
				<p>Methods: A general linear model was used to test for differences in chronic conditions and the health status between the groups while adjusting for covariates (age, education and monthly income). Models were run with and without the variable of education included as a covariate to present a conservative estimate of the effect of health literacy on health status as health literacy and education are very closely associated [Dewalt et al. 2004]. Data were analysed using SPSS Version 12.0 (SPSS Inc., Chicago, IL, USA).</p>	<p>Discussion: places findings in context</p>
				<p>Discussion: After removing education as a covariate, the magnitude of the difference between low and high literacy groups on health status was even larger: In addition to higher activity limitations and lower subjective health, individuals with low health literacy had even lower levels of physical function and higher levels of pain. Thus, the analyses with and without including education as a covariate in this study helps to rule out the possibility of misestimating the independent relationship between health literacy and</p>	

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
				health status from under- and over-adjustment [Dewalt et al. 2004].	
Greene J	2009	Medicaid consumers and informed decisionmaking	None		
Lokker N	2009	Parental misinterpretations of over-the-counter pediatric cough and cold medication labels	2	Many parents may have difficulty understanding the indications and appropriate dosing of OTC medications. In 2003, the National Assessment of Adult Literacy found that 90 million Americans have basic or below basic literacy skills, and 110 million people have basic or poor quantitative skills [22]. Low-literacy skills are associated with worse understanding of medication labels, worse knowledge of one's disease, and worse clinical outcomes [23–33]. The role of quantitative skills, or numeracy, has been less studied [34,35], but one recent study found that low numeracy was associated with poorer understanding of food labels [36]. Little is known about caregivers' ability to choose and dose medications appropriately for their infants and young children [37].	Introduction: supports problem statement
Volandes AE	2009	Video decision support tool for advance care planning in dementia: randomised controlled trial	None		
Osborn CY	2009	Diabetes numeracy: an overlooked factor in understanding racial disparities in glycemic control	None		
Sobel RM	2009	Asthma 1-2-3: a low literacy multimedia tool to educate African American adults about asthma	None		
Gatti ME	2009	Relationships between beliefs about medications and adherence	None		

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Galesi M	2009	Using icon arrays to communicate medical risks: overcoming low numeracy	None		
Galesi M	2009	Natural frequencies help older adults and people with low numeracy to evaluate medical screening tests	None		
Donelle L	2008	Health literacy and numeracy: key factors in cancer risk comprehension	None		
Jay M	2009	A randomized trial of a brief multimedia intervention to improve comprehension of food labels	None		
Waldrop-Valverde D	2009	Gender differences in medication management capacity in HIV infection: The role of health literacy and numeracy	1	As in previous research (Davis et al. 2006; Kripalani et al. 2006; Wolf et al. 2007), the present study also found a significant relationship between health literacy for verbal information and understanding of medication instructions. The ability to accurately read, understand and draw conclusions from verbal information is critically important for effective medication management. In a summary report developed by the Agency for Healthcare Research and Quality (AHRQ) [Berkman et al. 2004], a limited number of interventions to address low health literacy were identified. All of the studies attempted to improve presentation and understanding of verbal material and were largely successful. However, as results from the present study illustrate, further research to determine the mix of abilities required to be successful in the patient role are needed so that the essential skills for particular behaviors can be identified and intervened.	Discussion: supports research recommendations for future research

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Garcia-Retamero R	2010	Who profits from visual aids: overcoming challenges in people's understanding of risks [corrected]	None		
Yin HS	2010	Parents' medication administration errors: role of dosing instruments and health literacy	4, 11	[Both listed as references, but neither is cited in the article.]	
Gazmararian J	2010	Effect of a pharmacy-based health literacy intervention and patient characteristics on medication refill adherence in an urban health system	None		
Mbaezue N	2010	The impact of health literacy on self-monitoring of blood glucose in patients with diabetes receiving care in an inner-city hospital	None		
Cordasco KM	2009	A low-literacy medication education tool for safety-net hospital patients	5	Studies have shown an association between lower levels of health literacy and less medication knowledge and adherence [4–7]. Health literacy, “the ability to read, understand, and act upon health information” [8] is associated with multiple outcome disparities [9].	
Garcia-Retamero R	2009	Communicating treatment risk reduction to people with low numeracy skills: a cross-cultural comparison	None		
Bailey SC	2009	Predictors of misunderstanding pediatric liquid medication instructions	None		

**Table D2. Purpose of citation for health literacy update search (continued)**

<b>First Author</b>	<b>Year</b>	<b>Title</b>	<b>References</b>	<b>Text</b>	<b>Purpose of citation</b>
Yin HS	2009	The health literacy of parents in the United States: a nationally representative study	1	Increased national attention has been focused on the issue of health literacy, because a growing body of evidence has linked limited literacy skills to poorer health knowledge, worse health behaviors, and increased health care costs [1–4]. With an estimated \$106 to \$238 billion dollars in annual health care costs attributable to limited health literacy,5 organizations including the Agency for Healthcare Research and Quality, the Institute of Medicine, the Joint Commission, the American Medical Association, and the American Academy of Pediatrics have begun to prioritize health literacy as a key quality and patient-safety issue [1,2,4,6,7].	Introduction: supports problem statement

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Coffman MJ	2010	Demands of immigration, health literacy, and depression in recent Latino immigrants	2	<p>Ethnicity is associated with low health literacy; as many as 62% of Latinos have low or marginal health literacy, even when tested in Spanish (Paasche-Orlow, Parker, Gazmararian, Nielson-Bohlman, &amp; Rudd, 2005). Prior research has found relationships between low health literacy and inadequate preventive health care use (Scott, Gazmararian, Williams, &amp; Baker, 2002) and poor health outcomes [Dewalt, Berkman, Sheridan, Lohr, &amp; Pignone, 2004]. Several studies have also found a relationship between low health literacy and depressive symptoms. Though explained by their worse health status, one study found that elders with low health literacy were more than twice as likely to report symptoms of depression (Gazmararian, Baker, Parker, &amp; Blazer, 2000). Finally, a study that included Latina women who spoke Spanish, were recent immigrants, and were pregnant (Bennett, Culhane, McCollum, Mathew, &amp; Elo, 2007) found that those with inadequate health literacy had more than two times the risk of reporting depression symptoms.</p>	Introduction: state of science

**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Mancuso JM	2010	Impact of health literacy and patient trust on glycemic control in an urban USA population	12	<p>To date, there is limited research available that combines health literacy and patient trust as variables that influence glycemic control. One study (<math>n = 268</math>) was found that combined health literacy and patient trust with self-efficacy and patient involvement in decision-making to determine their influence on glycemic control. No relationship between health literacy, patient trust, self-efficacy, and patient involvement was found. In addition, no relationship was found between health literacy or patient trust and glycemic control [DeWalt et al., 2007].</p> <p>The significant positive correlation found between health literacy and diabetes knowledge was consistent with the previously discussed framework and literature [DeWalt et al., 2007; Powell et al., 2007].</p>	
Johnson VR	2010	Does social support help limited-literacy patients with medication adherence?: A mixed methods study of patients in the pharmacy intervention for limited literacy (PILL) study	1, 5	<p>Introduction: Another factor contributing to medication adherence is health literacy—the ability to understand and use health information to make important decisions affecting one’s health [26–34]. Previous studies have shown that limited-literacy patients have difficulty correctly identifying medicines [35,36] and understanding how to take medicine [4,28,37,38]. They are reluctant to ask providers questions, possibly because they are ashamed to admit they do not understand [39–41]. In interviews and focus groups, patients said they had not told anyone about their reading difficulties [39], not even their spouses or children [40,42]. They also said they had never brought anyone with them to the hospital to help them read materials or understand what</p>	Introduction: supports problem statement



**Table D2. Purpose of citation for health literacy update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
				they were reading [39].	
				About 77 million Americans lack the literacy skills needed to take perform tasks such as determining what time they should take prescription medication as it relates to food [43]. Most at risk are people with low incomes, immigrants who do not speak English well, people >65 years of age, those with chronic conditions or mental illnesses, and individuals in racial/ethnic minority populations [27,28]. People with limited literacy are more likely to be hospitalized and visit emergency rooms than those with stronger literacy skills [27].	Discussion: places findings in context
				Discussion: Patients in both of the limited-literacy focus groups said relatives began helping them after they were hospitalized for medication overdoses or interactions. These problems might have been associated with difficulty reading and understanding medication instructions. This explanation is in line with findings that limited-literacy patients are more likely to have difficulty understanding how to take their medicines [4,28,37,38] and are more likely to visit emergency rooms and hospitals than those with stronger literacy skills [27].	
Murphy DA	2010	Health literacy and antiretroviral adherence among HIV-infected adolescents	None		
Shieh C	2009	Health literacy and its association with the use of information sources with barriers to information seeking in clinic-based pregnant women	None		

**Table D2. Purpose of citation for health literacy update search (continued)**

<b>First Author</b>	<b>Year</b>	<b>Title</b>	<b>References</b>	<b>Text</b>	<b>Purpose of citation</b>
Osborn CY	2010	Health literacy in the context of HIV treatment: Introducing the Brief Estimate of Health Knowledge and Action (BEHKA)—HIV version	None		
Sharif I	2010	Relationship between child health literacy and body mass index in overweight children	11	Better health literacy, an individual's ability to read and interpret health information needed to make health decisions [1], has been correlated with better health outcomes in adults [2–36]. While some investigators have begun to explore the relationship between parental health literacy and child health outcomes [37,38], no recent studies have evaluated the contribution of children's own health literacy to health outcomes.	

**Table D3. Key to References for omega-3 update search**

<b>Citation</b>	
1	Balk E, Chung M, Lichtenstein A, et al. Effects of omega-3 fatty acids on cardiovascular risk factors and intermediate markers of cardiovascular disease. Evidence report/technology assessment no <b>93</b> (Prepared by Tufts-New England Medical Center Evidence-based Practice Center under Contract No. 290-02-0022). AHRQ publication no 04-E010-2. Rockville, Md: Agency for Healthcare Research and Quality; 2004. <a href="http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=hserta&amp;part=A136037">http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=hserta&amp;part=A136037</a> . Accessed November 6, 2009.
2	Balk EM, Lichtenstein AH, Chung M, Kupelnick B, Chew P, Lau J. Effects of omega-3 fatty acids on serum markers of cardiovascular disease risk factors: a systematic review. <i>Atherosclerosis</i> 2006;189:19–30.
3	Wang C, Harris WS, Chung M, et al. n–3 Fatty acids from fish or fish-oil supplements, but not alpha-linolenic acid, benefit cardiovascular disease outcomes in primary- and secondary-prevention studies: a systematic review. <i>Am J Clin Nutr</i> 2006;84:5–17.

**Table D4. Citation frequency and purpose for omega-3 update search**

First Author	Year	Title	References	Text	Purpose of citation
Dodin	2008	Flaxseed on cardiovascular disease markers in healthy menopausal women: a randomized, double-blind, placebo-controlled trial	None		
Maki	2008	Effects of Adding Prescription Omega-3 Acid Ethyl Esters to <i>Simvastatin</i> (20 mg/day) on Lipids and Lipoprotein Particles in Men and Women With Mixed Dyslipidemia	None		
Gajos	2010	Effects of Polyunsaturated Omega-3 Fatty Acids on Responsiveness to Dual Antiplatelet Therapy in Patients Undergoing Percutaneous Coronary Intervention	None		
Bays	2010	Effects of Prescription Omega-3-Acid Ethyl Esters on Non-High-Density Lipoprotein Cholesterol When Coadministered With Escalating Doses of Atorvastatin	1	From a safety and tolerability standpoint, the coadministration of P-OM3, 4 g/d, with atorvastatin was generally well tolerated. Although mild glucose elevations were observed in this trial, this finding is consistent with those from other randomized clinical trials involving omega-3 fatty acid administration [17,18]. Otherwise, no unexpected tolerability or safety concerns were found in this study.	Discussion: places findings in context

**Table D4. Citation frequency and purpose for omega-3 update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Hartweg	2007	Meta-analysis of the effects of n-3 polyunsaturated fatty acids on haematological and thrombogenic factors in type 2 diabetes	1	We are not aware of other systematic reviews including only randomised control trials that have evaluated the effect of n-3 PUFA on established and emerging cardiovascular risk factors in type 2 diabetes. A recent review included patients with diabetes as part of a high-risk-group analysis, but also included non-randomised control trials [41]. There are three previous systematic reviews evaluating the effect of n-3 PUFA on cardiovascular events, lipid and glycaemic markers in type 2 diabetes [42–44], which found n-3 PUFA reduced triacylglycerol, modestly increased LDL-cholesterol, and had no significant effect on fasting glucose, HbA1c, or total cholesterol and HDL-cholesterol. However, unlike previous systematic reviews, we also assessed the effects on other established and emerging cardiovascular risk factors.	Discussion: clarifies that study fills gap
Ramel	2008	Beneficial effects of long-chain <i>n</i> -3 fatty acids included in an energy-restricted diet on insulin resistance in overweight and obese European young adults	None		
Roth	2009	Prescription Omega-3 Fatty Acid as an Adjunct to Fenofibrate Therapy in Hypertriglyceridemic Subjects	None		
Sjoberg	2010	Dose-dependent increases in heart rate variability and arterial compliance in overweight and obese adults with DHA-rich fish oil supplementation	None		
Ninio	2008	Docosahexaenoic acid-rich fish oil improves heart rate variability and heart rate responses to exercise in overweight adults	None		
Carney	2010	Effect of Omega-3 Fatty Acids on Heart Rate Variability in Depressed Patients With Coronary Heart Disease	None		

**Table D4. Citation frequency and purpose for omega-3 update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Kelley	2009	DHA Supplementation Decreases Serum C-Reactive Protein and Other Markers of Inflammation in Hypertriglyceridemic Men <sup>1-3</sup>	None		
Davidson	2007	Efficacy and Tolerability of Adding 4 g/d to Simvastatin 40 mg/d in Hypertriglyceridemic Patients: An 8-Week, Randomized, Double-Blind, Placebo-Controlled Study	1	Fasting blood glucose was significantly increased with P-OM3 compared with placebo (P = 0.002). Two previous meta-analyses reported that elevations in glucose after omega-3 fatty acid supplementation were not accompanied by increases in HbA1c [26, 27]. The duration of the present study was too short to allow meaningful assessment of HbA1c, but a post hoc evaluation of fructosamine levels, which respond more rapidly to changes in blood glucose levels than HbA1c, found no significant difference in the change from baseline in fructosamine levels between the P-OM3 and placebo groups.	Discussion: places findings in context
Lindqvist	2007	Herring ( <i>Clupea harengus</i> ) supplemented diet influences risk factors for CVD in overweight subjects	None		
Engstrom	2003	Effects of Scandinavian caviar paste enriched with a stable fish oil on plasma phospholipid fatty acids and lipid peroxidation	None		
O'Keefe	2006	Effects of Omega-3 Fatty Acids on Resting Heart Rate, Heart Rate Recovery After Exercise, and Heart Rate Variability in Men With Healed Myocardial Infarctions and Depressed Ejection Fractions	None		
Morgan	2006	Effects of Dietary Omega-3 Fatty Acid Supplementation on Endothelium-Dependent Vasodilation in Patients With Chronic Heart Failure	None		
Ambring	2006	Mediterranean-inspired diet lowers the ratio of serum phospholipid n <sub>6</sub> to n <sub>3</sub> fatty acids, the number of leukocytes and platelets, and vascular endothelial growth factor in healthy subjects <sup>1-3</sup>	None		

**Table D4. Citation frequency and purpose for omega-3 update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Chan	2003	Randomized controlled trial of the effect of n-3 fatty acid supplementation on the metabolism of apolipoprotein B-100 and chylomicron remnants in men with visceral obesity <sup>1-3</sup>	Before report released		
Ma	2010	Effects of Walnut Consumption on Endothelial Function in Type 2 Diabetic Subjects	None		
Rajaram	2009	Walnuts and fatty fish influence different serum lipid fractions in normal to mildly hyperlipidemic individuals: a randomized controlled study <sup>1-4</sup>	2	Unlike walnuts, fatty fish did not lower cholesterol but, as shown by others (15, 26, 27), had a cholesterol-raising effect. Of the 2 long-chain n3 PUFA found in fish, DHA is reported to be more potent in raising cholesterol and this may be due to greater conversion of DHA-enriched VLDL to LDL cholesterol or downregulation of LDL cholesterol receptor [26, 28]. We found that the hypercholesterolemic effect of DHA was magnified in those subjects who had increased baseline cholesterol levels. The increase in LDL cholesterol from the fish diet may not suggest an increased risk of CVD as this may be counteracted by a shift of LDL cholesterol toward a larger, less atherogenic LDL cholesterol particle [29].	Discussion: places findings in context
Mostad	2006	Effects of n_3 fatty acids in subjects with type 2 diabetes: reduction of insulin sensitivity and time-dependent alteration from carbohydrate to fat oxidation	None		
Kabir	2007	Treatment for 2 mo with n_3 polyunsaturated fatty acids reduces adiposity and some atherogenic factors but does not improve insulin sensitivity in women with type 2 diabetes: a randomized controlled study <sup>1-4</sup>	None		

**Table D4. Citation frequency and purpose for omega-3 update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Brady	2004	Increased n <sub>6</sub> polyunsaturated fatty acids do not attenuate the effects of long-chain n <sub>3</sub> polyunsaturated fatty acids on insulin sensitivity or triacylglycerol reduction in Indian Asians <sup>1–3</sup>	None		
Stark	2004	Differential eicosapentaenoic acid elevations and altered cardiovascular disease risk factor responses after supplementation with docosahexaenoic acid in postmenopausal women receiving and not receiving hormone replacement therapy <sup>1–3</sup>	Could be before the release of the report		
Stirban	2010	Effects of n–3 fatty acids on macro- and microvascular function in subjects with type 2 diabetes mellitus <sup>1–3</sup>	None		
Kelley	2007	Docosahexaenoic acid supplementation improves fasting and postprandial lipid profiles in hypertriglyceridemic men <sup>1_4</sup>	None		
Patenaude	2009	Bioavailability of α-linolenic acid from flaxseed diets as a function of the age of the subject	None		
Goyens	2006	Effects of alpha-linolenic acid versus those of EPA/DHA on cardiovascular risk markers in healthy elderly subjects	None		
Olano-Martin	2010	Contribution of apolipoprotein E genotype and docosahexaenoic acid to the LDL-cholesterol response to fish oil	2	However, high dose EPA +DHA intakes have also been associated with a highly heterogeneous LDL-cholesterol (LDLC) raising effect which may negate the cardioprotective benefits in susceptible individuals [5–7]. In the 13 studies (n = 6969 participants) reviewed by Balk et al. [5], mean LDL-C responses to fish oil ranged from –3% to +14%, observations which are comparable to the mean 5% and 11% increases in LDL-C reported in normolipidaemic (fasting triglycerides (TG) <2.0mmol/l) and hypertriglyceridaemic (fasting TG >2mmol/l) participants, respectively, in the Harris analysis [6].	Introduction: lays out state of the science



**Table D4. Citation frequency and purpose for omega-3 update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Tuleta	2009	Antiplatelet effects of n-3 polyunsaturated fatty acids compared with aspirin: A pilot study with whole-blood aggregometry	None		
Wang	2008	Fish oil supplementation improves large arterial elasticity in overweight hypertensive patients	None		
Pedersen	2003	Influence of fish oil supplementation on in vivo and in vitro oxidation resistance of low-density lipoprotein in type 2 diabetes	Predates report		
Lara	2007	Benefits of salmon eating on traditional and novel vascular risk factors in young, non-obese healthy subjects	None		
Chan	2006	Factorial study of the effect of n-3 fatty acid supplementation and atorvastatin on the kinetics of HDL apolipoproteins A-I and A-II in men with abdominal obesity <sup>1-3</sup>	None		
Rizza	2009	Fish oil supplementation improves endothelial function in normoglycemic offspring of patients with type 2 diabetes	None		
Dyerberg	2004	Effects of trans- and n-3 unsaturated fatty acids on cardiovascular risk markers in healthy males. An 8 weeks dietary intervention study	May predate report		
Woodman	2003	Effects of purified eicosapentaenoic acid and docosahexaenoic acid on platelet, fibrinolytic and vascular function in hypertensive type 2 diabetic patients	Predates report		
Mita	2007	Eicosapentaenoic acid reduces the progression of carotid intima-media thickness in patients with type 2 diabetes	None		
Hill	2007	Combining fish-oil supplements with regular aerobic exercise improves body composition and cardiovascular disease risk factors <sup>1-3</sup>	None		
Rallidis	2003	Combining fish-oil supplements with regular aerobic exercise improves body composition and cardiovascular disease risk factors <sup>1-3</sup>	Predates report		
Lee	2006	Effects of omega-3 polyunsaturated fatty acids on plasma indices of thrombogenesis and inflammation in patients post-myocardial infarction	None		

**Table D4. Citation frequency and purpose for omega-3 update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Lovegrove	2004	Moderate fish-oil supplementation reverses low-platelet, long-chain n_3 polyunsaturated fatty acid status and reduces plasma triacylglycerol concentrations in British Indo-Asians <sup>1–3</sup>	May predate report		
Paschos	2007	Dietary supplementation with flaxseed oil lowers blood pressure in dyslipidaemic patients	None		
Rallidis	2004	The effect of diet enriched with $\omega$ -linolenic acid on soluble cellular adhesion molecules in dyslipidaemic patients	May predate report		
Tuttle	2008	Comparison of Low-Fat Versus Mediterranean-Style Dietary Intervention After First Myocardial Infarction (from The Heart Institute of Spokane Diet Intervention and Evaluation Trial)	None		
Dokholyan	2004	A Trial of Omega-3 Fatty Acids for Prevention of Hypertension	May predate report		
Bemelmans	2004	Increased $\alpha$ -linolenic acid intake lowers C-reactive protein, but has no effect on markers of atherosclerosis	May predate report		
Cazzola	2007	Age- and dose-dependent effects of an eicosapentaenoic acid-rich oil on cardiovascular risk factors in healthy male subjects	None		
Rasmussen	2006	Effects of dietary saturated, monounsaturated, and n_3 fatty acids on blood pressure in healthy subjects <sup>1–3</sup>	None		
Lindman	2004	The effects of long-term diet and omega-3 fatty acid supplementation on coagulation factor VII and serum phospholipids with special emphasis on the R353Q polymorphism of the FVII gene	May predate report		
Erkkila	2004	Fish intake is associated with a reduced progression of coronary artery atherosclerosis in postmenopausal women with coronary artery disease <sup>1–4</sup>	May predate report		
Maki	2010	Baseline Lipoprotein Lipids and Low-Density Lipoprotein Cholesterol Response to Prescription Omega-3 Acid Ethyl Ester Added to Simvastatin Therapy	None		

**Table D4. Citation frequency and purpose for omega-3 update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Sanders	2006	Effect of varying the ratio of n <sub>6</sub> to n <sub>3</sub> fatty acids by increasing the dietary intake of α-linolenic acid, eicosapentaenoic and docosahexaenoic acid, or both on fibrinogen and clotting factors VII and XII in persons aged 45–70 y: the OPTILIP Study1_3			
Griffin	2006	Effects of altering the ratio of dietary n <sub>6</sub> to n <sub>3</sub> fatty acids on insulin sensitivity, lipoprotein size, and postprandial lipemia in men and postmenopausal women aged 45–70 y: the OPTILIP Study1–3	None		
Grundt	2003	Changes in tissue factor and activated factor XII following an acute myocardial infarction were uninfluenced by high doses of n-3 polyunsaturated fatty acids	Precedes report		
Caslake	2008	Effect of sex and genotype on cardiovascular biomarker response to fish oils: the FINGEN Study1–3	2, 3	At intakes of 2 g EPA_DHA/d, additional cardioprotective benefits such as antithrombotic actions and a positive effect on vascular reactivity, blood pressure, plasma lipid concentrations, and lipoprotein subclass distribution have been reported [13–17]. The hypotriacylglycerolemic action of these relatively high fishoil n <sub>3</sub> FA intakes is well recognized; the degree of triacylglycerol (TAG) lowering is comparable to the response observed with commonly used pharmacologic treatments such as fibrates. Furthermore, as highlighted in a recent systematic review [8], data on the effects of EPA and DHA on cardiovascular disease (CVD) outcomes in different population subgroups are limited. The lipid response to fish-oil supplementation is known to be highly heterogeneous both within and between studies. In a previous study, our group [19] reported a group	Introduction: study fills gap

**Table D4. Citation frequency and purpose for omega-3 update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
				<p>mean reduction of 35% in fasting TAG and an increase of 7.1% in fasting LDLcholesterol concentrations after supplementation for 6 wk with 3 g EPA DHA/d, as compared with the control oil (CO). However, these mean responses represented ranges of 114% to 61% in TAG concentrations and of 49% to 87% in LDLcholesterol concentrations in the 55 participants [19]. It is likely that factors such as health status, medication use, background diet, age, sex, baseline lipid concentrations, and genetic variability account for this highly heterogeneous blood lipid response to fish-oil intervention, but the relative effect of these factors is unknown.</p>	
				<p>The ability to draw definitive conclusions from this earlier study was limited by the facts that it was conducted in subjects with an atherogenic lipoprotein phenotype and that it lacked adequate statistical power to examine genotype-phenotype associations. Therefore, in the present study, the FINGEN Study, prospective recruitment according to sex, age, and APOE genotype was used in a normolipidemic population to evaluate the effect of these factors on lipid responses to fish-oil supplementation by using EPADHA intakes that are achievable by the general population through an increase in the consumption of oily fish.</p>	

**Table D4. Citation frequency and purpose for omega-3 update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
Hjerkinn	2005	Influence of long-term intervention with dietary counseling, longchain n-3 fatty acid supplements, or both on circulating markers of endothelial activation in men with long-standing hyperlipidemia1-3	None		
Park	2009	Fruit, vegetable, and fish consumption and heart rate variability: the Veterans Administration Normative Aging Study1-3	None		
Niu	2006	Dietary long-chain n_3 fatty acids of marine origin and serum C-reactive protein concentrations are associated in a population with a diet rich in marine products1-3	None		
Djousse	2003	Dietary linolenic acid and carotid atherosclerosis: the National Heart, Lung, and Blood Institute Family Heart Study1-3	Predates report		
Hino	2004	Very long chain N-3 fatty acids intake and carotid atherosclerosis. An epidemiological study evaluated by ultrasonography	None		

**Table D4. Citation frequency and purpose for omega-3 update search (continued)**

First Author	Year	Title	References	Text	Purpose of citation
He	2008	Intakes of long-chain n-3 polyunsaturated fatty acids and fish in relation to measurements of subclinical atherosclerosis 1-3	2	The effects of LC n-3 PUFAs on atherosclerosis may be mediated through PUFAs' roles in lipoprotein metabolism. In the present study, we found that fish and LC n-3 PUFA intakes were associated with lower triglyceride concentrations. LC n-3 PUFAs and nonfried fish were positively related to HDL. LCn-3 PUFAs also were inversely associated with total:HDL cholesterol. No statistically significant associations were found for LDL and total cholesterol. A recent meta-analysis of 21 randomized controlled trials summarized the effects of fish-oil supplementation on lipid values [39]. The meta-analysis suggests that fish-oil consumption significantly reduces serum triglycerides and modestly improves HDL. However, fish-oil intake increases the concentration of LDL cholesterol and has no effect on total cholesterol. It is uncertain how these combined effects of LC n-3 PUFAs on lipid values affect the development or progression of atherosclerosis.	Discussion: places findings in context
He	2009	Associations of Dietary Long-Chain n-3 Polyunsaturated Fatty Acids and Fish with Biomarkers of Inflammation and Endothelial Activation (From the Multi-Ethnic Study of Atherosclerosis [MESA])	None		
Ohsawa	2008	Dietary intake of n-3 polyunsaturated fatty acids is inversely associated with CRP levels, especially among male smokers	None		

**Table D4. Citation frequency and purpose for omega-3 update search (continued)**

<b>First Author</b>	<b>Year</b>	<b>Title</b>	<b>References</b>	<b>Text</b>	<b>Purpose of citation</b>
Saito	2008	Effects of EPA on coronary artery disease in hypercholesterolemic patients with multiple risk factors: Sub-analysis of primary prevention cases from the Japan EPA Lipid Intervention Study (JELIS)	None		
Oikawa	2009	Suppressive effect of EPA on the incidence of coronary events in hypercholesterolemia with impaired glucose metabolism: Sub-analysis of the Japan EPA Lipid Intervention Study (JELIS)	None		

## Appendix E. Key Informant List

**Table E1. List of Key Informants**

<b>Omega-3 and cardiovascular disease case study</b>	<b>Literacy and health outcomes case study</b>
Ethan Balk, M.D., M.P.H. Tufts University Evidence-based Practice Center Boston, MA	Cynthia Baur, Ph.D. Centers for Disease Control and Prevention Atlanta, GA
Beth Collins Sharp, Ph.D., R.N. Agency for Healthcare Research and Quality Rockville, MD	Nancy Berkman, Ph.D. RTI International Research Triangle Park, NC
Rebecca Costello, Ph.D., F.A.C.N. National Institutes of Health- Office of Dietary Supplements Bethesda, MD	Cindy Brach, Ph.D., M.P.P. Agency for Healthcare Research and Quality Rockville, MD
William Harris, Ph.D. Sanford Health Sioux Falls, SD	Darren DeWalt, M.D., M.P.H. University of North Carolina School of Medicine Chapel Hill, NC
Penny Kris-Etherton, Ph.D., R.D., F.A.H.A. Pennsylvania State University University Park, PA	George Isham, M.D., M.S. HealthPartners Bloomington, MN
David Lathrop, Ph.D., F.A.H.A. National Heart, Lung, and Blood Institute Bethesda, MD	Joanne Schwartzberg, M.D. American Medical Association Chicago, IL
Alice H. Lichtenstein, D.Sc. Tufts University Boston, MA	