

Methods Future Research Needs Report
Number 9

Presentation of Future Research Needs



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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.

An important part of evidence reports is to not only synthesize the evidence, but also to identify the gaps in evidence that limited the ability to answer the systematic review questions. AHRQ supports EPCs to work with various stakeholders to identify and prioritize the future research that is needed by decisionmakers. This information is provided for researchers and funders of research in these Future Research Needs papers. These papers are made available for public comment and use and may be revised.

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 evidence reports undergo public comment prior to their release as a final report.

We welcome comments on this Future Research Needs document. 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 email to epc@ahrq.hhs.gov.

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Presentation of Future Research Needs

Structured Abstract

Objective: To recommend a more standardized and systematic approach to presenting and organizing future research needs in Future Research Needs (FRN) documents.

Methods: A workgroup representing five Evidence-based Practice Centers (EPCs) that are engaged in future research needs work reviewed prior effort on this topic and prepared a set of draft recommendations and frameworks, which were circulated to the remaining EPCs. Feedback on the working version was obtained from the EPC program at the May 2011 EPC meeting. All feedback was incorporated into the final report.

Findings: The workgroup developed separate frameworks for methods-related FRN recommendations and topic-specific FRN recommendations. Examples of methods-related issues include design issues, actions that facilitate the aggregation of results, inclusion of multiple disciplinary perspectives, and subgroup analysis. For topic-related FRNs, the PICOTS (Patient, Intervention, Comparator, Outcomes, Timing, and Setting) formulation should be used for each topic. The level of detail in presenting FRN recommendations will vary with the topic. Research in some areas may have sufficiently developed to the point where the gap can be precisely defined. EPCs should exercise judgment in determining the level of detail based on their understanding of the state of the science. The FRN should be presented in tiers rather than as a numerical ranking and should include a clear rationale for prioritization, based on considerations such as societal burden, feasibility, and likelihood of effect. An analytic framework should be used, if possible, and may be adapted. Specific recommendations for research design considerations should be made judiciously and framed as suggestions. Like the description of the future research need, the detail for these research design considerations may vary with the circumstance and topic. The executive summary should include the FRNs with the rationale for prioritization, without the PICOTS or research design considerations.

Contents

Introduction	1
Comparative Effectiveness Research.....	1
Future Research Needs	1
The Future Research Needs Process	2
Scope of This Paper	3
Background and Rationale.....	3
Aims.....	4
Methods	5
Results	6
Background Work.....	6
Review of Initial Eight FRN Reports	6
Panel Statements, NIH Consensus Development Conferences	8
Recommendations	10
General Recommendations	10
FRN Methods Framework	10
FRN Topics Framework	11
Considerations for Research Designs	13
Conclusion	15
References	16
Abbreviations	19
Tables	
Table 1. Potential Issues for Methodological Future Research Needs.....	10
Table 2. Excerpt from “Future Research Needs for Attention Deficit Hyperactivity Disorder”	11
Table 3. Excerpt from “Future Research Needs for Angiotensin-Converting Enzyme Inhibitors (ACEIs), Angiotensin II Receptor Antagonists (ARBs), or Direct Renin Inhibitors (DR) for “Treating Hypertension”	14
Figures	
Figure 1. Flowchart of Future Research Needs Process	2
Figure 2. Analytic Framework from “Future Research Needs to Reduce the Risk of Primary Breast Cancer in Women”	12

Introduction

This methods paper was commissioned by the Agency for Healthcare Research and Quality (AHRQ) as one of a series of papers addressing methods issues in the relatively new area of explicit discussion of future research needs (FRN) as part of comparative effectiveness research (CER). This paper is intended to reflect current and recommended practices for the AHRQ Evidence-based Practice Centers (EPC), but these methods will certainly be refined in the coming years through both the EPC program and related initiatives as envisioned by the Affordable Care Act. Other papers in this methods series on future research needs in comparative effectiveness research may be found on AHRQ's effective health care (EHC) Web site: www.effectivehealthcare.ahrq.gov/futureresearchneedsmethods.cfm.

Comparative Effectiveness Research

CER is the “generation and synthesis of evidence that compares the benefits and harms of alternative methods to prevent, diagnose, treat, and monitor a clinical condition or to improve delivery of care. The purpose of CER is to assist consumers, clinicians, purchasers, and policymakers to make informed decisions that will improve care both at the individual and the population levels.”¹ CER comprises a broad range of activities and types of study, encompassing systematic reviews, secondary data analyses, randomized controlled trials, prospective observational studies, health systems research, and dissemination of results to the public, providers, policymakers, and other key stakeholders. Key components of CER include comparisons between active treatments, policies, or diagnostic strategies with evidence from research conducted in settings similar to those in which most patients with a given condition are treated. The explicit nature of CER is demonstrated by the descriptions of proposed study questions through the PICOTS formalism, in which each Key Question is described using six dimensions: Population; Intervention; Comparator treatment or test; Outcomes assessed; Timeframe; Study setting.²

Future Research Needs

Systematic reviews of focused clinical and policy questions reach conclusions whenever feasible and describe the strength of evidence supporting those conclusions. However, many reviews find only low or moderate strength of evidence to address a given Key Question. Problems are often identified with the amount or quality of the literature examined, leading to an inability to address all of the components of the key study questions to sufficiently address the clinical and policy needs that led to the Key Questions. Gaps in the evidence remain. A common criticism of systematic reviews is that, while they generally contain a section describing the limitations of the research just reviewed, these limitations sections often are very general (e.g., “larger trials are needed”) and provide relatively little guidance to funders or the research community regarding the next study or series of studies needed to advance a given field.³ Yet a key, and to date, underutilized role of the systematic review process is to stimulate new research to address identified gaps in the literature.

With these FRN papers and accompanying methods papers, the AHRQ EPC Program distinguishes between the evidence gaps that are identified from within a systematic review and those that are prioritized and clearly defined as research needs by stakeholders based on their potential impact on practice or care. A more explicit and prioritized listing of research needs,

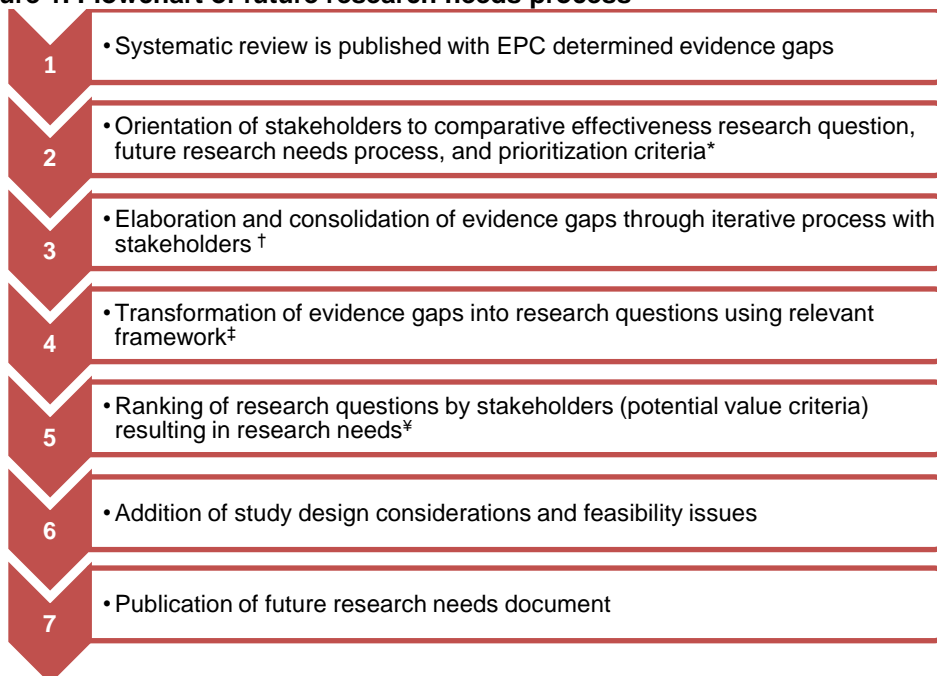
with guidance regarding how to address those needs, could allow the impact of systematic reviews to be more fully realized and increase the pace of research to provide meaningful answers. The audience for future research needs reports includes the research community, funders, policymakers, and advocacy groups. Reducing the time between synthesis of evidence, identification of future research needs, and initiation of studies to address those needs is urgently needed in the current health care environment.

The Future Research Needs Process

In the AHRQ EHC program, FRN documents are derived from systematic reviews of CER questions. The FRN document follows online publication of the systematic review and serves as a standalone document. Figure 1 shows the flow of an FRN project.

Each FRN report begins with identifying a list of evidence gaps from the systematic review (in draft or final form), which may be augmented with input from a multidisciplinary panel of stakeholders familiar with both the research methods and the clinical and policy content of the systematic review. The EPC then works with the stakeholder group to elaborate and consolidate the evidence gaps, taking into consideration any ongoing or planned research that may already be addressing gaps. Potential research questions are then elaborated following the PICOTS framework with the exception of methodological questions, which may be organized differently.⁴ Once the questions have been formalized, they are given a final ranking by the stakeholders according to potential value criteria. The final list of 4–12 high priority Future Research Needs with specific questions, including PICOTS definition (as appropriate) and potential study designs, is published in a final document intended for use by researchers and funders of research.

Figure 1. Flowchart of future research needs process



* May include identification of additional evidence gaps.

† Reduction through topic consolidation, preliminary prioritization, and consideration of ongoing research (duplication criteria).

‡ Evidence gaps that address specific methods issues would not use PICOTS framework

¥ May require iterative steps

Scope of This Paper

This paper is one of a series of papers that provide recommendations and best practices on the steps in identifying and prioritizing Future Research Needs. (This particular paper addresses issues around presenting the findings from an FRN analysis, which are covered in steps 4, 6, and 7. This paper does not address other related issues around determining research gaps, orienting stakeholders to CER questions, FRN process and prioritization criteria, elaboration of evidence gaps, and ranking research needs, within steps 1, 2, 3, and 5, which are covered in related papers.⁵⁻⁷) Other papers that address other steps in the FRN process will be posted as they are completed at www.effectivehealthcare.ahrq.gov/futureresearchneedsmethods.cfm.

Background and Rationale

The goal of the FRN documents is to encourage further research based on the shortcomings identified in the comparative effectiveness (CE) reviews, by extending the discussion raised in those reports. We walk a fine line between stimulating action and appearing overly prescriptive. The question of the “desirable” level of detail in laying out future research needs is related to larger questions of:

- Who is the primary audience for the reports (funding agencies, researchers)?
- Is the prioritization activity a technical exercise in which solutions (highly specified research studies to address research needs) are found?
or
- Are stakeholders engaged in a prioritization activity that leads to insights and broad understanding of research needs?

These questions may also be related to the extent of the evidence base in the underlying field of research. It is possible that fields with a large evidence base are more amenable to focused prioritization efforts that yield highly specified research questions.

Stakeholder perspective offers some clues about which approach (technical or broader insights) may be the most appropriate. In some cases, stakeholders may move the identification to a broader plane than was originally anticipated. For example, the future research needs report on weight gain in pregnancy offered the following narrative: “Stakeholders were reluctant to dictate a specific form of study design because they felt that many of the research areas were at a nascent stage that might benefit from a multiplicity of approaches. In addition, while the group was inspired to map the identified research priorities to study approaches, they were reluctant to specify a single, correct next step. They expressed confidence in the collective energy and creativity of the scientific community, suggesting that agencies and organizations seeking to advance research in this area solicit and amply fund investigator-initiated research rather than prespecifying study designs to answer high priority questions. Likewise there was confidence that robust expertise and appropriate study populations are available to realize answers to the prioritized questions quickly in order to bring practical tools and new knowledge to advancing the care of women and their children.”⁸

Stakeholder reactions varied for other topics. For example, members of the stakeholder panel on treatment for localized prostate cancer⁹ took into account two large, lengthy randomized controlled trials that were then underway and sought to identify potential studies and research designs that could enrich the evidence base while awaiting the results of those trials. They also

shifted the emphasis from specific treatments to determining which patients should be treated and when, because of their concern about substantial overtreatment in this patient population.

In addition to the pilot work in FRN documents, recognizing that this was a new area of work, these eight centers were also engaged in methodological development to provide an underpinning for eventual programmatic guidance. One of these projects was devoted to defining an optimal format for presenting research needs.¹⁰

As a result of these early experiences in piloting approaches to FRN development and prioritization, and exploration of methods, AHRQ has identified the need for program guidance on a structured and consistent method for presenting FRNs. Initial efforts have been made to create guidance, but initial experience has suggested that further refinements are indicated.

Aims

This project explores how recommendations for FRNs beyond the work done in CE reviews can be best organized and presented across a variety of topics. It delineates the elements and presentation that are most helpful in a standalone future research needs document.

In the context of the FRN document, this relates specifically to the way the prioritized list of research needs (the “future research needs”) are presented. Early experience suggests two categories of research gaps, one related to the topic area and another related to methodological issues. This report will inform presentation elements and the level of detail that are appropriate for each.

Methods

A workgroup, with representation across five EPCs currently engaged in FRN work, undertook the task to develop guidance in this area. The workgroup developed drafts and discussed them via conference calls.

To evaluate variation and to identify exemplars, we reviewed the initial set of FRN pilot reports^{8, 9, 11-16} to assess how the research needs were presented. We also reviewed methods papers from the Tufts EPC¹⁰ on defining an optimal framework for presenting research needs, based on systematic review and expert input, and the RTI EPC report¹⁷ on the advantages and disadvantages of different study designs for FRN. The workgroup also scanned relevant sections of panel statements produced by National Institutes of Health (NIH) Consensus Development Conferences,¹⁸⁻²² to assess their level of detail and scope. Other relevant material included an EPC report on the development of a framework for the identification of gaps from systematic reviews.^{5, 23} Lastly, the workgroup reviewed current content guidance for FRN documents, which were initially revised in response to methods work by EPCs in future research needs and consensus by EPCs at the November 2010 EPC meeting.

The workgroup conducted a series of teleconferences to identify preferred strategies and discuss lessons learned. Drafts were reviewed by all members.

The group solicited EPC input from the other EPCs at the May 2011 EPC meeting.

Results

Background Work

The panel built upon a number of earlier efforts.

Review of Initial Eight FRN Reports

Eight EPCs developed pilot FRN documents based on a previously completed AHRQ systematic review. These eight reports were:

- Prioritizing Research Needs in Gestational Diabetes Mellitus (Johns Hopkins University EPC)¹¹
- Integration of Mental Health/Substance Abuse and Primary Care (RTI International—University of North Carolina at Chapel Hill EPC)¹²
- Reducing the Risk of Primary Breast Cancer (Oregon EPC)¹³
- Outcomes of Maternal Weight Gain (Vanderbilt EPC)⁸
- Treatments of Common Hip Fractures (Minnesota EPC)¹⁴
- Clinically Localized Prostate Cancer (Blue Cross and Blue Shield Association Technology Evaluation Center EPC)⁹
- Comparative Effectiveness of Angiotensin Converting Enzyme Inhibitors or Angiotensin II Receptor Blockers Added to Standard Medical Therapy for Treating Stable Ischemic Heart Disease (Duke EPC)¹⁵
- Comparative Effectiveness of Percutaneous Coronary Interventions and Coronary Artery Bypass Grafting for Patients with Coronary Artery Disease (Tufts EPC)¹⁶

Of the initial eight Future Research Needs reports, half followed a broad, conceptual approach to identifying future needs^{8, 13, 14, 16} and the other half used a more focused approach.^{9, 11, 12, 15} The type of approach dictated the type and level of detail provided in laying out future needs. Reports that followed a broad, conceptual approach, specified future research needs at the level of research areas or questions and presented lists of research questions that were sometimes organized as categories. These reports also tended to separate research questions from methodological considerations.

For example, the Vanderbilt EPC⁸ supplemented the gaps identified in the original CE review with additional gaps identified through a horizon scan of literature; they illustrated the content with an annotated causal framework. The Oregon EPC¹³ categorized the research gaps identified in the original CE review according to the most applicable element of the population(s), interventions, comparators, outcomes (PICO) framework. The Tufts EPC¹⁶ expanded the initial list of gaps based on the original CE review and feedback from a group of key informants with additions based on literature search and review of ongoing trials and refined in one-to-one interviews with key informants. They organized into the gaps four thematic areas: comparative effectiveness and safety of PCI (percutaneous coronary intervention) versus CABG (coronary artery bypass graft), role of testing to inform choice of revascularization procedure, methods to enhance patient population, and methods for assessing performance.

Tufts EPC Methods Report

The Tufts EPC methods report¹⁰ on defining an optimal framework for presenting research needs offered a number of recommendations that serve as a jumping off point for the workgroup's deliberations. (We have added some annotations.)

1. Provide succinct yet adequate description of methods and results following guidelines for reporting of health care research (for example, there are reporting guidelines for qualitative research and modeling). Aim for a level of detail similar to that found in papers addressed to a general medical audience.
2. Be cognizant of the importance of the face validity of the process. Justify the selection of the stakeholders who participated in identifying or prioritizing research needs, and be clear on their degree of engagement.
3. Consider reporting the results of the future research needs assessment at two levels of detail. A suggestion would be to first present general areas that merit future research without specifying research designs or specific details on, for example, PICOTS elements. A second set of results could further elaborate on potential research designs, details on PICOTS elements, or other details as applicable.
4. Frame the more specific set of results as "examples" rather than as strict recommendations. (For example, it may be better to avoid specific numerical rankings and cluster recommendations into high and medium categories.)
5. Avoid explicit prioritization of research needs when there are no clear differences in the perceived strength of alternative recommendations, but acknowledge strong beliefs when they exist. Consider a tiered presentation of future research needs by grouping them in thematic entities (after the priorities have been established).
6. Clearly define how "feasibility" of future research was assessed. It may be instructive to perform power analyses for specific research designs for a range of assumptions and compare with the size of existing studies in the field.

RTI EPC Methods Project

The RTI EPC methods project¹⁷ on the advantages and disadvantages of different study designs for FRN discusses the terminology and presentation that could be used in FRN reports to describe study design considerations. The paper outlines common terminology for study designs and criteria for consideration of study designs. These criteria include resource use, size, and duration; availability of data and ability to recruit; ethical, legal and social issues; and advantages of study design for producing a valid result. Points taken from the paper for consideration by the workgroup include:

- Study design consideration comments may assist researchers and funders in determining whether to examine a given research question and guide the resources needed to address the research need. We anticipate that this information will provide a starting point for study planning and stimulate discussion. The FRN documents are intended to stimulate additional discussion among researchers and stakeholders, not truncate debate or planning. We do not intend that the future research considerations be prescriptive or exclude creative study designs or innovative use of existing data for CER.

- The criteria and terminology comments are generic, and will almost certainly need to be modified in a given FRN exercise, given the clinical and policy context of the condition under consideration.
- A degree of flexibility is necessary to apply these guidelines to considerations of study designs for future research needs. The advantages and disadvantages of a study design might change depending on the study question or the setting. The resources required for a study design depend on the intervention proposed. In addition, some study designs could be better suited for certain future research needs than other designs. Considerations should include an understanding of the context of the research including the nature of the factor being investigated and potential utility and quality of the data.

Panel Statements, NIH Consensus Development Conferences

The NIH Consensus Development Program organizes conferences that generate evidence-based consensus statements addressing controversial issues important to health care providers, policymakers, patients, researchers, and the general public. The final key question of each NIH Consensus Development Conference relates to research needs, based on the evidence presented in these conferences. The workgroup scanned the relevant portions of these panel statements.

The scope of questions asked was variable and depended on the state of the science.

Examples include:

- Preventing Alzheimer’s Disease and Cognitive Decline. If recommendations for interventions cannot be made currently, what studies need to be done to provide the quality and strength of evidence necessary to make such recommendations to individuals?¹⁹
- Vaginal Birth After Cesarean: New Insights. What are the critical gaps in the evidence for decisionmaking, and what are the priority investigations needed to address these gaps?²⁰
- Inhaled Nitric Oxide Therapy for Premature Infants. What are the future research directions needed to better understand the risks, benefits, and alternatives to nitric oxide therapy for premature infants who receive respiratory support?¹⁸
- Lactose Intolerance and Health. What are the future research needs for understanding and managing lactose intolerance?²¹
- Enhancing Use and Quality of Colorectal Cancer Screening. What research is needed to make the most progress and have the greatest public health impact in promoting the appropriate use of colorectal cancer screening?²²

The scope, detail, and organization of recommended research directions varied across the panel statements. Methods of presentation included a numerical list, thematic approach, and narrative. Types of identified research needs were both methodological and topical and also included recommendations for infrastructure development as well as basic research in the field. Methods type research needs included use or development of consistent measures, reporting, and study design methodology. Often the description of the research need included a rationale that highlighted the importance of filling the need in terms of a patient outcome. Research design considerations were also frequently included, though the level of detail was also variable. While almost no one advocated a particular research design, many made mention of considerations related to power, subgroups, appropriate comparators, intervention details (timing, dosing, etc.), relevant outcomes, and contextual factors. When research designs were mentioned, they were

frequently presented as an example among other potential approaches. For research designs presented as a recommendation, the panel included a rationale and did not include specifics in terms of sample size or other details.

Recommendations

General Recommendations

The FRN, whether methodological or topic-specific in nature, should be presented as a top tier rather than a numerical list. The level of detail of the FRN description will depend on the state of the science, and EPCs should use their judgment based on their understanding of the topic and field.

Basic principles include:

- Rationale for prioritization if possible.
- Research design considerations for the FRN should be offered as suggestions only to avoid appearing overly prescriptive.

The workgroup recommended separating the presentation of two elements of potential future research: methods issues and specific topics. Methods issues tend to transcend specific topics. They should be ranked separately.

FRN Methods Framework

The workgroup identified a number of potential methodological issues that an FRN might address. Table 1 identifies elements that should be considered when addressing methods issues.

For each relevant issue, the FRN should address elements and level of detail and explain how this fills the evidence gap.

An example of a methodological gap identified in an FRN relates to treatments for localized prostate cancer. Because of the lengthy course of this disease, some randomized controlled trials have been published with high crossover rates in which patients have taken the initiative to receive the treatment to which they were not randomized. This is understandable from the patient’s perspective but may greatly reduce the ability to draw conclusions from the trial. Research was therefore recommended on “Exploring methods to increase patient adherence with randomization scheme.” This might include surveys to help understand participants’ decision-making; and measuring the effectiveness of approaches intended to reduce unplanned crossing over to another arm. Research was also recommended to increase the use of statistical modeling and other advanced methods in studies on localized prostate cancer.

Table 1. Potential issues for methodological future research needs

Issues	Potential Details To Be Addressed for Each Issue
Designs	<ul style="list-style-type: none"> • What research designs are most appropriate for specific questions? What are the barriers to conducting the optimal kind? • How much information is needed regarding the study design and study elements such as intervention and patient characteristics? • Where possible, future research needs reports should allude to elements needed to improve the strength of evidence from the initial Comparative Effectiveness Review.
Actions that facilitate aggregations of results	<ul style="list-style-type: none"> • For each clinical area, to facilitate comparisons and aggregation across studies, we need common measures and definitions for condition(s) under investigation, elements of interventions, major outcomes, and harms. • Focus on harms as well as benefits when appropriate.
Inclusion of multiple perspectives	<ul style="list-style-type: none"> • Incorporate various disciplinary perspectives. The focus of different disciplines in terms of the emphasis on patients or treatments may vary.
Statistical analysis	<ul style="list-style-type: none"> • Specify interactions to identify differences in effects across subgroups. • Specify when certain diagnostic categories should be in or out of a study.

FRN Topics Framework

The steps in this process may be summarized as follows:

- Include reason why the FRN is prioritized as high. May include criteria used (burden, feasibility, impact).
- Organize by PICOTS.
- Use analytic framework if possible, and adapt if needed. Consider including relevant issues such as subgroups, settings, and other contextual issues.
- Level of detail of FRN description depends on the state of the science.
- Research design considerations for the FRN should be offered as suggestions only to avoid appearing overly prescriptive.

The presentation of specific research topics should include a rationale as well as an organized presentation of each topic. Provide text description of why the prioritized questions are particularly urgent to be answered. Criteria for choosing topics should reflect why answers to the prioritized questions are particularly urgent. Proposed criteria include:

- Societal burden
 - Costs
 - Harms
- Feasibility of research
- Likelihood results will affect practice/policy (for patients as well as others)

The PICOTS formulation should be used to present each recommended topical research question in a separate table for each question. An example of using the PICOTS framework to structure future research recommendations comes from the report *Future Research Needs for Attention Deficit Hyperactivity Disorder: Effectiveness of Treatment in At-Risk Preschoolers; Long-Term Effectiveness in All Ages; and Variability in Prevalence, Diagnosis, and Treatment*²⁴ (see Table 2).

Table 2. Excerpt from “Future Research Needs for Attention Deficit Hyperactivity Disorder”

P	I	C	O	T	S
Age <6 years Diagnosed with ADHD or at risk for ADHD or diagnosed with Disruptive Behavior Disorder (including Oppositional defiant disorder (ODD) and Conduct disorder (CD)	Initial treatment with psychosocial and/or pharmacologic treatments or Addition of a psychosocial and/or pharmacological treatment to an existing treatment after treatment failure	Initial treatment with psychosocial and/or pharmacologic treatments or Continuation of existing treatment without addition of psychosocial and/or pharmacologic treatment or switch to different treatment	Outcomes for children and parents*	Months/ Years	Private clinic, community clinic, school, home

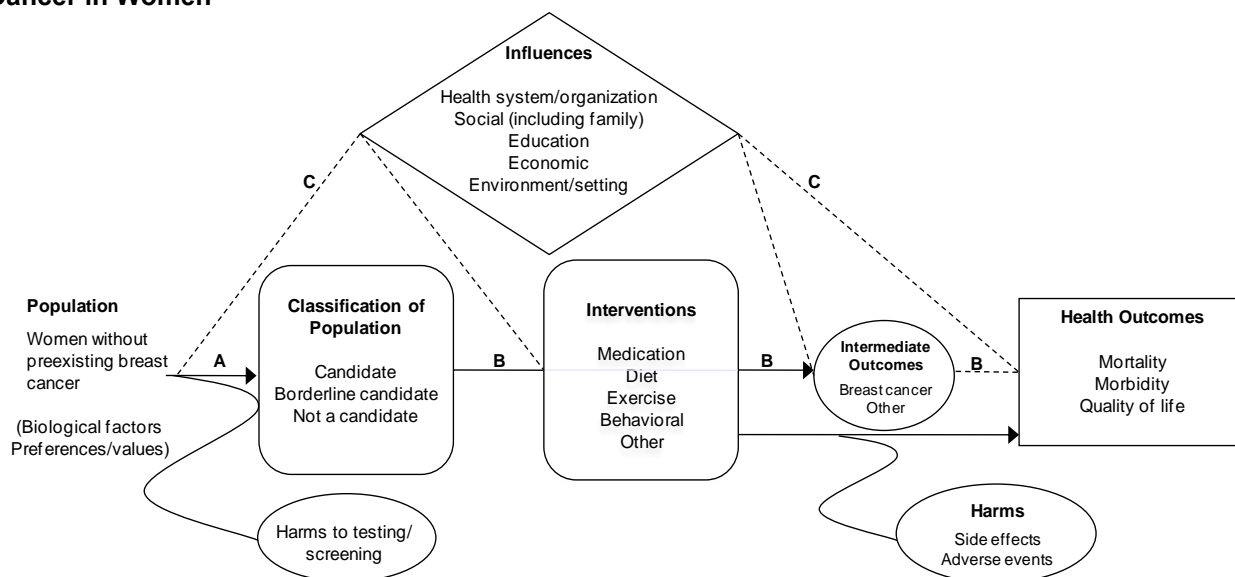
*Outcomes for children and parents include change in ADHD symptoms, social functioning, emotional regulation, executive functioning, treatment adherence, behavior problems, global functioning, academics, and parent competence, and harms, such as behavioral side effects, sleep difficulties, appetite/metabolic concerns, and cardiovascular changes.

Graphical frameworks are often used in grants to clearly communicate ideas, linkages, and assumptions to demonstrate that the research proposed is well-integrated, well-reasoned, and appropriately designed to advance a field of research. Analytic frameworks have been used to structure comparative and systematic reviews but were not intended to guide discussions of

future research, although work is underway to adapt them to FRNs when feasible. However, analytic frameworks depict the population, interventions, comparators, outcomes, timing, and settings (PICOTS) which are often key elements in research study designs. Future research chapters of CE reviews often mention the need for more research on special populations (including racial, ethnic, and genetic variations), settings (e.g., community or geographic), contextual features such as patient-provider communication and decisionmaking, and influencing factors as important topics for future research. Thus an analytic framework may be an effective method to display these considerations and their linkages to interventions and their outcomes. The report should employ a conceptual model or logic diagram when appropriate; not all FRN topics may be suitable for this. For example, research questions may address prevalence in subgroups. The model should be based on current thinking and not limited to what was in the parent report.¹⁶

An example of the use of a framework adapted for an FRN document comes from Future Research Needs To Reduce the Risk of Primary Breast Cancer in Women,¹³ which used an analytic framework that incorporated the priority research area, research needs, and potential study designs (Figure 2). This flowchart depicts an enhanced conceptual framework to illustrate priorities for future research to reduce the risk of primary breast cancer in women. The chart emphasizes high priority research domains and depicts “influencing factors” important to stakeholders and integral to patient-centered care: health system/organization, social, educational, economic, and environmental factors. A series of research questions are applied to these high priority research domains, with the overall goal of understanding which interventions are most effective to reduce risk of breast cancer for which patients under what circumstances.

Figure 2. Analytic framework from “Future Research Needs to Reduce the Risk of Primary Breast Cancer in Women”



As part of the process of the most salient FRNs, EPCs engage a wide variety of stakeholders who may identify a broad list of new potential research areas. It should be noted that these new areas of research will likely not be based on an assessment of the evidence (or lack of evidence) because they fall outside of the scope of the parent evidence report.

The level of detail in presenting recommendations will vary with the topic. Research in some areas may have sufficiently developed to the point where the gap can be precisely defined (e.g., testing a specific intervention or comparing two specific interventions). In other areas, the suggestions may be couched more broadly about types of questions or interventions. Likewise, the specificity of research design considerations may vary with the circumstance. In some cases, but not all, the appropriate design will be evident. There may be design tradeoffs or specific issues to consider. Include any research design considerations or comments if relevant. For example, it would be inappropriate to recommend that you must do an RCT with X number of people, but it would be fitting to suggest (as opposed to recommend) that future research should be appropriately powered to study X subpopulation. EPCs will need to decide when the research design issues are sufficiently clear that they can be urged.

Considerations for Research Designs

In looking at the entirety of the literature, evidence reviews may uncover important insights regarding study designs that would help advance the science. For example, in a review of the treatment of hip fracture, it became clear that the studies conducted by epidemiologists emphasized patient characteristics, and those by orthopedic surgeons emphasized treatments, but neither captured the whole terrain. FRN authors may want to consider including appropriate research considerations. FRN documents aim to delineate where there is an absence of studies and also to describe limitations of existing studies to the extent that researchers could improve upon those limitations. It can be a delicate balance to provide sufficient detail to be helpful to researchers while not being so prescriptive that research creativity and discovery are stifled. As opposed to identifying gaps in research, there may be important design issues to consider. When there are fatal flaws in prior study designs, future research needs documents should describe the flaws and potential design remedies in sufficient detail that interested researchers could improve their study designs accordingly. The amount of detail that should be shared in FRN documents will depend on the topic and specifics of the report. In fields with relatively little evidence, a broad translational table presenting the spectrum of study designs that would be acceptable to inform certain research gaps may be most useful. In other areas, where there is a substantial body of literature, a deeper description of important flaws in existing studies that are hampering the strength of certainty in results is appropriate.

A common issue that future research documents can inform across topics addresses the role for observational studies and comments about the context in which observational studies may be suitable or even preferable for certain needs. For example, while there may be randomized controlled trials of screening, the question about the adverse consequences of screening (or the long-term effects) may be best answered through an observational study. While each report will differ on the extent to which details about study designs can be discussed, it is the general intent to describe important flaws and provide insights into possible solutions while promoting the creativity that advances discovery.

An example of how study design can be addressed while leaving reasonable latitude can be found in the future study recommendations in Future Research Needs for Angiotensin-Converting Enzyme Inhibitors (ACEIs), Angiotensin II Receptor Antagonists (ARBs), or Direct Renin Inhibitors (DRI) for Treating Hypertension²⁵ (Table 3).

For specific details related to considerations of research designs in FRN documents, please refer to the RTI EPC methods paper on Advantages and Disadvantages of Different Study Designs for Future Research Needs.¹⁷

Table 3. Excerpt from “Future Research Needs for Angiotensin-Converting Enzyme Inhibitors (ACEIs), Angiotensin II Receptor Antagonists (ARBs), or Direct Renin Inhibitors (DRI) for Treating Hypertension”

Research area	RCT?	Meta-analysis or individual patient data analysis across RCTs?	Meta-analysis of observational studies?	New observational study?	Analysis of existing data?	Model?
What is the comparative effectiveness of these medications on cardiovascular and cerebrovascular events measured over several years?	Maybe: Large number of studies recently completed or ongoing in patients with other comorbidities may make new RCTs unnecessary	Maybe: If recent data is not included in original CER or if it is methodologically valid to combine studies of medication impact across different conditions (such as hypertension, ischemic heart disease, chronic kidney disease)	Maybe: If sufficient number of studies available; adjustment for confounding could be an issue	Maybe: Most direct way to address long-term outcomes; however, resource requirements for longer-term studies are potential limitations	Yes: Most efficient method for evaluating long-term outcomes given the large number of existing studies; appropriate coding for covariates an issue	Maybe: Potential role for helping determine clinically important differences
What is the impact of comorbidities (such as ischemic heart disease, CHF, diabetes, peripheral arterial disease, chronic kidney disease) on ACEI/ARB/DRI effectiveness or harms in patients with hypertension?	Maybe: May be feasible for common comorbidities; existing or ongoing studies might be sufficient for some	Yes: If individual patient data or separate subgroup data not reported in current trials could be obtained and pooled for analysis; would require cooperation from the multiple sponsors of RCTs in this area	Yes: If individual patient data or separate subgroup data not reported in current trials could be obtained and pooled for analysis; would require cooperation from the multiple sponsors; if available, could address less common comorbidities, long-term safety/ effectiveness	Maybe: Most direct way to address less common comorbidities; allows for adjustment for confounding; sample size and resources needed for longer follow-up are potential limitations	Yes: Most efficient method for evaluating less common comorbidities over longer time frames; appropriate coding of covariates a potential limitation	No: Except for potential role in defining clinically or economically meaningful differences

Conclusion

The workgroup reviewed relevant documents from sources within the EPC program and external sources. The recommendations are based on the information gleaned from previous experience of the workgroup members, recommendations from methods work, and from exemplars of this work from multiple sources. We expect that further development in this area will continue as EPCs gain more experience in FRN work and the program receives feedback from stakeholders.

The methodology committee of the newly formed Patient Centered Outcomes Research Institute has been tasked with creating a translation table, which is intended to “provide guidance and act as a reference...to determine research methods that are most likely to address each specific research question (U.S. Public Law 111-148, section 301). This additional guidance will also contribute to the development of FRN work within the EPC program.

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Abbreviations

AHRQ	Agency for Healthcare Research and Quality
CABG	coronary artery bypass graft
CE	comparative effectiveness
CER	comparative effectiveness research
EPC	Evidence-based Practice Center
FRN	future research needs
PCI	percutaneous coronary intervention
PICO	Population(s), Interventions, Comparators, Outcomes
PICOTS	Population(s), Interventions, Comparators, Outcomes, Timing, Settings