Methods Future Research Needs Report

Number 1

Finding Evidence on Ongoing Studies

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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 in 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.

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Background

Comparative effectiveness reviews synthesize evidence to inform questions about healthcare topics, but the evidence is not always sufficient to completely answer those questions. Therefore systematic reviews and specifically Evidence-based Practice Center (EPC) reports may identify research gaps and make recommendations for future research to address these unanswered questions. One useful adjunct to these recommendations is an analysis of the research that is currently in the pipeline. This additional information can be used to prioritize the research gaps in the report. Identified research gaps on topics for which several large studies are underway can be described as a lower priority future research need. Identified research gaps on topics with few studies underway may rise as priorities for future research. Prioritizing the research gaps this way can also guide funding agencies in decisions about which topics may need additional research funding. The information provided about ongoing studies can provide indications about when to update reviews.

This project assessed this potential adjunct of reviewing ongoing studies when addressing future research needs through two aims. First sources of information that can be used to identify ongoing studies relevant to the research gaps were analyzed. Second, we evaluated the value that could be added by utilizing these sources in refining the research recommendation section of an EPC report. The second aim was to determine if there are characteristics of ongoing studies that can be used to predict which studies will be completed as planned and published in a timely manner. We addressed the following key questions during the completion of this project:

1. What sources of information are available to identify ongoing studies?
    a. Is the metadata provided, and are indexing and search capabilities in these sources easy to use and understand in identifying studies pertaining to specific research questions?
    b. What are the strengths and weaknesses of these sources?

2. For research questions pertaining to research gaps identified in past EPC reports, how often do these information sources list relevant ongoing studies?
    a. Are there study characteristics that can be used to predict which studies will be completed as planned and published in a timely manner (sponsorship, topic area, etc.)?
    b. Can study characteristics predict which studies will be completed as planned and published in a timely manner (sponsorship, topic area, etc.)?

Methods

The aims of this project were investigated primarily qualitatively in several steps. First, we reviewed literature to develop the background on this topic. Second, we solicited expert opinion from EPC librarians to generate a list of sources (i.e., trial registries, funded research databases, other grey literature sources) useful in identifying ongoing studies. Librarians were also queried regarding the strategies and techniques they use when searching for ongoing studies.

For the next phase of this project, we identified all AHRQ EPC reports published in 2004-2005. We evaluated whether the completed and published EPC reports identified research gaps. We then searched for studies ongoing at the time the reports were published. From this group of 49 EPC reports, 4 were analyzed in more detail. The four were selected because they represented topics with significant research activity and they represented different areas of comparative effectiveness research (i.e., pharmacological or surgical interventions, complex disease management, or health services research) and a variety of topics. We searched topically for ongoing studies that were relevant for each of the four selected reports in the identified databases. We pragmatically evaluated the databases using the following criteria:

- How can the database be searched (i.e., topic, study design)?
- Can information about studies be downloaded for efficient analysis?
- Do databases provide study completion dates and links to publications in peer reviewed journals?
- Does the database provide sufficient information about the study?

We assessed relevance of each ongoing study according to EPC report criteria for study inclusion. Relevance was subjectively determined on topic by one study author. We evaluated completeness of the study according to recruitment status. We evaluated publication status in peer reviewed journals and a presentation of the results in scientific meetings. Sponsorship, topic (cancer, heart disease, etc.) and/or context area (i.e., devices, drugs, procedures, diagnostic methods) were qualitatively assessed to suggest factors that might predict relevance and utility of the completed study and associated end-products in meeting the future research needs identified in the EPC report.

Results

Several online information sources are available to search for ongoing studies. Librarians typically search a few of these sources to identify ongoing studies (Executive Summary Table 1). The single most commonly used source for identifying ongoing clinical trials appears to be ClinicalTrials.gov. Beyond ClinicalTrials.gov, additional international trials are sometimes identified through the International Clinical Trials Registry Platform (ICTRP) which is a search portal maintained by the World Health Organization (WHO) that aggregates information from several registries. Several sources that maintain databases of funded research are also available to search for ongoing studies. These are especially useful when searching for studies that are not clinical trials. The two sources most frequently utilized to search for funded research included the National Library of Medicine's Health Service Research Projects in Progress (HSRProj) and the National Institutes of Health Research Portfolio Online Reporting Tools Expenditures and Results (RePORTER). Questionnaire respondents found HSRProj to have a more pleasing interface than the RePORTER. The RePORTER seemed to be more comprehensive as it includes all National Institutes of Health (NIH) funded research where HSRProj focuses on health services research topics. Grey literature sources were also important to librarians searching for ongoing studies. Other grey literature sources mentioned included Food and Drug Administration databases, topic-specific conference proceedings, and Web sites recommended by content experts.

Table A. Data sources used to find ongoing studies

Data Source	Always (N)	Always (%)	Sometimes (n)	Sometimes (%)	Never (n)	Never (%)
Portals						
ICTRP	1	11.0%	6	67.0%	2	22.0%
IFPMA	0	0%	0	0%	8	100%
International and National Registries						
Clinicaltrials.gov	7	87.5%	1	12.5%	0	0%
ISCTRN	2	25.0%	1	12.5%	5	62.5%
Other government	0	0%	4	50.0%	4	50.0%
Industry						
Specific pharmaceutical company	1	12.5%	4	50.0%	3	37.5%
PhRMA clinicalstudyresults.org	1	12.5%	0	0%	7	87.5%
Specialty						
Academic	0	0%	2	25.0%	6	75%
Subject specific	1	12.5%	3	37.5%	4	50.0%
Databases of Funded Research						
HSRProj	2	25.0%	2	25.0%	4	50.0%
RePORT	3	37.5%	0	0%	5	62.5%
AHRQ GOLD	1	12.5%	1	12.5%	6	75%
Specific Foundations	0	0%	2	28.6%	5	71.4%

The majority of the EPC reports published in 2004-2005 included future research recommendations. However, reports did not address ongoing studies when making research recommendations. The number of ongoing studies at the time when the reports were completed varied across topics without visible patterns. The following four EPC titles were selected for more detailed analysis of related ongoing studies:

- *Quality of Care in Minority Health*
- *Islet Cell Transplantation*
- *Diagnosis and treatment for Acute Stroke*
- *Pharmacological Treatments for Dementia*

The next phase of the project included following the ongoing studies relevant to these four reports forward through the next 5 to 6 years. Several observations were made during this process. Trial registries and funded research databases did not provide complete information about all ongoing studies. One registry, ClinicalTrials.gov, and two funded research databases, NIH RePORTER and AHRQ GOLD, allowed for comparatively efficient searching by topic or study design. Retrieved data can be downloaded from ClinicalTrials.gov and most of the funded research databases we evaluated. Trial registries typically provided sponsor name but not exact grant numbers. Funded research databases do not appear to provide study registration status. In general, trial registries and funded research databases did not appear to link to each other. ClinicalTrials.gov complies with the WHO minimum dataset requirements providing detailed study design, recruitment activities, ethics review of research, target sample size, subject inclusion criteria, and primary and secondary outcomes.[1] ClinicalTrials.gov included links to publications in Medline. Two funded research databases are linked to all publications in which the project was mentioned, but all are not necessarily results of the exact study that was funded. ClinicalTrials.gov and ClinicalStudyResults.org allow posting of study results. Trial registries do not have information about all funded studies. Only the NIH REPORTER has a complete list of all grants sponsored by NIH.

The precision of searches for ongoing studies in different sources varied across databases. Generally, for the searches we performed, ClinicalTrials.gov provided the most precise search results. Information about study status (i.e., recruiting, completed, terminated) was available only in trials registries and not in funded research databases. Publication rates varied among our four topics. Publications appeared more common among the ongoing studies we identified in the NIH RePORTER than in ClinicalTrials.gov, consistent with previous results concerning sponsorship and publication. In the four studies we investigated, drug studies seemed to be published less often than other interventions. The studies with posted results tended to be published more often than those without posted results. Publication rates appeared to differ across sponsorship category with government sponsored research being published more frequently than industry sponsored research in three of our four topics.

Conclusions

In general, it seems there is little certainty that ongoing studies will be completed in a manner that contributes useful evidence. Searching for ongoing studies may not warrant a significant investment of resources. However, information about ongoing studies is useful in prioritizing the identified research gaps. Therefore, searching these sources as efficiently as possible is important and useful to refining the future research needs section of EPC reports. To do this, the highest priority should be to search those sources that are likely to provide the largest yield and provide the most useful data on the ongoing studies in a useable way.

Based on our qualitative assessment of identifying ongoing studies, we recommend searching at least two sources for clinical studies, ClinicalTrials.gov and the ICTRP. These two sources should provide a fairly complete list of registered studies, they are relatively easy to use, and data on selected studies can be downloaded from ClinicalTrials.gov. Searching for nonclinical ongoing studies should be conducted in a more targeted manner. The NIH RePORTER provides complete information about NIH funded studies but few details regarding study design and protocol. HSRProj and AHRQ GOLD also provided information on studies and were considered excellent sources for finding ongoing studies that would not necessarily be in a clinical trials registry (observational studies or health services research topics). Supplementing these sources with targeted grey literature searching may uncover a portion of ongoing studies.

Completeness rates were high for all topics. Publication rates were higher but less accurate among studies identified in the NIH RePORTER. Nearly half of the registered studies were not published. Sponsor factors were the most obviously associated with publication.

It is also important that caveats regarding the potential of ongoing studies to fill the research gap be addressed when listing ongoing studies. The extent of protocol changes and low publication rates among registered studies indicates that identified ongoing studies should be watched for completion, publication, and posting of results (as is now required by law) and not automatically relied upon to fill a research gap.

Chapter 1. Background

The conclusion of each Evidence-based Practice Center (EPC) report typically presents a set of research recommendations based on the research gaps identified in the review. These recommendations can address new interventions, outcomes, populations, or analyses. One useful adjunct to these recommendations would be an analysis of the research that is currently in the pipeline. In effect, this analysis would help to refine the research gaps remaining after accounting for those gaps currently addressed by ongoing studies. This additional information can be used to prioritize the research gaps in the report. Identified research gaps pertaining to issues for which several large studies are underway can be described as a lower priority future research need. Identified research gaps with few studies underway may rise as priorities for future research. Prioritizing the research gaps this way can guide funding agencies in their funding decisions to best fill high priority research gaps and can also provide indications for updating the review.

The Cochrane handbook describes the importance of identifying ongoing studies as part of the process of completing systematic reviews.[2] A table called "4.6.5. Characteristics of Ongoing Studies" is used to include identified related ongoing studies in the analysis.[2] Unfortunately, several limitations restrict the extent that ongoing studies can be relied upon to fill a particular research gap. For instance, not all ongoing studies are completed or completed as planned. Studies that are completed are not always published. Studies that are published may significantly change their protocols such that they no longer fill the identified research gap.

The value of providing information about ongoing studies depends on the quality of the information available on the ongoing study. Ideally, available information regarding ongoing studies should be efficiently identifiable and sufficient to allow judgment about its likelihood to be completed and published as planned. Additionally, information about the study that helps predict the eventual study quality would also be beneficial. Therefore, ongoing studies can be listed along with an assessment of their potential to fill the research gap and the likelihood of completion and publication.

This project aims to provide insight to EPCs in finding ongoing studies by identifying the key resources, the most efficient approach to these sources and predictors that may help to determine the degree of reliance on a particular study to fill the identified research gap. Finding information about research studies underway but not (yet) published has long been challenging. For several reasons, searching for these studies has become faster and easier. The electronic age, pushes toward openness, transparency, and full disclosure, and studies demonstrating bias in published medical literature have all led to improved access to information on ongoing studies.

Development of Sources for Finding Information About Ongoing Studies

Progress toward increased access to information about ongoing studies began with a focus on clinical trials. In 1997 the U.S. Food and Drug Administration Modernization Act (FDAMA 113) required NIH to establish a registry of clinical trials for both federally and privately funded trials of experimental treatments for serious or life threatening diseases.[3] A Clinical Trials Registry (CTR) is a database of planned, ongoing, or completed clinical trials, published as well as unpublished, in which details concerning the trial's objectives, main design features, sample size, and tested treatments are stored.[4] ClinicalTrials.gov was created and launched in February 2000.[5] Trial registration was required only for certain trials, those

conducted under U.S. Food and Drug Administration investigational new drug applications that evaluate drug efficacy for serious diseases.[5] However, few consequences resulted from not registering,[6] and registration rates were initially poor. Research on oncology trials found that only 16 of 20 qualifying trials were registered.[6]

In September 2004, in an effort to improve the registration, the International Committee of Medical Journal Editors (ICMJE) required that clinical trials be registered as a condition for publication in member journals.[5] Trials beginning after July 1, 2005, had to be registered in a publically available registry before beginning enrollment. Trials that began enrollment prior to July 1, 2005, were given a deadline of September 13, 2005, to register their trials in a registry.[7]

Authors were permitted to register trials in any registry that met certain qualifications. At that time, only ClinicalTrials.gov met the registry requirements of being publicly available for no cost, was managed by a not-for-profit organization, included a mechanism to ensure validity, and was electronically searchable.[7] To raise awareness of this new requirement, an editorial with the statement requiring registration for publication was authored by 11 medical journal editors and published in several medical journals, including the *Annals of Internal Medicine*, the *Journal of the American Medical Association*, the *New England Journal of Medicine*, *The Lancet*, and others. This action by the ICMJE inspired a dramatic increase in trial registration. The number of trials registered in Clinicaltrials.gov went from just over 13,000 to over 22,000 one month after the policy went into effect.[8]

The pharmaceutical industry also responded to calls for greater transparency. In 2004 a U.S. based pharmaceutical trade organization, the Pharmaceutical Research and Manufacturers of America (PhRMA), created a registry for trial results. In 2005 the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA), a global trade group, issued a position paper committing to trial registration consistent with FDAMA 113.[6] This group also recommended the reporting of results of clinical trials.

Shortly after adding the trial registration requirement for publication, the ICMJE recommended that trial registrations comply with the WHO minimum dataset.[6,9] This minimum set of data includes:

- Primary registry and trial identification number
- Trial registration date
- Secondary identification numbers
- Sources of funding
- Primary sponsor
- Secondary sponsor
- Responsible contact person
- Research contact person
- Study title (brief)
- Official title
- Research ethics review (yes/no)/countries of recruitment
- Health condition or problem studied
- Intervention
- Inclusion and exclusion criteria
- Study type
- Anticipated date of first enrollment
- Target sample size

- Recruitment status
- Primary outcome
- Secondary outcome(s)

In September 2007 the Food and Drug Administration Amendments Act (FDAAA) 801 expanded the scope of clinical trial registration to include all drug and device trials (except early phase trials) and add results to the database.[5] The expanded scope of registration requirements went into effect in December 2007. Registration rates in ClinicalTrials.gov grew in response to this legislation. A National Library of Medicine spokesman estimated an increase from about 250 trial registrations a week to 350.[10] Additional components of this legislation went into effect at later dates; results reporting in September 2008; and adverse events reporting in September 2009. Penalties for noncompliance with FDAAA 801 could result in loss of grant funding and daily fines.[10] The secretary of Health and Human Services is expected to advise on enhancing results reporting in late 2010.[5]

Other factors improved access to information on clinical trials. In May of 2007 WHO launched its ICTRP. While not a registry, this site offers a search engine allowing users to search several registries simultaneously.[10] Another search engine enabling users to find trial registration and results information in several registries was established by IFPMA in 2005.[6]

Studies of Clinical Trials Registries

As previously mentioned, information about ongoing clinical trials was the first to become available and accessible to the public in a systematic way. The number of CTRs and the number of registered trials has multiplied during the last several years. As the number of CTRs, registered trials, and policies regarding trial registration grew, so did research on CTRs. Incomplete and vague information about the trials seemed to be common as trial registration was gaining acceptance.[11,12] Findings from some of these studies suggest that many study results are never published, especially those with negative or insignificant results;[13-17] time to publish is longer for insignificant results and study outcomes and protocols may be adjusted based upon study results for publication purposes.[13] While publication rates of registered trials were generally low, those sponsored by industry were less likely to be published than those sponsored by government/nongovernment sources.[13,16] Several studies find evidence of selective reporting of outcomes in published studies, providing an indication that published reports may have different primary outcomes as a result of study results than is described in registered study protocols.[13,18] One recent study found that selective outcome reporting is prevalent in published studies when compared to the trial registration, and only 45 percent of studies were registered before the end of the trial.[18] The proportion of trials registered was greater for studies published in general medicine journals compared with specialty journals; and authors identified 69 trials published in journals that specifically mention in their instructions to authors that registration is a requirement for publication that were not registered.[18] While the movement toward improved access to information about ongoing trials is not yet perfect, information is more freely available and accessible than ever before.

CTRs are not a new concept. Several authors describe inventories of CTRs. Easterbrook[19] reports on results of a 1989 international survey of organizations and individuals known to be active in the field of clinical trials in 13 countries to create a directory of clinical trials registries. Survey results include the identification of 24 current and six planned registries. Registries were developed as early as 1974. Subject-specific registries were prevalent, especially in AIDS/HIV

and Cancer.[19] Most registries were based in the United States, including two general clinical trials registries collecting information on clinical trials at the national level (one at NIH and one at the Veterans Administration).[19] These registries collected information on trials primarily through funding agencies and surveys of organizations known to conduct trials. While many of these registries are no longer in existence, they likely set the stage for current clinical trials registries.

A report by the Public Citizen's Health Research Group included a listing of four public registries and 18 private registries.[20] A study of registry compliance with WHO minimum dataset requirements used a convenience sample of 21 registries.[9] They categorize their registries as international, national, specialty, and industry. Web sites for search portals list their registry sources.[21,22]

The most widely recognized international clinical trials registries include Clinicaltrials.gov and the ISRCTN registry. This is not surprising given that these are the two largest clinical trials registries. In July of 2010 ClinicalTrials.gov listed nearly 95,000 studies and ISRCTN listed over 9,000 studies.[23,24] However, in addition to these, international or national trial registries are administered by governments in other countries, including Australia and New Zealand, China, Germany, India, Iran, Japan, Korea, The Netherlands, Pan African countries, and Sri Lanka.[21]

In addition to the international and national registries, the pharmaceutical industry has been prolific in the development of trials registries. Several authors describe media attention to unpublished trial information on antidepressant drugs as the impetus behind pharmaceutical companies beginning to create registries.[6,25] While the trade group PhRMA was organizing and preparing their database of clinical trial results, a couple of pharmaceutical companies created their own registries. Eli Lilly appears to have created the first independent pharmaceutical company registry which began registering trials initiated by July 1, 2004.[25] The pharmaceutical company currently known as GlaxoSmithKline and others followed.[6] Currently, most of the major pharmaceutical companies appear to maintain registries of their ongoing and completed trials.

Specialty registries or databases are also common sources listing ongoing studies. These include subject-specific, institution-specific, or other special interest collections of ongoing trials. For instance, the University of Michigan maintains a searchable database describing studies currently ongoing at the university.[26] The Stroke Center Registry maintains a listing of stroke related trials.[27] Many of the specialty databases seem intended to inform and recruit patients and are less valuable for researchers because they often do not provide sufficient information about the study.

Several search portals have been established to allow simultaneous searching of several registries, eliminating the need for individuals to search through all registries to compile their list of studies. WHO developed the International Clinical Trials Registry Platform (ICTRP) Search Portal. Here users can search for trials registered in any of the included registries and obtain links to the full record in the respective registry. The metaRegister of Controlled Trials (mRCT) also administered and available though Current Controlled Trials[28] searches at least seven registries including Clinicaltrials.gov and the ISRCTN Register. The IFPMA Clinical Trials Portal allows federated searching of four general trial registries and 24 pharmaceutical registries, including PhRMA's clinical trials results database.[29]

Sources other than those including registered clinical trials are also important especially when looking for ongoing observational studies or for ongoing studies relevant to health services

research questions. While a recent editorial suggests registering health services research projects in ClinicalTrials.gov,[30] currently other databases are more useful in identifying these types of ongoing studies. There are newly available databases that were designed to describe funded research studies. The NIH RePORTeER is a database including all research funded by the National Institutes of Health. A database specific to health services research topics was developed by the National Library of Medicine. Other sponsors also list studies that they have funded. Other topic specific grey literature sources are also important to finding ongoing studies that may not be registered. These may be best identified with assistance from content experts on relevant topic-specific conferences and/or websites.

This project aims to shed light on the best way to approach ongoing studies for EPC reports. The value of this additional information as well as the costs are also described.

Key Questions

To shed light on the value and process of searching for and including ongoing studies in EPC reports, this project set out to address the following key questions:

1. What sources of information are available to identify ongoing studies?
    a. Is the metadata provided, and are indexing and search capabilities in these sources easy to use and understand in identifying studies pertaining to specific research questions?
    b. What are the strengths and weaknesses of these sources?
2. For research questions pertaining to research gaps identified in past EPC reports, how often do these information sources list relevant ongoing studies?
    a. What proportion of registered studies yield publications?
    b. Can study characteristics predict which studies will be completed as planned and published in a timely manner (sponsorship, topic area, etc.)?

Chapter 2. Methods

Key Question 1

Addressing the first key question regarding identifying sources for ongoing studies involved two activities. First, we reviewed the literature discussing ongoing studies and databases or other resources that could be searched to identify ongoing studies. The literature search was conducted in Ovid Medline using the MeSH heading "Clinical trials as topic and the multipurpose key word 'trials' regist?" This electronic database search was complemented with hand searching the reference lists of included articles. Literature was searched through July of 2010.

Prior knowledge and the literature searches were used to compile a preliminary list of sources for finding ongoing studies. These primarily included trial registries and databases of funded research. The preliminary listing was used to develop an electronic questionnaire for EPC librarians. The questionnaire sought information about their current practices used in searching for ongoing studies and/or funded research when assisting in the development of EPC reports. The librarians or EPC staff members were asked about specific sources for information about ongoing studies and their experience with those sources.

- How do you conduct a search for ongoing studies (what sources are searched [registries, funded research databases, other sources of grey literature]?
- How do you rate the quality and usefulness of the sources you search for ongoing studies (comments and critiques for identified sources)?

The questionnaire was pretested among colleagues at the University of Minnesota. An e-mail requesting participation and a link to the final electronic questionnaire administered via Survey Monkey™[31] were sent out on July 20, 2010, to 14 EPC staff identified by AHRQ as librarians or librarian contact persons. Two individuals listed as EPC librarian contacts responded to the request, explaining that their EPC did not routinely use librarians to assist with their searching and that research staff typically performed the searches relevant to EPC reports. When the survey reminder was sent out via e-mail 1 week later, respondents other than librarians were invited to participate. A copy of the questionnaire appears in Appendix A.

The questionnaire included statements regarding the sources used to conduct searches for ongoing studies. In response to these statements, respondents selected 'always,' 'sometimes,' or 'never.' The first set of statements pertained to general procedures about searching for ongoing studies (if they did it, whether they used several sources, and whether these sources included trial registries, databases of funded research, and grey literature). The next series of statements asked about specific sources or a category of sources and the extent to which each of these is used. Respondents indicating usage of a particular source (ClinicalTrials.gov, controlled-trials.org, ICTRP or IFPMA search engines, clinicalstudyresults.org, HSRProj, NIH RePORTER, AHRQ GOLD) by selecting "sometimes" or "always" were asked to agree or disagree on a 5-point Likert scale with statements about that source:

- It is easy to use.
- It provides adequate instructions to assist in searching.
- The data provided about the ongoing studies are sufficient to gain a basic understanding of the research underway.

- It appears to provide a comprehensive listing of studies.

Respondents were also asked open-ended questions about specific attributes of the source that they found valuable or beneficial and/or difficult or frustrating. They were also asked for advice they could offer regarding the source. Due to the number of registries available, those detailed questions were not asked of all identified sources for ongoing studies. Other registries were asked about in a categorical fashion (government registries other than U.S., professional organization/condition specific registries, academic institution registries, and specific pharmaceutical company registries). If respondents used one of these categories of registries, they were asked to list the specific registry they had used and why. The next section of the survey asked about general approaches to using grey literature to identify ongoing studies and what sources were frequently used for these searches. Lastly, respondents were asked to list other sources they knew of for finding ongoing studies and were provided the opportunity to list other information or comments relevant to finding ongoing studies. From the 14 EPC contacts, we received nine responses for a response rate of 60 percent.

Key Question 2

Two sequential tasks were completed to address the second research question. First, we analyzed whether completed and published evidence-based reports identified the research gaps. We made a list of reports completed in 2004-2005. We wanted to ensure that evidence reports published after 2004 (when trial registration became more prevalent) are evaluated. We checked to see whether the reports included future research recommendations and in what format (e.g. narrative, list of gaps based on available evidence).

To select topics for the second task of this research question, we searched ClinicalTrials.gov to identify studies relevant to each EPC report topic that were ongoing at the time of report publication. This was necessary to ensure that the reports selected to follow relevant ongoing studies forward to completion and publication included a variety of topics and interventions and had a fairly high amount of ongoing research. A table describing these first steps of quantifying ongoing studies related to each EPC report published in 2004/2005 appears in Appendix B.

Second, we selected four EPC reports representing different areas of comparative effectiveness research, including pharmacological and surgical treatments, diagnostic studies, and health services research. We looked for ongoing studies relevant to those four reports in several sources that were identified through the literature and the librarian questionnaire. The trials registries included ClinicalTrials.gov and the International Standard Randomized Controlled Trial Number (ISRCTN) registry. Additionally, we searched the industry-sponsored database of clinical study results. We searched several websites with information about funded studies including the NIH RePORTER database, the Foundation Directory Online, the National Information Center on Health Services Research and Health Care Technology, Web site, and AHRQ grants On-Line Database (AHRQ GOLD). We selected four reports representing high priority research areas for AHRQ and high research activity.

Using the four selected topics, we evaluated the databases where ongoing studies could be identified. We evaluated the databases using the following criteria:

- What is the search capability (vocabulary used for indexing, advanced searching, Boolean operators, keyword searching only, etc.)?
- Can identified information about studies be downloaded for efficient analysis?

- Do trial registries provide grant numbers to link registries and funding agencies' databases?
- Do databases provide completion dates for the studies and links to publications in peer reviewed journals?
- Is the data provided complete in each database when compared to other databases?

We retrieved the studies that were ongoing at the time when the EPC reports were published; inclusion criteria for the ongoing studies were similar to the inclusion criteria for the published EPC reports. We used similar search strings to those used in the original report to identify and retrieve ongoing studies. Then we individually reviewed available information about each ongoing study to decide relevance to the published EPC reports. One author screened retrieved studies and subjectively determined their relevance to the EPC reports and inclusion into analysis. We followed these included studies forward in time to the present to evaluate study completion and publication. We defined study status according to the status mentioned in the trial registry or funded research database:

- Completed: the study has concluded normally; participants are no longer being examined or treated (i.e., last patient's last visit has occurred).
- Suspended: recruiting or enrolling participants has halted prematurely but potentially will resume.
- Terminated: recruiting or enrolling participants has halted prematurely and will not resume; participants are no longer being examined or treated.
- Withdrawn: study halted prematurely, prior to enrollment of first participant.

Then we examined completeness and publication rates of ongoing studies. We also analyzed study or sponsor characteristics associated with a publication of the ongoing studies. We separately analyzed publication of the study in peer reviewed journals versus a presentation of the results in scientific meetings. We looked at the publication status of ongoing studies in the database in which we found them. We also searched for publications indexed in MEDLINE® using study identifiers from either the registries or grant numbers from funded research databases. We searched the Cambridge Scientific Abstracts' Conference Paper Index and Web of Science databases (using both study title and study identifiers from registries and grant numbers from funded research databases) to find out whether the identified ongoing studies were presented at scientific meetings. Conference and meeting abstracts were treated separately from publications, as many studies presented in abstracts may not go on to be published in journals. We qualitatively compared proportions of published and unpublished registered studies by sponsorship and topic.

Chapter 3. Results

Key Question 1

In an effort to collect information about sources of information regarding ongoing studies, the EPC Librarian Ongoing Studies questionnaire first sought to identify practices among EPC librarians and other staff with regard to finding ongoing studies. It appears that searching for ongoing studies is a common practice when working on EPC reports. Nearly all respondents participate in searches for ongoing studies. Three indicated that they always search for ongoing studies while working on EPC reports and five said they sometimes do. Only one respondent indicated never searching for ongoing studies and therefore was not eligible for finishing the questionnaire. The eight respondents who reported searching for ongoing studies were asked generally about the sources they used for these searches. Five respondents always use several sources when searching for ongoing studies and three respondents sometimes use multiple sources. Seven of eight respondents always included CTRs in their searches; one sometimes does. Three always search the grey literature in their searches for ongoing studies; four sometimes do, and one never does.

Many sources were identified that can be used to search for ongoing studies. Several sources were identified by previous studies of clinical trials registries.[6,9] However, many mentioned in older studies were no longer in existence. The results from the review of literature identified via MEDLINE® and hand searching, Internet searching, personal communication with an EPC librarian while developing the questionnaire, and the EPC Librarian Ongoing Studies Questionnaire identified over 50 sources including portals, clinical trials registries and other searchable databases for identifying ongoing studies. A listing of the sources we identified for finding ongoing studies appears in Appendix C. The sources most frequently used by respondents to our questionnaire were ClinicalTrials.gov and the ICTRP (Table 1).

Table 1. Data sources used to find ongoing studies

Data Source	Always (n)	Always (%)	Sometimes (n)	Sometimes (%)	Never (n)	Never (%)
Portals						
ICTRP	1	11.0%	6	67.0%	2	22.0%
IFPMA	0	0%	0	0%	8	100%
International and National Registries						
Clinicaltrials.gov	7	87.5%	1	12.5%	0	0%
ISCTRN	2	25.0%	1	12.5%	5	62.5%
Other government	0	0%	4	50.0%	4	50.0%
Industry						
Specific pharmaceutical company	1	12.5%	4	50.0%	3	37.5%
PhRMA clinicalstudyresults.org	1	12.5%	0	0%	7	87.5%
Specialty						
Academic	0	0%	2	25.0%	6	75%
Subject specific	1	12.5%	3	37.5%	4	50.0%
Databases of Funded Research						
HSRProj	2	25.0%	2	25.0%	4	50.0%
RePORT	3	37.5%	0	0%	5	62.5%
AHRQ GOLD	1	12.5%	1	12.5%	6	75%
Specific Foundations	0	0%	2	28.6%	5	71.4%

Clinical Trials Registries and Databases

The major sources for finding ongoing studies identified in the literature were used in developing the questionnaire. The number of sources available for finding information on ongoing studies demonstrates that searching for ongoing studies can be extremely time consuming. This is one reason we sought guidance from librarians and other EPC staff, to identify which of the resources provide the greatest yield and efficiency in these searches. EPC staff were asked which sources they used in searching for ongoing studies. Clinicaltrials.gov was the most commonly used source. All of the survey respondents that search for ongoing studies (n=8) reported using ClinicalTrials.gov and reported on its attributes.

Opinions based on experience with ClinicalTrials.gov:

- Was easy to use (6/8 respondents agreed, 2/8 were neutral)
- Provided adequate instructions (6/8 respondents agreed, 2/8 were neutral)
- Provided a sufficient amount of information on the trials (6/8 respondents agreed, 2/8 were neutral)
- Appeared to provide a comprehensive listing of studies (5/8 respondents agreed, 2/8 were neutral, 1/8 strongly disagreed)

Valuable or beneficial attributes of ClinicalTrials.gov:

- Straightforward (mentioned by 1 respondent)
- Comprehensive study status (mentioned by 1 respondent)
- Ability to download the trials' data (mentioned by 2 respondents)
- Ability to customize the search and display (mentioned by 1 respondent)

Difficult or frustrating attributes of ClinicalTrials.gov:

- Out-of-date information (mentioned by 1 respondent)
- Inability to directly perform certain searches, such as searching for only completed trials (mentioned by 1 respondent)
- Not yet comprehensive (mentioned by 1 respondent)
- Can be frustrating to figure out which reports have been published (mentioned by 1 respondent)

Advice offered regarding searching ClinicalTrials.gov:

- Create a filter to import downloaded results into EndNote.
- Drop down menu for downloading format on the search results page.

The second most commonly used source for finding ongoing trials was the ICTRP. However, users of the portal were not as positive as the users of ClinicalTrials.gov. One respondent reported always and six reported sometimes using the ICTRP when searching for ongoing studies. Only six completed questions regarding their experience with the ICTRP.

Opinions based upon experience with the ICTRP:

- Was easy to use (1/6 respondents agreed, 2/6 were neutral, 1/6 disagreed)
- Provided adequate instructions (5/6 respondents were neutral, 1/6 disagreed)
- Provided a sufficient amount of information on the trials (3/6 respondents agreed, 3/6 were neutral)

- Appeared to provide a comprehensive listing of studies (3/6 respondents agreed, 2/6 were neutral, 1/6 disagreed)

Valuable or beneficial attributes of the ICTRP:

- Lists the registry it came from and study contact information (mentioned by 1 respondent)
- Nice to have one place to search (mentioned by 1 respondent)
- Trust in World Health Organization to keep track of national registries (mentioned by 1 respondent)
- Ability to sort list of studies by column (mentioned by 1 respondent)
- Good way to get to non-U.S. registries (mentioned by 1 respondent)

Difficult or frustrating attributes of the ICTRP:

- Different results when searching home page vs. advanced search page with same search terms (mentioned by 1 respondent)
- Out of date information (mentioned by 1 respondent)
- Exporting results (mentioned by 1 respondent)
- Limiting searches (mentioned by 1 respondent)
- Overlap with ClinicalTrials.gov (mentioned by 1 respondent)

Advice offered regarding searching the ICTRP:

- Sorting by registry helps to quickly bypass registries already searched

Industry and specialty registries or databases were also occasionally utilized by EPC librarians and staff. The only industry database mentioned specifically was the clinical study results database maintained by the PhRMA. While specific pharmaceutical company registries were not mentioned, two respondents indicated that they would specifically search a certain company's registry if they were looking for trials on a particular drug. Specific specialty sources used by questionnaire respondents included the National Cancer Institute registry and a "breast cancer registry."

Funded Research Databases

CTRs are useful for identifying ongoing clinical studies. However, many EPC reports address health services research topics. Databases of funded research are a more recent source for identifying these types of ongoing studies. Literature discussing databases that index observational or ongoing health services research studies was not found. Prior knowledge, consultations with librarians, and internet searches identified several sources for identifying ongoing funded research studies. These sources were included in our EPC Librarian Ongoing Studies Questionnaire to assess experience and opinions regarding using these sources.

Half of the questionnaire respondents had used the National Library of Medicine's Health Services Research database, HSRProj.

Opinions based upon experience with HSRProj:

- Was easy to use (3/4 respondents agreed, 1/4 strongly agreed)
- Provided adequate instructions (2/4 respondents were neutral, 1/4 agreed, 1/4 strongly agreed)

- Provided a sufficient amount of information on the trials (1/4 respondents disagreed, 1/4 were neutral, 1/4 agreed, and 1/4 strongly agreed)
- Appeared to provide a comprehensive listing of studies (3/4 respondents were neutral, 1/4 agreed)

Valuable or beneficial attributes of HSRProj:
- Similar to other National Library of Medicine databases (mentioned by 1 respondent)

Difficult or frustrating attributes of HSRProj:
- Inability to download results (mentioned by 1 respondent)

Advice offered regarding searching HSRProj:
- Able to tag files for downloading.

The National Institute of Health's Research Portfolio Online Reporting Tool (RePORTER) database was also utilized by a few questionnaire respondents. Three of the eight EPC librarians or staff responded that they always search RePORTER when searching for ongoing studies. The other five had never used the database.

Opinions based upon experience with RePORTER:
- Was easy to use (1/3 respondents strongly disagreed, 1/3 agreed, 1/3 strongly agreed)
- Provided adequate instructions (1/3 respondents strongly disagreed, 1/3 agreed, 1/3 strongly agreed)
- Provided a sufficient amount of information on the trials (1/3 respondents disagreed, 1/3 agreed, 1/3 strongly agreed)
- Appeared to provide a comprehensive listing of studies (1/3 respondents were neutral, 1/3 agreed, 1/3 strongly agreed)

Valuable or beneficial attributes of RePORTER:
- Provides information not available elsewhere (mentioned by 1 respondent)

Difficult or frustrating attributes of RePORTER:
- Very difficult to use, limited searching and downloading capabilities (mentioned by 1 respondent)

Advice offered regarding searching RePORTER:
- Breaking results into smaller groups helps with downloading.

The last specific database of funded research listed on the questionnaire was the Agency for Healthcare Research and Quality's AHRQ GOLD. Only two respondents reported having used this database, but responses were positive regarding ease of use, adequacy of instructions, sufficiency of data, and comprehensiveness. The one comment provided about this database describes that because it is a small database, it is fairly quick and easy to search.

Other nongovernmental funding organizations mentioned by one respondent, included the "Breast Cancer Research Foundation," the "Flight Attendant Medical Research Institute,' and the "Komen Foundation,' This respondent also described her process in identifying potential funding

sources and therefore lists of funded research from which to search for ongoing studies. She uses her institution's grants listing and performs a topic search to identify topic-specific funding agencies. She then searches the websites of these sponsors individually to identify ongoing studies relevant to that topic.

Grey Literature

Questionnaire respondents also reported that they frequently performed searches of the grey literature to identify ongoing studies. Of those conducting searches for ongoing studies, five respondents (62.5 percent) reported "always" and three (37.5 percent) reported "sometimes" searching the grey literature to identify ongoing studies. Strategies used to find grey literature, other than that included in the sources previously mentioned, included internet searches from a search engine such as Google, relying on the EPC Scientific Research Center to provide packages of grey literature, conference abstracts, obtaining recommendations of relevant sources for information from experts. Web of Science was also mentioned as an excellent resource for locating conference abstracts. While not mentioned on our questionnaire, we have found that the Cambridge Scientific Abstracts' Conference Paper Index database is another useful source in identifying conference abstracts. Other sources identified by questionnaire respondents as useful in these searches included the Food and Drug Administration databases, the Grey Literature Report, and topic-specific scientific meeting abstracts.

Key Question 2

Research Gaps in Published Evidence-based Reports

We first assessed the population of reports published in 2004-2005 to gather additional information on which to base the selection of the four studies with research gaps to use to identify ongoing studies and follow forward in time to completion and/or publication. Of the 49 EPC reports completed in 2004-2005 (Appendix Table B1), 46 included future research recommendations. The reports did not search for ongoing studies when making research recommendations. One report mentioned an ongoing project that should be available in the near future to fill some evidence gaps pertaining to that topic.[34] The number of ongoing studies that we retrospectively identified as relevant at the time when the reports were completed varied across topics without visible patterns. The four EPC reports selected to follow forward in time included:

- Pharmacological treatments of Dementia[32]
- Acute Stroke: Evaluation and Treatment[33]
- Islet Transplantation in Patients with Type 1 Diabetes Mellitus[34]
- Strategies for Improving Minority Healthcare Quality[35]

Evaluation of the Databases Searched for Ongoing Studies

In addition to the general information about databases presented for Question 1, here we present more pragmatic evaluation of the data sources used to identify ongoing studies. Funded research databases provided title and a short description about funded studies. Not all funded studies were registered. Only one funded research database, the NIH RePORTER, has a complete list of all grants sponsored by NIH. Trial registries provided more detailed protocols of the registered studies. Trial registries do not have information about all funded studies. More

complete information about funded and registered studies was available by combining these two sources (Table 2). One registry, ClinicalTrials.gov, and one funded research database, NIH RePORTER, allowed a sufficiently efficient search by specific conditions or study type. Retrieved data can be downloaded from ClinicalTrials.gov and each of the three funded research databases we evaluated (NIH RePORTER, HSRProj, and AHRQ GOLD).

Trial registries provide sponsor name but not specific grant numbers. Funded research databases do not provide study registration status. In general, trial registries and grant databases do not have a single variable identifying funding and registration of the same studies. One registry, ClinicalTrials.gov, complies with WHO minimum dataset requirements providing detailed study design, recruitment activities, ethics review of research, target sample size, conditions of eligibility for subjects to participate in the study, and primary and secondary outcomes.[21] ClinicalTrials.gov also links to publications indexed in MEDLINE® via PubMed®. The NIH RePORTer, has links to all publications in which the grant was mentioned. However, these links often were not directly related to the exact study that was funded. ClinicalTrials.gov and ClinicalStudyResults.org allow posting of study results.

Searches for ongoing studies in different databases varied in the proportion of relevant studies from those retrieved with a simple subject search (Table 3). Generally, searches in ClinicalTrials.gov were the most efficient. Searches in the ICTRP yielded a small number of eligible studies in addition to those already identified in ClinicalTrials.gov. Searches in funded research databases yielded a large number of funded research studies with small proportions of funded research relevant to answer treatment related research questions.

Table 2. Evaluation of the databases to search for ongoing studies

	Search Terms	Data Downloadable	Grant No.	Lists Publications	Provided Registration Status	Allow Results Posting	Comprehensive When Compared to Other Sources
Registries							
ClinicalTrials.gov	Yes	Yes	No	Yes		Yes	No
ICTRP	No	No	No	No		No	No
ISRCTN Current Controlled Trials	No	No	No	Yes		No	No
PhRMA study results	No	No	No	No, references in slides	Link to registry	Yes	No
IFPMA Clinical Trials Portal	No	No	No	No	Link to registry	No	No
Funded Research Databases							
NIH RePORTER	Yes	Yes	Yes	Yes but not accurate	No	No	Yes
Foundation Directory Online (FDO)	Yes	Yes	Yes	No	No	No	No
HSRProj	No	Yes	Yes	No	No	No	No
AHRQ GOLD	No	Yes	Yes	Yes but not accurate	No	No	No

Table 3. EPC report-specific retrieval and relevance of results

	Pharmacological Treatments for Dementia			Islet Transplantation			Acute Stroke: Evaluation and Treatment			Strategies for Improving Minority Healthcare Quality		
	N	n	%	N	n	%	N	n	%	N	n	%
ClinicalTrials.gov	408	47	12	91	22	24	211	44	21	234	80	34
ICTRP (in addition to www.clinicaltrials.gov)	1	1	100	1	1	100	4	4	100	6	6	100
NIH RePORTER	1160	160	14	125	40	32	2082	464	22	2	1	50
HSRProj										24	24	100
AHRQ GOLD										2,797	127	5

N =number of retrieved studies; n=number of relevant studies; %=percentage of relevant among retrieved.

Evaluation of Completeness and Publication of the Studies

Information about study completion was available in trial registries. Relevancy of studies retrieved to topic varied across topics and databases (Table 3). The completeness rates (participants are no longer being examined or treated) were analyzed for registered studies only. The majority of registered studies were completed. Completion rates were high for studies determined relevant**.** All relevant studies of pharmacological treatments for dementia, 99 percent of the relevant studies on quality of care in minority groups, 86 percent of the relevant studies of diagnosis and treatments for acute stroke, and 77 percent of the relevant studies of islet cell transplantation were completed from the time of the EPC report publication and July 2010 (Appendix D).

Publications of ongoing studies were analyzed separately for studies registered in ClinicalTrials.gov (Figure 1) and studies found in the NIH RePORTER (Figure 2). Publications percentages, calculated as the proportion of studies with related publications indexed and identified in MEDLINE®, were generally lower for studies registered in ClinicalTrials.gov than for the NIH sponsored studies. For instance, the publication rate for the studies of pharmacological treatments for dementia was 99 percent according to the flags in the NIH grants database but 62 percent among studies registered in ClinicalTrials.gov. Publication rates were less than 50 percent among registered studies of diagnosis and treatments for acute stroke (46 percent), islet cell transplantation (36 percent), or quality of care in minority populations (43 percent).The NIH RePORTER provided publications for more than 80 percent of the studies of diagnosis and treatments for acute stroke (87 percent) and islet cell transplantation (83 percent). The publication rate in the NIH RePORTER was lowest for quality of care in minority populations (50 percent). The NIH RePORTER lists all publications where the grant number was mentioned. Many of the publications do not appear to be directly related.

Figure 1. Proportion of relevant studies (registered in ClinicalTrials.gov) published in peer-reviewed journals

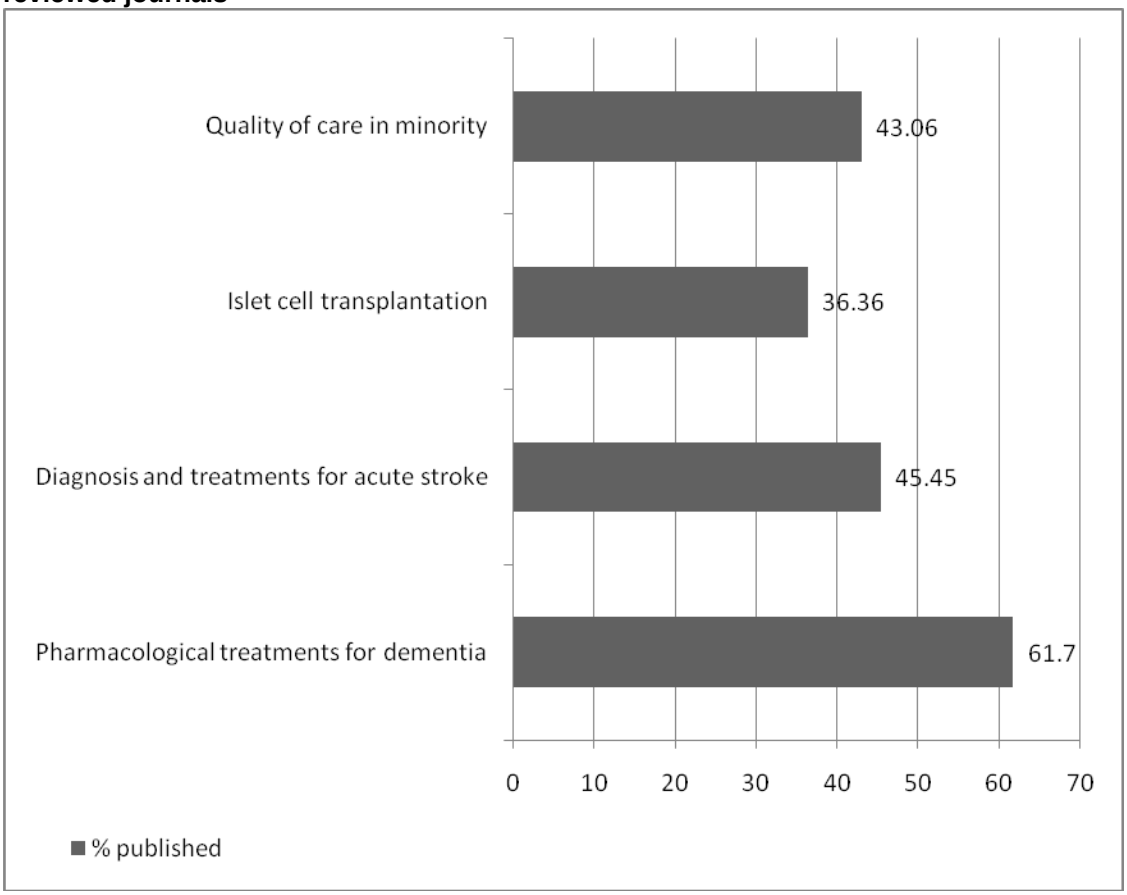
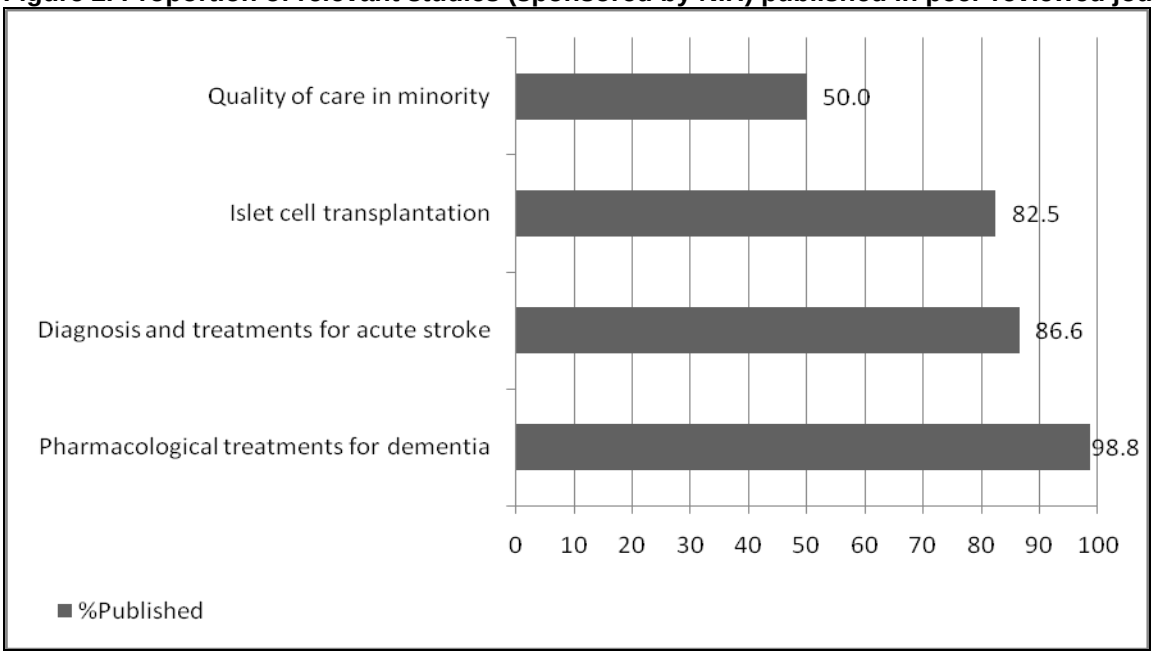


Figure 2. Proportion of relevant studies (sponsored by NIH) published in peer-reviewed journals



Characteristics of Ongoing Registered Studies

We also examined the characteristics of the registered ongoing studies relevant for the four selected topics. The majority of ongoing studies recruited both sexes. Recruitment of age subgroups depended solely on the topic. The majority of ongoing studies we identified for the four topics we evaluated recruited adults or seniors. Inclusion of age subgroups depended on the research topic.

The majority of registered ongoing studies were interventions. However, observational design was used in 24 percent of ongoing studies of quality of care improvement in minorities. Study design of the studies identified in the NIH RePORTER was difficult to judge because the database does not provide detailed information about study characteristics. More than 80 percent of registered ongoing studies across all four topics posted changes to study protocols. A judgment about the significance of the impact of such changes on the results of the studies was difficult to determine without a time consuming evaluation of archived records for each change and for each study. This was considered beyond the scope of the current research. Less than 5 percent of the ongoing studies across the four topics had the results posted in ClinicalTrials.gov. As we noted before, publication rates of registered studies differed slightly across the four topics. We compared publication status among topics and sponsorship category for the four selected EPC report topics (Table 4). Publication rates varied across topics and by sponsorship category within topics.

The NIH RePORTER provides complete information about NIH grants but very few details about study design and protocols. Completeness rates were high for all topics. When we compared publication status of the studies that were relevant to different topics, we found out that publications seemed to vary depending on the topic and on the registration status. Publication rates were higher among the studies found in NIH RePORTER than those found in ClinicalTrials.gov. The NIH RePORTER lists all publications that mention the particular grant or funded study. However, in our examination these listed publications frequently did not report results from the particular ongoing study from which the link was obtained. For instance, the funded study aimed to test treatment effects, but linked publications did not report the results of the tested hypothesis.

Nearly half of registered studies did not appear to be published at the time of our search. Ongoing studies that focused on subpopulations seemed to be published less often. Sponsor factors seemed most obviously associated with the publication of the study results.

Table 4. Summary tables. Distribution of publication status by study topic and sponsor

Study Topic and Sponsorship	Not Published	Published	% Published in Peer Reviewed Journals
Pharmacological Treatments for Dementia			
Total Ongoing Studies	18	29	62
By source of Funding*			
Federal Government	7	20	74
Nongovernment, nonprofit	0	3	100
Industry	11	6	35
Acute Stroke: Evaluation and Treatment			
Total Ongoing Studies	24	20	45
By Source of Funding			
Federal Government	4	4	50
Nongovernment, nonprofit	9	5	36
Industry	11	11	50
Islet Transplantation in Patients with Type 1 Diabetes Mellitus			
Total Ongoing Studies	13	8	38
By Source of Funding			
Federal Government	1	2	67
Nongovernment, nonprofit	9	6	40
Industry	3	0	0
Strategies for Improving Minority Healthcare Quality			
Total Ongoing Studies	41	31	43
By Source of Funding			
Federal Government	23	24	51
Nongovernment, nonprofit	15	7	32
Industry	3	0	0

* Source of funding was downloaded from ClinicalTrials.gov

Chapter 4. Discussion

The objective of this methods project was to assess the sources and strategies for finding ongoing studies relevant to the identified research gaps in EPC reports. We identified several sources that can be useful in identifying ongoing studies. For finding ongoing clinical trials, ClinicalTrials.gov offers a fairly comprehensive registry of clinical trials, is relatively easy to use, and provides sufficient data about trials from which to estimate study quality. Results of a study by Moja et al. (2009) support the EPC staff assessments that ClinicalTrials.gov provides a sufficient amount of data to adequately describe the ongoing research.[9] Moja et al. found that ClinicalTrials.gov was one of only three registries that complied with the WHO minimum data set for trial reporting. Clearly, this resource is the most valuable to finding ongoing clinical trials. One downside is that solely using ClinicalTrials.gov could miss important trials of interventions that are not marketed in the United States. Fortunately, a convenient resource exists to perform federated searches of multiple clinical trials registries—the ICTRP. Because the ICTRP is frequently updated and can be searched to find trials in several countries, it is a very valuable source for finding ongoing clinical studies. Yield of additional registered clinical trials beyond those found in these two trials sources is likely to be low.

Searching ClinicalTrials.gov and the ICTRP is likely valuable to all EPC reports on clinical interventions. There may be special circumstances where utilizing other sources may be warranted. For instance, it may be worthwhile to search pharmaceutical company registries when studying a new drug developed by certain manufacturers. In this case, researchers may want to supplement the above sources by adding searches in industry registries. Leads to appropriate grey literature sources are best identified with assistance from content experts representing the full range of stakeholders to the topic.

Funded research databases are useful in finding ongoing studies that are observational or address health services research topics. In these cases, it seems reasonable to check the NIH RePORTER, HSRProj, and/or AHRQ GOLD, depending upon which seems most important to the topic at hand. These sources should be supplemented by targeted searches of the grey literature.

Our brief comparison of the major trial registries and a major funded research database demonstrated that publication rates appear to be higher for ongoing studies identified through the NIH RePORTER than those identified in ClinicalTrials.gov. This could be an indication that federally sponsored research may be more likely to result in publication as opposed to studies published by any sponsor identified in ClinicalTrials.gov. However, this finding could also have implications relevant to study designs as well. We identified one other potentially misleading data element in reviewing these sources. This includes our observation that the publications listed in ClinicalTrials.gov and especially the NIH RePORTER frequently did not always report the results from the ongoing study description for which they were listed. This was confusing and extends screening time to insure that publications listed are truly relevant to the EPC report. One other observation included that nearly half of studies identified in ClinicalTrials.gov did not appear to be published according to our search results. This observation is consistent with previous research. Our examination seemed to indicate that of the factors we examined, topic and sponsor factors were most obviously associated with publication of results.

This study was largely qualitative and suffers from several limitations. Being qualitative, generalizability to other topics and time frames is not possible. This lack of generalizability is demonstrated by the wide variability across our four topics. Additionally, the time frame

examined in this project is at an early stage when trial registration was just beginning to rise. We were constrained to this time frame because when following studies forward, a long followup period is necessary between subject enrollment and publication of study results. We expect time frames after those selected for this project to offer improved reporting of ongoing studies and potentially improved publication rates. There is little research on finding ongoing studies, and it is a topic undergoing rapid change. Additionally, we obtained input from only eight individuals with expertise in the area of finding ongoing studies. Opinions about individual databases were sometimes only informed by one or two questionnaire respondents that had experience with the source. Results should be interpreted as an examination of four topics for one time period, a time period that hopefully provides a fairly pessimistic study of registration, reporting, and identification ongoing studies.

Other limitations to the comprehensiveness of this project should also be recognized. Because Clinicaltrials.gov and the ICTRP were identified as the highest priority sources for identifying ongoing trials, we did not analyze other trial registries. We did not analyze the importance of the posted changes in the protocols in relation to study completeness and publication of the results. We did not conduct a comprehensive search of all abstracts that were presented in the meetings. We did not search for the results of unpublished registered studies on the FDA Web site. Nevertheless, our analyses indicated a substantial difference in publication rates across different topics.

Having the information about current ongoing trials in hand is only part of the process of refining the future research needs discussion of EPC reports. The true potential these studies have to fill a particular research gap rests with the quality of the completed published study or completed study results posted to a trials registry. Therefore, a listing of ongoing studies is incomplete without some assessment of how likely these ongoing studies are to fill the identified gaps. At this point, we have little certainty that the ongoing studies identified will be published in a manner consistent with the published protocols. An improved understanding of this for the EPC topic can assist in determining level of resources to invest in these activities. Aside from the positive trend toward publication of federally funded research when compared to industry funded research and more confidence in topics with several studies as opposed to just one, our research sheds little light on this issue. The authors of evidence-based reports have to list future research needs based upon available evidence and describe the current research in process that may assist in filling those needs. A coherent synthesis of existing and expected evidence should result in a greater understanding of future research needs and the priorities among those needs.

Chapter 5. Conclusion

Searching for ongoing studies in relevant information sources and screening those results for relevance to an identified research gap is a time consuming process. Because it appears that there is little certainty that identified ongoing studies will be conducted and completed in a manner that contributes useful evidence, searching for ongoing studies may not warrant a significant investment of resources. However, the identification of ongoing studies is valuable in helping to prioritize identified research gaps. Research gaps for which there exist many large federally funded studies may not be as important as research gaps where there are few industry sponsored studies. This information is also valuable in determining timelines for updating reports and provides a listing of studies that should be watched by topic stakeholders. Searching for ongoing studies as efficiently as possible is important. To do this, the highest priority should be to first search those sources that are likely to provide the largest yield and provide a sufficient amount of data on ongoing studies in the most useable way. For this reason, we recommend first using ClinicalTrials.gov and supplementing that data identified and downloaded from this source with a search of the ICTRP.

Efficiently searching for ongoing studies regarding health services research topics or for observational studies is not as straightforward. However, a strategy of selecting one or two general sources of funded research (NIH RePORTER, HSRProj, AHRQ GOLD) supplemented by topic-specific grey literature searches is likely the best method of finding ongoing studies for these topics. Guidance in identifying subject-specific sources should be obtained by reviewing websites of sponsors of similar funded research or via sources identified by content experts affiliated with the project.

And finally, when addressing the ongoing studies relevant to EPC reports it is also important that caveats regarding the potential of these ongoing studies to fill the research gap be addressed. The extent of protocol changes and low publication rates for registered studies indicates that ongoing studies should be watched for completion and publication or results posted to the registry (as is now required by law) and not relied upon to fill a research gap. We have even less information about which to base reliance on ongoing health services research or observational studies to eventually fill research gaps. Therefore, staying abreast of research regarding ongoing studies is another important activity to EPC practice.

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Acronyms and Abbreviations

AHRQ	Agency for Healthcare Research and Quality
CITR	Collaborative Islet Transplant Registry
CSA	Cambridge Scientific Abstracts
CTR	Clinical Trials Registry
EPC	Evidence-based Practice Center
FDAAA	Food and Drug Administration Amendments Act
FDAMA	Food and Drug Administration Modernization Act
FDO	Foundation Directory Online
ICMJE	International Committee of Medical Journal Editors
IFPMA	International Federation of Pharmaceutical Manufacturers Association
ICTRP	International Clinical Trials Registry Platform
ISRCTN	International Standard Randomised Controlled Trial Number
mRCT	metaRegister of Controlled Trials
NIH	National Institutes of Health
PhRMA	Pharmaceutical Research and Manufacturers of America
RePORTER	Research Portfolio Online Reporting Tool
WHO	World Health Organization

Appendix A. EPC Librarian Questionnaire

1. Please take a few minutes to provide your expertise and guidance about identifying ongoing studies while working with the Evidence-based Practice Center program at your institution.

Please mark the extent to which you agree or disagree with the following statements:

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
I regularly search for ongoing studies when assisting in the completion of reports for the Evidence-based Practice Center.					
I typically use several sources when searching for ongoing studies.					
My searches for ongoing studies usually include searching clinical trials registries.					
My searches for ongoing studies usually include searching grey literature.					
My searches for ongoing studies usually include searching databases and/or websites that list funded research.					

2. The World Health Organization (WHO) compiles data from multiple registries with the International Clinical Trials Registry Platform (ICTRP) at http://www.who.int/ictrp/en /. Do you use the ICTRP to identify ongoing studies?
    i. Always (Go to 2a)
    ii. Sometimes (Go to 2a)
    iii. Never (Go to 3)

    2a. Please mark your level of agreement or disagreement with the following statements regarding the WHO International Clinical Trials Registry Platform (ICTRP):

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
It is easy to use.					
It provides adequate instructions to assist in searching.					
The data provided about the ongoing studies are sufficient to gain a basic understanding of the research underway.					
It appears to provide a comprehensive listing of studies					

3. The International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) Clinical Trials Portal at http://clinicaltrials.ifpma.org/no_cache/en/myportal/ also compiles data from multiple registries, including registries of member pharmaceutical companies. Do you use the IFPMA Clinical Trials Portal to identify ongoing studies?
    i. Always (Go to 3a)
    ii. Sometimes (Go to 3a)
    iii. Never (Go to 4)

3a. Please respond to the following statements regarding using the IFPMA Clinical Trials Portal to identify ongoing studies:

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
It is easy to use.					
It provides adequate instructions to assist in searching.					
The data provided about the ongoing studies are sufficient to gain a basic understanding of the research underway.					
It appears to provide a comprehensive listing of studies.					

4. ClinicalTrials.gov is a clinical trials registry maintained by the U.S. National Institutes of Health. Do you use ClinicalTrials.gov to search for ongoing studies?
    i. Always (Go to 4a)
    ii. Sometimes (Go to 4a)
    iii. Never (Go to 5)

4a. Please mark your level of agreement or disagreement with the following statements regarding ClinicalTrials.gov:

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
It is easy to use.					
It provides adequate instructions to assist in searching.					
The data provided about the ongoing studies are sufficient to gain a basic understanding of the research underway.					
It appears to provide a comprehensive listing of studies					

5. Governments other than the United States maintain clinical trials registries (i.e., the Australian New Zealand Clinical Trials Registry). Do you ever use an online government-sponsored clinical trials registry other than clinicaltrials.gov to identify ongoing studies?
    i. Always (Go to 5a)
    ii. Sometimes (Go to 5a)
    iii. Never (Go to 6)

5a. Other than registries maintained by United States government agencies, please list registries maintained by other governments that you have used to identify ongoing studies (i.e. Australian New Zealand Clinical Trials Registry, German Clinical Trials Register):

5b. Why did you choose to use this/these particular registry/ies?

6. Professional organizations and specific government agencies sometimes create disease-specific clinical trials registries (i.e., Stroke Trials Directory or the registry that is part of the National Cancer Institute's Physician Data Query). Do you use a disease-specific clinical trials registry to identify ongoing studies?
    i. Always (Go to 6a)
    ii. Sometimes (Go to 6a)
    iii. Never (Go to 7)

6a. Please list any disease-specific registries that you have used to identify ongoing studies:

1._____
2._____
3._____

6b. Why did you choose to use this/these particular registry/ies?

7. Current Controlled Trials (http://www.controlled-trials.com) is a clinical trials registry maintained by a publishing house. Do you use this registry to identify ongoing studies?
   i. Always (Go to 7a)
   ii. Sometimes (Go to 7a)
   iii. Never (Go to 8)

7a. Please mark your level of agreement or disagreement with the following statements regarding Current Controlled Trials:

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
It is easy to use.					
It provides adequate instructions to assist in searching.					
The data provided about the ongoing studies are sufficient to gain a basic understanding of the research underway.					
It appears to provide a comprehensive listing of studies					

8. Universities, hospitals and medical centers often create registries of their institutions' clinical trials. Do you use university, hospital or medical center registries to identify ongoing studies?
   i. Always (Go to 8a)
   ii. Sometimes (Go to 8a)
   iii. Never (Go to 9)

8a. Please list any academic institution or health center registries that you have used to identify ongoing studies:

1._____
2._____
3._____

8b. Why did you choose to use this/these particular registry/ies?

9. Pharmaceutical companies often create registries of their company's clinical trials. Do you use pharmaceutical company registries to identify ongoing studies?
   i. Always (Go to 9a)
   ii. Sometimes (Go to 9a)
   iii. Never (Go to 10)

9a. Please list any pharmaceutical company registries that you have used to identify ongoing studies:

1._____
2._____
3._____

9b. Why did you choose to use this/these particular registry/ies?

10. Pharmaceutical Researchers and Manufacturers of America (PhRMA) Clinical Study Results Database (http://www.clinicaltrialresults.org) was one of the first registries to allow clinical trials results to be registered. Do you use the PhRMA Clinical Study Results Database to identify ongoing studies?
    i. Always (Go to 10a)
    ii. Sometimes (Go to 10a)
    iii. Never (Go to 11)

10a. Please mark your level of agreement or disagreement with the following statements regarding PhRMA Clinical Study Results Database:

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
It is easy to use.					
It provides adequate instructions to assist in searching.					
The data provided about the ongoing studies are sufficient to gain a basic understanding of the research underway.					
It appears to provide a comprehensive listing of studies.					

11. The National Library of Medicine maintains the Health Services Research Projects in Progress (HSRProj) database at http://wwwcf.nlm.nih.gov/hsr_project/home_proj.cfm to provide information about ongoing studies in health services research. Do you use HSRProj to identify ongoing studies?
    i. Always (Go to 11a)
    ii. Sometimes (Go to 11a)
    iii. Never (Go to 12)

11a. Please mark your level of agreement or disagreement with the following statements regarding Health Services Research Projects in Progress (HSRProj):

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
It is easy to use.					
It provides adequate instructions to assist in searching.					
The data provided about the ongoing studies are sufficient to gain a basic understanding of the research underway.					
It appears to provide a comprehensive listing of studies.					

12. The National Institutes of Health maintains the Research Portfolio Online Reporting Tools (RePORT) database at http://report.nih.gov/ to provide information about funded research and other federal health-related activities. Do you use RePORT to identify ongoing studies?
    i. Always (Go to 12a)
    ii. Sometimes (Go to 12a)
    iii. Never(Go to 13)

    12a. Please mark your level of agreement or disagreement with the following statements regarding RePORT:

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
It is easy to use.					
It provides adequate instructions to assist in searching.					
The data provided about the ongoing studies are sufficient to gain a basic understanding of the research underway.					
It appears to provide a comprehensive listing of studies.					

13. The Agency for Healthcare Research and Quality maintains a database of their projects called AHRQ Grants On-Line Database (GOLD) at http://gold.ahrq.gov/projectsearch/ to provide information about funded research and other federal health-related activities. Do you use AHRQ GOLD to identify ongoing studies?
    i. Always (Go to 13a)
    ii. Sometimes (Go to 13a)
    iii. Never (Go to 14)

    13a. Please respond to the following statements regarding using AHRQ GOLD:

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
It is easy to use.					
It provides adequate instructions to assist in searching.					
The data provided about the ongoing studies are sufficient to gain a basic understanding of the research underway.					
It appears to provide a comprehensive listing of studies					

14. Specific foundations or other not-for-profit organizations, such as the Robert Wood Johnson Foundation, often provide information on research they have funded. Do you use a foundation or other not-for-profit's website to identify ongoing studies?
    i. Always (Go to 14a)
    ii. Sometimes(Go to 14a)
    iii. Never(Go to 15)

    14a. Please list the specific non-governmental funding organization websites you have used to identify ongoing research.
    1._____
    2._____
    3._____

14b. Why did you choose to use this/these particular registry/ies?

15. Please describe your general approach to searching the grey literature (reports and literature other than that published in journals indexed by bibliographic databases) to identify ongoing studies.

16. In searching the grey literature to identify ongoing studies, please describe the sources you use most often and why.

17. Please list any other resources that you use to identify ongoing studies, studies currently in progress, or studies completed but not yet published.

18. Please provide any other information and/or comments regarding identifying ongoing studies here.

Thank you for your time!

Appendix B. EPC Reports Published in 2004/2005

Table B1. Research gaps and ongoing studies in completed evidence-based reports

Study Name	Institution	Includes Future Research Recommen-dations	Format (Narrative, List, etc.)	Notes	Number of Ongoing Studies: Clinicaltrials.gov	Number of Ongoing Studies: Other Sources
Likely to have clinical trials						
Effectiveness of Portable Monitoring Devices for Diagnosing Obstructive Sleep Apnea: Update of a Systematic Review http://www.cms.gov/determinationprocess/downloads/id24TA.pdf	RTI International–University of North Carolina	No	No	Year: 2005	**0**	**0**
RANDOMIZED TRIALS OF SECONDARY PREVENTION PROGRAMS IN CORONARY ARTERY DISEASE: A SYSTEMATIC http://www.cms.gov/determinationprocess/downloads/id31TA.pdf	the University of Alberta Evidence-based Practice Center	Yes	Narrative in Discussion	Year: 2005	**5**	**0**
Usual Care in the Management of Chronic Wounds http://www.cms.gov/determinationprocess/downloads/id37TA.pdf	Tufts-New England Medical Center EPC	No	No	Year: 2005	**3**	**4**
Effectiveness of Antimicrobial Adjuncts to Scaling and Root-Planing Therapy for Periodontitis http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta88	RTI International–University of North Carolina	Yes	Narrative	Separate chapter of future research	1	1
Health Effects of Omega-3 Fatty Acids on Lipids and Glycemic Control in Type II Diabetes and the Metabolic Syndrome and on Inflammatory Bowel Disease, Rheumatoid Arthritis, Renal Disease, Systemic Lupus Erythematosus and Osteoporosis http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta89	Southern California/RAND	Yes	List	Year: 2004	5	1
Health Effects of Omega-3 Fatty Acids on Asthma http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta91	University of Ottawa	Yes	Narrative	Research Implications and Possibilities Year: 2004	0	1
Health Effects of Omega-3 Fatty Acids on Arrhythmogenic Mechanisms in Animal and Isolated Organ/Cell Culture Studies http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta92	Tufts-New England Medical Center	Yes	Tables and narrative	Year: 2004	0	0
Effects of Omega-3 Fatty Acids on Cardiovascular Risk Factors and Intermediate Markers of Cardiovascular Disease http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta93	Tufts-New England Medical Center	Yes	List	Year: March 2004	4	1

Table B1. Research gaps and ongoing studies in completed evidence-based reports (continued)

Study Name	Institution	Includes Future Research Recommen-dations	Format (Narrative, List, etc.)	Notes	Number of Ongoing Studies: Clinicaltrials.gov	Number of Ongoing Studies: Other Sources
Health Effects of Omega-3 Fatty Acids on Cardiovascular Disease http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta94	Tufts-New England Medical Center	Yes	List	Year: March 2004	2	1
Pharmacological Treatment of Dementia http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=hserta&part=A140440#A140514	McMaster University	Yes	List		13	10
Islet Transplantation in Patients with Type 1 Diabetes Mellitus http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=hserta&part=A148269	Blue Cross and Blue Shield	Yes	Reports from the Collaborative Islet Transplant Registry (CITR) are expected to be available in the near future.	Discussion includes mention of "uncertainties" that remain, but no explicit research recommenda-tions	5	9
Economic Incentives for Preventive Care http://www.ahrq.gov/clinic/tp/ecinctp.htm	University of Minnesota	Yes	Narrative	Year: August 2004	0	0
Effectiveness of Behavioral Interventions to Modify Physical Activity Behaviors in General Populations and Cancer Patients and Survivors	University of Minnesota	Yes	Narrative	"Future Direction"	3	14
Pharmacological and Surgical Treatment of Obesity	Southern California-RAND	Yes	Narrative		4	15
Celiac Disease http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta104	University of Ottawa	Yes	Narrative	Year: September 2004	1	4

Table B1. Research gaps and ongoing studies in completed evidence-based reports (continued)

Study Name	Institution	Includes Future Research Recommen-dations	Format (Narrative, List, etc.)	Notes	Number of Ongoing Studies: Clinicaltrials.gov	Number of Ongoing Studies: Other Sources
Cardiac Resynchronization Therapy for Congestive Heart Failure	University of Alberta	see note		Conclusion notes: "a marked paucity of data exists for the efficacy and complication rates with CRT devices beyond one year"—presumably a possibility for future research	0	1
Preventing Violence and Related Health-Risking Social Behaviors in Adolescents http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta107	Southern California Evidence-based Practice Center	Yes	Narrative	Future research opportunities was one of the Key Questions Year: October 2004	2	10
Melatonin for Treatment of Sleep Disorders http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta108	University of Alberta	Yes	Narrative	Year: November 2004	3	
Wound-Healing Technologies: Low-Level Laser and Vacuum-Assisted Closure	Blue Cross and Blue Shield	Yes	Narrative		0	0
Effects of Omega-3 Fatty Acids on Cancer http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta113	Southern California/RAND	Yes	Narrative	Year: February 2005	2	0
Effects of Omega-3 Fatty Acids on Cognitive Function with Aging, Dementia, and Neurological Diseases http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta114	Southern California/RAND	Yes	List	Year: February 2005	1	2

Table B1. Research gaps and ongoing studies in completed evidence-based reports (continued)

Study Name	Institution	Includes Future Research Recommen-dations	Format (Narrative, List, etc.)	Notes	Number of Ongoing Studies: Clinicaltrials.gov	Number of Ongoing Studies: Other Sources
Effects of Omega-3 Fatty Acids on Organ Transplantation http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta115	Tufts-New England Medical Center	Yes	List	Year: February 2005	0	0
Effects of Omega-3 Fatty Acids on Mental Health http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta116	University of Ottawa	Yes	Narrative	Research Implications and Directions" Year: July 2005	5	4
Effects of Omega-3 Fatty Acids on Eye Health http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta117	University of Ottawa	Yes	Narrative	"Research Implications and Directions" Year: July 2005	1	2
Effects of Omega-3 Fatty Acids on Child and Maternal Health http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta118	University of Ottawa	Yes	Narrative	"Research Implications and Directions" Year: August 2005	0	0
Management of Menopause-Related Symptoms http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta120	Oregon Health & Science University	Yes	Narrative	Roughly 1 sentence on future research per Key Question in "discussion" section Year: March 2005	9	5
Use of Spirometry for Case Finding, Diagnosis, and Management of Chronic Obstructive Pulmonary Disease (COPD) http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta121	University of Minnesota	Yes	List	Year: September 2005	2	0

Table B1. Research gaps and ongoing studies in completed evidence-based reports (continued)

Study Name	Institution	Includes Future Research Recommen-dations	Format (Narrative, List, etc.)	Notes	Number of Ongoing Studies: Clinicaltrials.gov	Number of Ongoing Studies: Other Sources
Post-Myocardial Infarction Depression http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta123	Johns Hopkins University	Yes	Narrative	One paragraph per Key Question Year: May 2005	2	5
Manifestations and Management of Chronic Insomnia in Adults http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta125	University of Alberta	Yes	Narrative	"Limitations of the Review and Future Research" Year: June 2005	2	2
Acute Stroke: Evaluation and Treatment http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta127	University of Ottawa	Yes	Narrative	"Research and Clinical Implications" Year: July 2005	7	2
Diagnosis, Prognosis, and Therapy of Impaired Glucose Tolerance and Impaired Fasting Glucose http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta128	McMaster University	Yes	Narrative	Year: September 2005	6	2
Diagnosis and Management of Work-Related Asthma	University of Alberta	Yes	List		1	4
Percutaneous Myocardial Laser Revascularization and Transmyocardial Laser Revascularization http://www.cms.gov/DeterminationProcess/downloads/id125.pdf	Duke Center for Clinical Health Policy Research and Evidence-based Practice Center	No	No	Year: 2004	**1**	**2**
May have clinical trials						
Strategies for Improving Minority Healthcare Quality http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta90	Johns Hopkins University	Yes	List	Year: January 2005	4	4
The Use of Episiotomy in Obstetrical Care: A Systematic Review	RTI International-University of North Carolina	Yes	Narrative		1	0

Table B1. Research gaps and ongoing studies in completed evidence-based reports (continued)

Study Name	Institution	Includes Future Research Recommen-dations	Format (Narrative, List, etc.)	Notes	Number of Ongoing Studies: Clinicaltrials.gov	Number of Ongoing Studies: Other Sources
Update on Acute Bacterial Rhinosinusitis http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta124	Tufts-New England Medical Center	Yes	Narrative	Year: June 2005	0	0
Effects of Soy on Health Outcomes http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta126	Tufts-New England Medical Center	Yes	Narrative	Year: August 2005	16	19
Gastroesophageal Reflux Disease, Management Strategies (December 2005) http://effectivehealthcare.ahrq.gov/ehc/products/1/42/GERDExecSum.pdf	Tufts-New England Medical Center EPC	Yes	December 2005, Remaining issues	Year: December 2005	**2**	**0**
Unlikely to have clinical trials						
Literacy and Health Outcomes http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta87	RTI International–University of North Carolina	Yes	Narrative	Year: January 2004	1	18
Training of Hospital Staff to Respond to a Mass Casualty Incident http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta95	JHU EPC/ Johns Hopkins University Bloomberg School of Public Health	Yes	Narrative	Year: July 2004	0	1
Regionalization of Bioterrorism Preparedness and Response http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta96	Stanford–UCSF	Yes	Narrative	Year: April 2004	0	0
Community-Based Participatory Research http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta99	RTI International-University of North Carolina	Yes	Narrative	Notes that several studies are upcoming (as of publication date) Year: July 2004	0	0
Criteria to Determine Disability Related to Multiple Sclerosis http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta100	Duke	Yes	Narrative	Year: May 2004	1	21

Table B1. Research gaps and ongoing studies in completed evidence-based reports (continued)

Study Name	Institution	Includes Future Research Recommen-dations	Format (Narrative, List, etc.)	Notes	Number of Ongoing Studies: Clinicaltrials.gov	Number of Ongoing Studies: Other Sources
Measuring the Quality of Breast Cancer Care in Women http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta105	University of Ottawa	Yes	Narrative	Refers to key upcoming study from ASCO Year: October 2004	0	14
Sexuality and Reproductive Health Following Spinal Cord Injury http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta109	University of Ottawa	Yes	Narrative	"Research and Clinical Implications" Year: November 2004	1	2
End-of-Life Care and Outcomes http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta110	Southern California-RAND	Yes	Narrative with 12 "Considera-tions" highlighted	Year: December 2004	1	0
Perinatal Depression: Prevalence, Screening Accuracy, and Screening Outcomes http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta119	RTI-University of North Carolina	Yes	Narrative	Year: February 2005	0	6
Knowledge and Access to Information on Recruitment of Underrepresented Populations to Cancer Clinical Trials http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=erta122	JHU EPC / Johns Hopkins University Bloomberg School of Public Health	Yes	List	Recommen-dations and Research Opportunities" Year: June 2005	1	0

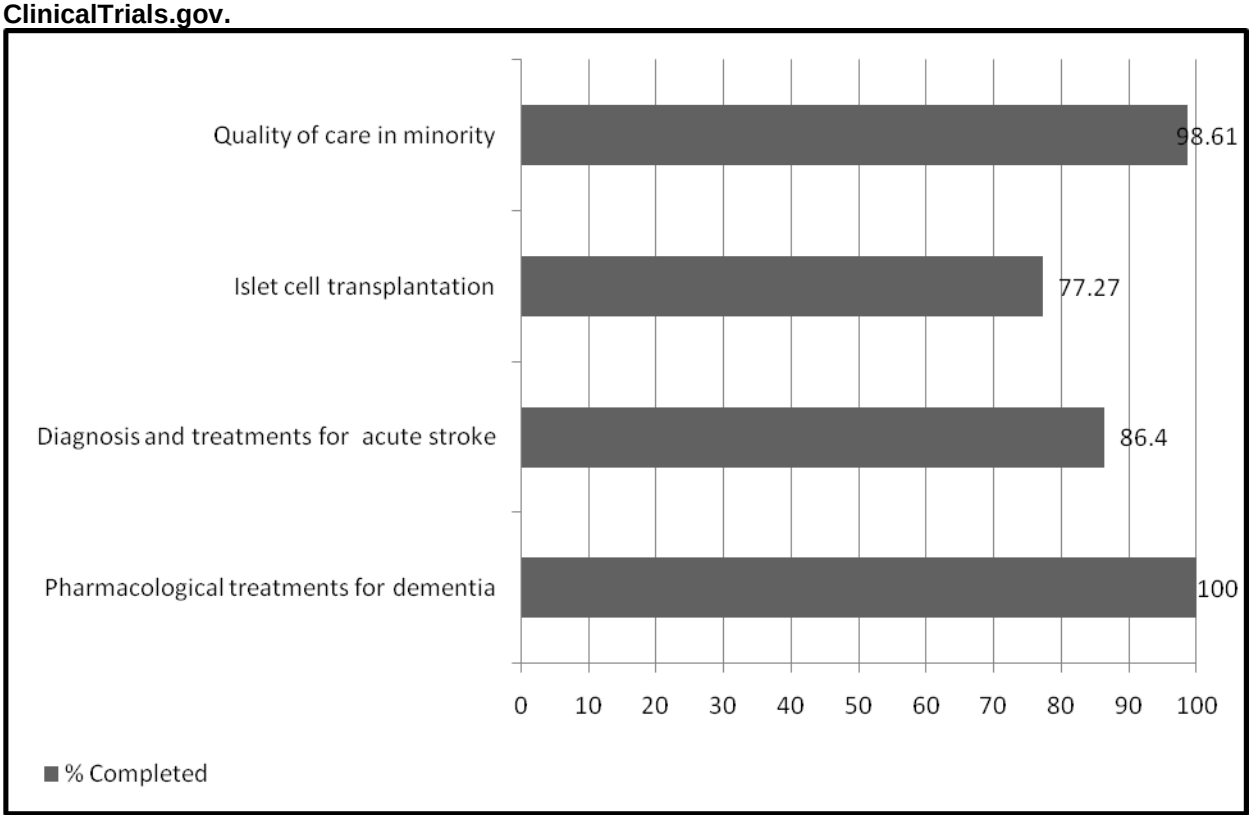
Appendix C. Sources for Finding Ongoing Studies

Source for finding ongoing studies Web address
Portals
WHO International Clinical Trials Registry Platform (ICTRP) Search Portal http://apps.who.int/trialsearch
IFPMA Clinical Trials Portal http://clinicaltrials.ifpma.org
mRCT http://www.controlled-trials.com
TrialsCentral http://www.trialscentral.org Not an authoritative site
Centerwatch http://www.centerwatch.com/
International and National
ClinicalTrials.gov http://clinicaltrials.gov
ISRCTN *Current Controlled Trials* http://www.controlled-trials.com
Australian New Zealand Clinical Trials Registry http://www.anzctr.org.au
Canada Trials http://www.canadatrials.com/
Chinese Clinical Trial Registry http://www.chictr.org
Clinical Trials Registry – India http://www.ctri.in/Clinicaltrials/index.jsp
German Clinical Trials Register http://www.drks.de
Iranian Registry of Clinical Trials http://www.irct.ir
*Japan Primary Registries Netw*ork http://rctportal.niph.go.jp/link.html
Pan African Clinical Trial Registry http://www.pactr.org
The Netherlands National Trial Register http://www.trialregister.nl
Sri Lanka Clinical Trials Registry http://www.slctr.lk
Industry Clinical Trials
Almirall http://www.almirall.com/webcorp2/cda/ImD_03_02.jsp
Amgen http://www.amgentrials.com/
AstraZeneca http://www.astrazeneca.com/research/our-pipeline-summary/
Bayer HealthCare - Trial Finder http://www.bayerhealthcare.com/scripts/pages/en/research_development/clinical_trials/trial_finder/index.php
Bristol-Myers Squibb http://www.bms.com/research/pipeline/Pages/default.aspx
Genentech http://www.gene.com/gene/pipeline/status/
GlaxoSmithKline http://www.gsk-clinicalstudyregister.com/

Lilly http://www.lillytrials.com/
Merck http://www.merck.com/research/pipeline/home.html?WT.svl=mainnav
Novartis http://www.novartisclinicaltrials.com
Novo Nordisk http://www.novonordisk.com/science/pipeline/rd_pipeline.asp
Roche http://www.roche-trials.com/
Takeda http://www.takeda.com/research/product-pipeline/article_1044.html
Specialty Clinical Trials
AIDS Clinical Trials Group http://www.aactg.org/
Centre for Clinical Trials, Clinical Trials Registry – Chinese University of Hong Kong http://www.cct.cuhk.edu.hk/cctwebsite/Home/tabid/38/Default.aspx
Clinical Trial Registry of the University Medical Center Freiburg http://www.uniklinik-freiburg.de/zks/live/uklregister/Oeffentlich_en.html
European Leukemia Trial Registry http://www.leukemia-net.org/content/e58/e3956/e3957/index_eng.html
German Registry for Somatic Gene-Transfer Trials http://www.dereg.de/dereg_new/dereg_extern/index.faces
Harvard Bipolar Research Program http://www.mainicdepressive.org/currentstudies.php#
National Cancer Institute http://www.cancer.gov/clinicaltrials
North Shore-Long Island Jewish Health System http://www.northshorelij.com/NSLU/Clinical+Trials
PhRMA Clinical Study Results Database http://www.clinicalstudyresults.org/
Stroke Trials Directory http://www.strokecenter.org/trials
University of Alabama Comprehensive Cancer Center http://www2.ccc.uab.edu/CSUWEB/ClinicalTrialsListing.asp
University of California at San Francisco (UCSF) Cancer Center http://medschool.ucsf.edu/clinical_trials/
University of Michigan Clinical Trials https://www.umms.med.umich.edu/engage/disp_pub_condition.do
Winship Cancer Institute of Emory University http://winshipcancer.emory.edu/WinshipContentPage.aspx?nd=759
Health Services Research Ongoing Studies
AHRQ GOLD http://gold.ahrq.gov/projectsearch/
HSRProj (Health Services Research Projects in Progress) http://wwwcf.nlm.nih.gov/hsr_project/home_proj.cfm
NIH REPORT http://report.nih.gov/index.aspx
RWJF http://www.rwjf.org/grants/pg.jsp

Appendix D. Trial Completion by Topic

Figure D1. Proportion of Completed Studies Among All Eligible Studies That Were Registered in ClinicalTrials.gov.



Appendix E. Sponsors of Eligible Ongoing Studies

Table E1. Sponsors of the ongoing studies that were relevant to selected evidence-based reports

Categories	Dementia	Minority	Stroke	Type 1 Diabetes	Total
Total	47	72	44	22	185
National Heart, Lung, and Blood Institute (NHLBI)	0	7	1	0	8
National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)	0	5	0	3	8
National Institute of Mental Health (NIMH)	8	0	0	0	8
National Institute of Neurological Disorders and Stroke (NINDS)	4	1	3	0	8
Department of Veterans Affairs	3	0	2	0	5
National Institute on Aging (NIA)	4	0	0	0	4
Forest Laboratories	2	0	1	0	3
Mount Sinai School of Medicine/Agency for Healthcare Research and Quality (AHRQ)	0	3	0	0	3
National Institutes of Health Clinical Center (CC)	0	2	1	0	3
Novartis	3	0	0	0	3
Astellas Pharma Inc./Astellas Pharma US, Inc.	0	0	2	0	2
Bristol-Myers Squibb	2	0	0	0	2
Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)	0	2	0	0	2
Johnson & Johnson Pharmaceutical Research & Development, L.L.C.	2	0	0	0	2
Johnson & Johnson Pharmaceutical Research & Development, L.L.C./Ortho-McNeil Neurologics, Inc.	2	0	0	0	2
National Cancer Institute (NCI)	0	2	0	0	2
National Center for Complementary and Alternative Medicine (NCCAM)	1	1	0	0	2
National Institute of Environmental Health Sciences (NIEHS)	0	2	0	0	2
National Institute on Aging (NIA)/Alzheimer's Disease Cooperative Study (ADCS)	2	0	0	0	2
National Institute on Drug Abuse (NIDA)	0	2	0	0	2
Ono Pharma	1	0	1	0	2
PAION Deutschland GmbH	0	0	2	0	2
Pfizer	0	0	2	0	2
Sanofi-Aventis	0	0	2	0	2
Transition Therapeutics	0	0	0	2	2
Voyager Pharmaceutical Corporation	2	0	0	0	2
Abbott Vascular	0	0	1	0	1
Agency for Healthcare Research and Quality (AHRQ)	0	1	0	0	1
Alzheimer's Association	1	0	0	0	1
Alzheimer's Disease Cooperative Study (ADCS)/National Institute on Aging (NIA)	1	0	0	0	1
Arkansas Children's Hospital Research Institute	0	1	0	0	1
AstraZeneca	0	0	1	0	1
AVI BioPharma, Inc.	0	0	1	0	1
AZ-VUB/Fund for Scientific Research, Flanders, Belgium/Belgian Government	0	0	0	1	1

Table E1. Sponsors of the ongoing studies that were relevant to selected evidence based reports (continued)

Categories	Dementia	Minority	Stroke	Type 1 Diabetes	Total
AZ-VUB/Vrije Universiteit Brussel/Universitaire Ziekenhuizen Leuven/Universiteit Antwerpen/Erasme University Hospital	0	0	0	1	1
Barts & The London NHS Trust/Asthma UK/Social Action for Health/Department of Health (Service Support)/Noreen Clarke, Professor of Public Health, Michigan University	0	1	0	0	1
Bayer	0	0	1	0	1
Baylor College of Medicine/U.S. Army Medical Research and Materiel Command	0	1	0	0	1
Baylor Research Institute/Baylor University/Diabetes Research Institute, Miami, Florida	0	0	0	1	1
Beth Israel Deaconess Medical Center/Joslin Diabetes Center	0	0	0	1	1
Boston Medical Center	0	1	0	0	1
Bristol-Myers Squibb/Otsuka America Pharmaceutical	1	0	0	0	1
Centers for Disease Control and Prevention/Philadelphia Health Management Corporation	0	1	0	0	1
Centers for Disease Control and Prevention/University of North Carolina	0	1	0	0	1
Children's Hospital Boston	0	1	0	0	1
Complejo Hospitalario Universitario de Albacete/Instituto Ciencias de la Salud, Junta de Comunidades de Castilla-La Mancha	0	0	1	0	1
Danish Heart Foundation/Fonden for Lægevidenskabelig Forskning for Fyns Amt./Novo Nordisk/AJ Andersen og Hustrus Fond/Overlægerådet Legatudvalg/Raimond og Dagmar Ringgård Bohns Fond/Bankdirektør Hans Stener og hustru Agnes Steners legat/Odense University	0	0	1	0	1
Eisai Inc./Pfizer	1	0	0	0	1
Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)/National Institute on Drug Abuse (NIDA)/National Institute of Mental Health (NIMH)/National Institute on Alcohol Abuse and Alcoholism (NIAAA)	0	1	0	0	1
Federico II University/Azienda Ospedaliera \D Cotugno\ Hospital of Infectious Diseases	0	1	0	0	1
Florida International University/Sigma Theta Tau International (Nursing Honor Society)	0	1	0	0	1
Fuzhou General Hospital	0	0	0	1	1
Gates Malaria Partnership/Yunnan Institute	0	1	0	0	1
Global Biotech	0	0	1	0	1
IRCCS San Raffaele/Fondazione Telethon	0	1	0	0	1
IRCCS San Raffaele/PRIN MIUR/Juvenile Diabetes Research Foundation/Telethon-JDRF Center for Beta cell replacement: clinical core.	0	0	0	1	1
Janssen, LP	1	0	0	0	1
John Douglas French Foundation/Institute for the Study of Aging (ISOA)	1	0	0	0	1
Johns Hopkins University/National Institutes of Health (NIH)	0	0	1	0	1
Kaiser Permanente	0	1	0	0	1
Kantonsspital Baden/407 Doctors	0	0	1	0	1
Kantonsspital Baden/RehaClinic Zurzach	0	0	1	0	1
Lawson Health Research Institute/London Health Sciences Centre	0	0	0	1	1
M.D. Anderson Cancer Center	0	1	0	0	1
Mayo Clinic/Aventis Pharmaceuticals	0	1	0	0	1
McMaster University	0	1	0	0	1

Table E1. Sponsors of the ongoing studies that were relevant to selected evidence based reports (continued)

Categories	Dementia	Minority	Stroke	Type 1 Diabetes	Total
Memorial Sloan-Kettering Cancer Center/National Cancer Institute (NCI)	0	1	0	0	1
Memorial Sloan-Kettering Cancer Center/North General Hospital, New York/Ralph Lauren Center for Cancer Care and Prevention	0	1	0	0	1
Mitsubishi Tanabe Pharma Corporation/Kyowa Hakko Kogyo Co., Ltd.	0	0	1	0	1
National Center for Research Resources (NCRR)	0	1	0	0	1
National Center for Research Resources (NCRR)/Alzheimer's Association/Pfizer/Eisai Inc.	1	0	0	0	1
National Center for Research Resources (NCRR)/University of Alabama at Birmingham	0	1	0	0	1
National Human Genome Research Institute (NHGRI)	0	1	0	0	1
National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)	0	1	0	0	1
National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)/National Center for Research Resources (NCRR)/National Institute of Allergy and Infectious Diseases (NIAID)/Eunice Kennedy Shriver National Institute of Child Health and Human Development	0	1	0	0	1
National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)/National Institute of Allergy and Infectious Diseases (NIAID)/National Center on Minority Health and Health Disparities (NCMHD)/National Cancer Institute (NCI)/Hoffmann-La Roche	0	1	0	0	1
National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)/National Institute on Aging (NIA)/Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)/National Center on Minority Health and Health Disparities (NCMHHD)	0	1	0	0	1
National Institute of Neurological Disorders and Stroke (NINDS/Yale University	0	0	1	0	1
National Institute of Nursing Research (NINR)	0	1	0	0	1
National Institute of Nursing Research (NINR)/National Institutes of Health (NIH)	0	1	0	0	1
National Institute on Aging (NIA)/Alzheimer's Disease Cooperative Study (ADCS)/Neuro-Hitech	1	0	0	0	1
National Institute on Aging (NIA)/UCLA Resource Centers for Minority Aging Research/Center for Health Improvement of Minority Elderly (RCMAR/CHIME)	0	1	0	0	1
Novocell/Diabetes & Glandular Disease Research Associates, P.A., San Antonio, TX/CHRISTUS Santa Rosa Healthcare	0	0	0	1	1
Oregon Health and Science University/National Institute on Aging (NIA)/National Center for Complementary and Alternative Medicine (NCCAM)	1	0	0	0	1
Princess Alexandra Hospital, Brisbane, Australia/The Broad Foundation/Townsville Hospital/James Cook University, Queensland, Australia/Walter and Eliza Hall Institute of Medical Research/Queensland Institute of Medical Research	0	1	0	0	1
Pronova Biocare/Danish Heart Foundation/The Danish Kidney Association/North Jutland County	0	0	1	0	1
Royal Perth Hospital/Royal Perth Hospital Medical Research Foundation	0	0	1	0	1
Rush University Medical Center	0	1	0	0	1
Sahlgrenska University Hospital, Sweden/Stockholm South General Hospital/University Hospital Orebro/Norra Alvsborgs Lans Hospital, Trollhattan/Varberg Hospital, Varberg	0	0	1	0	1
Saint Antoine University Hospital/French Cardiology Society	0	0	1	0	1
Sanofi-Aventis/Bristol-Myers Squibb	0	0	1	0	1
Second University of Naples	0	0	1	0	1
Stanford University/Northeastern University	0	1	0	0	1
State University of New York - Upstate Medical University/Bristol-Myers Squibb	0	1	0	0	1

Table E1. Sponsors of the ongoing studies that were relevant to selected evidence based reports (continued)

Categories	Dementia	Minority	Stroke	Type 1 Diabetes	Total
Takeda Global Research & Development Centre (Europe) Ltd./Eli Lilly and Company	0	0	1	0	1
The Cleveland Clinic/Sanofi-Aventis	0	0	1	0	1
The Shiley Family Trust/Institute for the Study of Aging (ISOA)/University of California, San Diego	1	0	0	0	1
Universidad de Antioquia	0	1	0	0	1
University Hospital, Grenoble	0	0	0	1	1
University Hospital, Lille/Institut National de la Santé Et de la Recherche Médicale, France	0	0	0	1	1
University Hospital, Strasbourg, France	0	0	1	0	1
University Hospital, Toulouse/Ministry of Health, France	0	0	1	0	1
University of Alberta/Juvenile Diabetes Research Foundation	0	0	0	1	1
University of California, Irvine	0	1	0	0	1
University of California, Irvine/Juvenile Diabetes Research Foundation	0	0	0	1	1
University of Connecticut Health Center/Agency for Healthcare Research and Quality (AHRQ)	0	1	0	0	1
University of Glasgow/South Glasgow University Hospitals NHS Trust/The Stroke Association, United Kingdom	0	0	1	0	1
University of Hawaii/National Center on Minority Health and Health Disparities (NCMHD)	0	1	0	0	1
University of L'Aquila	0	1	0	0	1
University of Maryland	0	1	0	0	1
University of Minnesota - Clinical and Translational Science Institute/Hoffmann-La Roche/Juvenile Diabetes Research Foundation	0	0	0	1	1
University of Minnesota - Clinical and Translational Science Institute/Juvenile Diabetes Research Foundation	0	0	0	1	1
University of Minnesota - Clinical and Translational Science Institute/Juvenile Diabetes Research Foundation/National Institutes of Health (NIH)/Novartis	0	0	0	1	1
University of Minnesota - Clinical and Translational Science Institute/National Institutes of Health (NIH)/Juvenile Diabetes Research Foundation	0	0	0	1	1
University of North Carolina/National Institutes of Health (NIH)/Indiana University School of Medicine/Wishard Health Services	0	1	0	0	1
University of Oxford/Sanofi-Aventis/AstraZeneca	0	0	1	0	1
University of Pennsylvania	0	1	0	0	1
University of South Carolina/Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)	0	1	0	0	1
University of Texas Southwestern Medical Center	0	1	0	0	1
University of Tromso/The Research Council of Norway/The Council on Health and Rehabilitation, Norway/The Norwegian Council on Cardiovascular Disease/The Royal Norwegian Ministry of Health/The Norwegian Red Cross/Foundation to Promote Research into Function	0	0	1	0	1
University of Wisconsin, Madison	1	0	0	0	1
University of Zurich/Eli Lilly and Company	0	0	1	0	1
University of Zurich/Schweizerische Herzstiftung/Eli Lilly and Company	0	0	1	0	1
Washington University School of Medicine	0	1	0	0	1
Washington University School of Medicine/National Institute of Environmental Health Sciences	0	1	0	0	1

Table E1. Sponsors of the ongoing studies that were relevant to selected evidence based reports (continued)

Categories	Dementia	Minority	Stroke	Type 1 Diabetes	Total
(NIEHS)					
Weill Medical College of Cornell University	0	0	0	1	1