

# **The Refinement of Topics for Systematic Reviews: Lessons and Recommendations from the Effective Health Care Program**

## **Appendixes**

# Appendix A: EPC Topic Refinement Template

*Note: This document is undergoing revision*

This document outlines and documents the evolution of topics in the process of topic refinement. Topic refinement is intended to further develop the key questions and scope from the original nomination with input from Key Informants. The product of the topic refinement process (background, draft key questions, PICOTS, and provisional analytic framework) forms the basis of a separate document, the Key Question Posting Document, which will be posted for public comment on the Effective Health Care website.

The topic was presented to the EHC Topic Triage Group and was selected to go forward for further topic refinement by an Evidence-based Practice Center (EPC) in preparation for a Comparative Effectiveness Review or Effectiveness Review for the EHC program.

All nominations to the EHC program are presented at Topic Triage which represents stakeholder, scientific, and clinical perspectives, and the programmatic authority vested in AHRQ. In preparation for Topic Triage, SRC or EPC staff prepares a topic brief that outlines the evidence that evaluates the topic against the following EHC Selection Criteria: 1.) Appropriateness, 2.) Importance, 3) Desirability of New Research/Duplication, 4.) Feasibility, and 5.) Potential Impact. Topics are selected by this group for further development within the program. For each topic are the following documents are uploaded on the MMA secure site (<https://www.kpchr.org/MMA/system/login.aspx>)

1. Original Nomination;
2. Topic Triage brief, which includes (1) cover sheet; (2) selection criteria table, and (3) existing guidance table.

The remainder of this document describes and documents the Topic Refinement Process. It may be used as a template for a final deliverable for topic refinement.

## 1. Initial Topic Refinement

Initial topic refinement moves the topic from the nomination stage to a point where it is ready to be discussed with key informants. The background and clinical context is expanded and preliminary key questions are clarified. An important aspect to the initial topic refinement is the proposal of an analytic framework.

### Nomination Data:

	Fill in boxes with info as it appears in Topic Triage documents
<b>Topic Name:</b>	
<b>Topic Number:</b>	
<b>Topic Triage Review Date:</b>	
<b>Topic Investigator(s):</b>	
<b>Nominator:</b>	
<b>Nominator Liaison:</b>	

### Summary of Nomination:

The Summary of Nomination will review pertinent information from the Topic Triage or nomination documents. This section explains the clinical and current context under which the topic and key questions were developed.

This preliminary PICO develops as a guide to the rest of the Topic Refinement Document, since it underlies the structure of the Key Questions and the logic of the Analytic Framework. The PICO resulting from topic refinement may be different than the PICO originating from Topic Triage.

<b>P:</b>	
<b>I:</b>	
<b>C:</b>	
<b>O:</b>	
<b>Narrative:</b>	

**Background and Context:**

The purpose of the Background section is to describe the condition(s), role of the intervention, relevant claims about comparative effectiveness and safety, and outline the rationale for a systematic review on the topic.

The background section will be a work in progress. This initial section developed for distribution to Key Informants should set the context for their discussion of the topic and include information on the nature and burden of disease, the current interventions that are available, recommendations from current guidelines, interventions that are currently available in the United States and the FDA status of each, and a list of relevant outcomes that have been studied.

The final background section of 2-5 pages will describe the importance of the topic, the current state of understanding on the topic and what practices are currently available. Justification for the review should include a description of the theoretical and potential benefits or harms of the intervention or technology being studied and how the review questions will help readers understand how this intervention or technology fits with what is currently available. The background should be informed by the input from the Key informants.

In addition, the background may include any information regarding the possible use of the report (e.g., issues in guidelines, coverage decisions, or benefit design).

This will require a targeted literature search by the EPC on the current state of the literature (including guidelines, outcomes studied, scope of literature). If there is a large body of literature, the EPC will work with key informants to focus the questions on those most essential. The exact literature search and sources can be further refined after discussions with the Technical Experts during the review portion of the project.

Elements that should be included are:

- Population:
  - Nature and burden of condition
  - Description of subpopulations, if appropriate
- Intervention, Comparator
  - Current treatment or standard of care and/or existing guidelines
  - Mechanism of action
  - Availability in the United States; FDA approval status
  - Are there interventions for which there is uncertainty regarding use?
  - Proposed advantages and disadvantages of the intervention (cost, invasiveness, harms, etc)
- Outcomes
  - What are the outcomes with the current standard of care?
  - What are the outcomes of importance for stakeholders?
- Setting and context
- Rationale for an evidence review

- Controversy or uncertainty about a topic
- Literature is confusing or conflicting
- Relevant literature not in one place
- Clinical decisions are complicated
- Relevance of research question to clinical decision making or policymaking
  - Weighing benefits and harms
  - Targeting specific populations
  - Applicability to general practice
  - Patient preferences
  - Cost, if relevant
  - Coverage
- Availability of scientific data to support the systematic review and analysis
- Assessment of other ongoing work in this topic area.
- Other contextual factors (such as training, facility requirements, advocacy positions)

### Citations

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### Additional References

For the benefit of the Key Informant discussions, additional sources not directly cited in the Background materials may be included.

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### Preliminary Key Questions

During refinement, Preliminary Key Questions are refined into the Draft Key Questions that are posted for public comment.

The Preliminary Key Questions serve as a starting point for Key Informant discussions and aid in the development of Draft Key Questions. These Preliminary Key Questions on the proposed topic should reflect important decisional dilemmas in health care for stakeholders. Key Informants should comment on how well the questions reflect what they need to know in making their decisions.

With this in mind, the Key Questions must clearly define the logic and scope of the topic. (For further discussion of the significance of Key Questions, consult the Methods Guide).

**KQ 1:**

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**KQ 2:**

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**KQ 3:**

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**KQ 4:**

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**KQ 5:**

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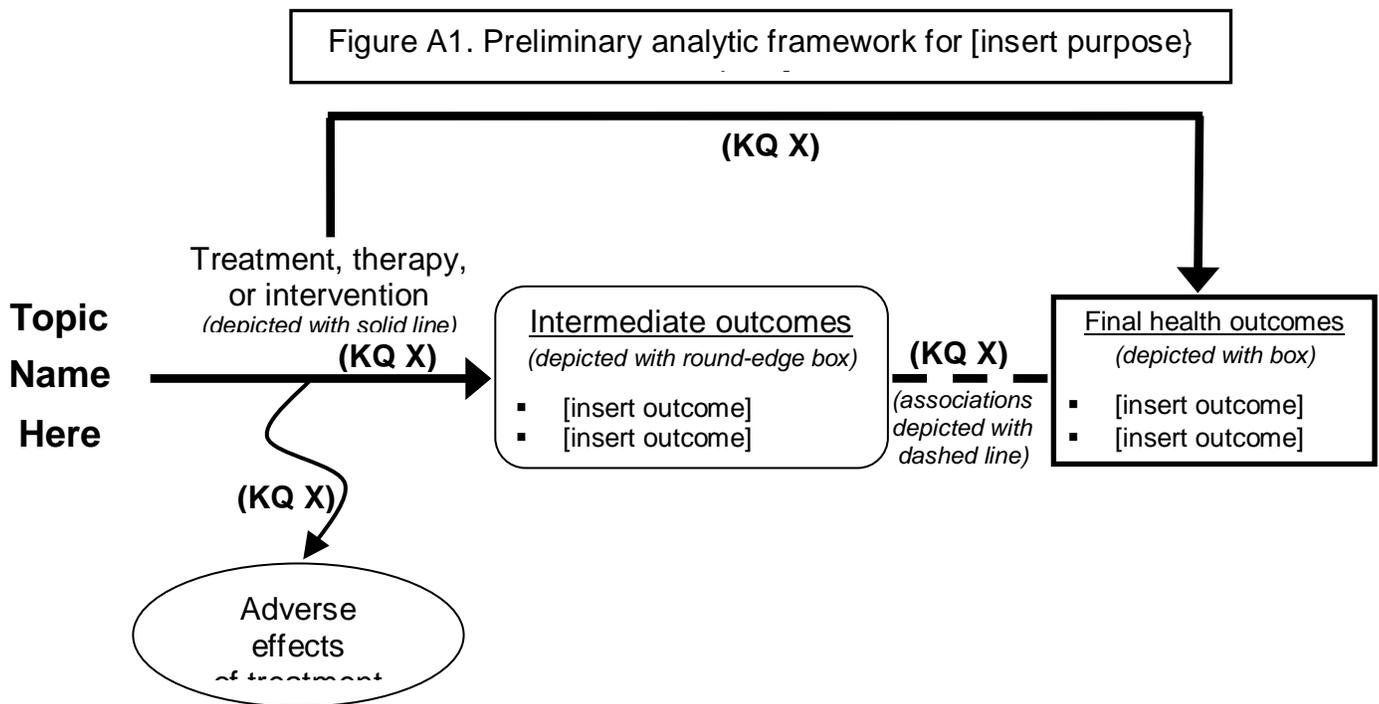
**KQ 6:**

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## Preliminary Analytic Framework

The Preliminary Analytic Framework is to encompass preliminary patients, interventions, comparators, harms, intermediate outcomes, and health outcomes. Its purpose is to provide a visual representation of the clinical logic and final PICOTS. The Key Informant process will then use this framework to guide further refinement of these issues. (For example, a preliminary Analytic Framework for IMRT might indicate “More precise guidance for radiation treatments” as a potential intermediate outcome and “better health outcomes” as the final outcome, even though Key Informant input would be used to identify which “better health outcomes” are the intended result of “more precise guidance.”)

Additionally, the Preliminary Analytic Framework should be linked to the Preliminary Key Questions (KQs). A template for linking KQs to the Analytic Framework is described in the Methods Guide. If an Analytic Framework is not included, the KQs can be formatted according to the Posting Document Template. Based on Key Informant input, this preliminary analytic framework may be modified. It will be referred to as the Draft Analytic Framework in the Key Question Posting Document.



## Key Considerations for Key Informants

Input will be solicited from Key Informants - a small number of individuals (no more than 9) including patients and consumers, practicing clinicians, relevant professional and consumer organizations, purchasers of health care, and others who will use the findings from the report to make healthcare decisions for themselves or others. EPCs should ask Key Informants directed questions that can help them to understand the questions that decision-makers are struggling with so that the review can be sure to address these questions within the scope of the review. These informants are distinct from the Technical Expert Panel which is constituted to inform the scientific processes (i.e. literature available) of the subsequent research review.

The purpose of Key Considerations from Topic Refinement is to structure the discussions of the Key Informants by clarifying the Preliminary Key Questions, Analytic Framework, and other salient aspects of the topic. While there is no specific content requirement, this section may be used to brief the Key Informants on information and points of interest that are not included elsewhere. This typically includes a well-considered set of issues and questions to guide and structure the Key Informant discussion. Key considerations may also include issues that the EPC staff is not able to adequately address in the limited literature search or discussion with a local expert and/or because the issues require the perspective,

experience and/or technical knowledge of experts, or the perspective of other stakeholders. These issues and questions should be as detailed as necessary and/or possible.

Key Informants are meant to help define the decisional dilemmas and define the scope of the questions. Some sample questions for their input may be:

- What interventions or technologies are you currently using? What is the current perception or understanding of guidelines or standards of care?
- What is your current understanding of outcomes with the current standard of care? (or if no current treatments are available, what is your understanding of the natural progression of disease?)
- What are the potential advantages or disadvantages of the intervention or technology over those that are currently available? (i.e. ease of use, access, cost, invasiveness, patient preference, use of other resources or tests) Why might you be interested in this intervention or technology? What would keep you from using it?
- Benefit or harms on which outcomes would influence whether you would use or recommend this intervention or technology?

1.	
2.	
3.	
4.	
5.	
6.	

**Attachment(s):** EPC may add attachments or relevant documents to inform the Key Informants.

## 2. Input from Key Informants

### Summary of Key Informant Discussions

This section summarizes the Key Informant discussions, and outlines how the background, preliminary key questions, preliminary analytic framework, and/or scope have been changed based on these discussions.

Insert

## 3. Final Topic as Proposed for Posting

This section should include the draft key questions, provisional analytic framework and/or PICOTS if changed.

### Contacts for Scientific Information Packets

List of known pharmaceutical or device companies or other professional entities or researchers from whom Scientific Information Packets (SIP) should be requested at the time of finalizing the protocol. If contact information is known, please include.

Additional information about the SIP process can be found in the EPC procedure guide, and at <http://effectivehealthcare.ahrq.gov/index.cfm/submit-scientific-information-packets/>

Insert

**Submit the Posting Document for public comment on key questions as a separate file.**

The Key Question Posting Document includes the Draft Key Questions and Draft Analytic Framework. Please see the Key Question Posting Document Content Guidance for further details.

## Appendix B. Example of Selected Aspects of a Topic Refinement

Figure B1. Nomination: The effectiveness of disease-modifying anti-rheumatic drugs in children with juvenile idiopathic arthritis<sup>1</sup>

### **Nominated PICO**

*Population:* Children and subgroups of children diagnosed with JIA

*Intervention:* Corticosteroids; Synthetic DMARDs; Biologic DMARDs

*Comparator:* Comparisons of different DMARDs

*Outcome:* Outcomes include looking at potential harms and benefits of various treatments.

### **Nominated Key Question**

For children with juvenile idiopathic arthritis, do drug therapies differ in their ability to reduce patient-reported symptoms, to slow or limit progression of radiographic joint damage, or to maintain remission (feeling healthy, not experiencing pain, functioning well, and not having flare-ups)?



### **Refined PICO**

*Population:* Children and subgroups of children diagnosed with JIA

*Intervention:* Various DMARDs

*Comparator:* Placebo, NSAIDs and/or corticosteroids, or other DMARDs

*Outcome:* Patient-centered outcomes (such as pain control, clinical remission, and quality of life); intermediate outcomes (laboratory measure of inflammation, number of joints with limited range of motion); and adverse effects of treatment.

### **Refined Key Questions**

In children with JIA

**KQ1:** Does treatment with any of a variety of DMARDs, alone or in combination, improve health outcomes (i.e. pain control; clinical remission; quality of life; parent/patient global assessment; mortality; function; or growth and development) compared with placebo, NSAIDs and/or corticosteroids, or other DMARDs?

**KQ2:** Does treatment with any of a variety of DMARDs, alone or in combination, improve other outcomes (i.e. active joint count; number of joints with limited ROM; laboratory measures of inflammation; physician global assessment; or radiographic change) compared with placebo, NSAIDs and/or corticosteroids, or other DMARDs?

**KQ3:** Is improvement with other outcomes associated with improvement in health outcomes?

**KQ4:** Does treatment with any of a variety of DMARDs, alone or in combination, result in additional troublesome or serious harms compared with placebo, NSAIDs and/or corticosteroids, or other DMARDs?

**KQ5:** How do the efficacy, effectiveness, safety or adverse effects of treatment with DMARDs differ between each of the various subtypes of JIA?

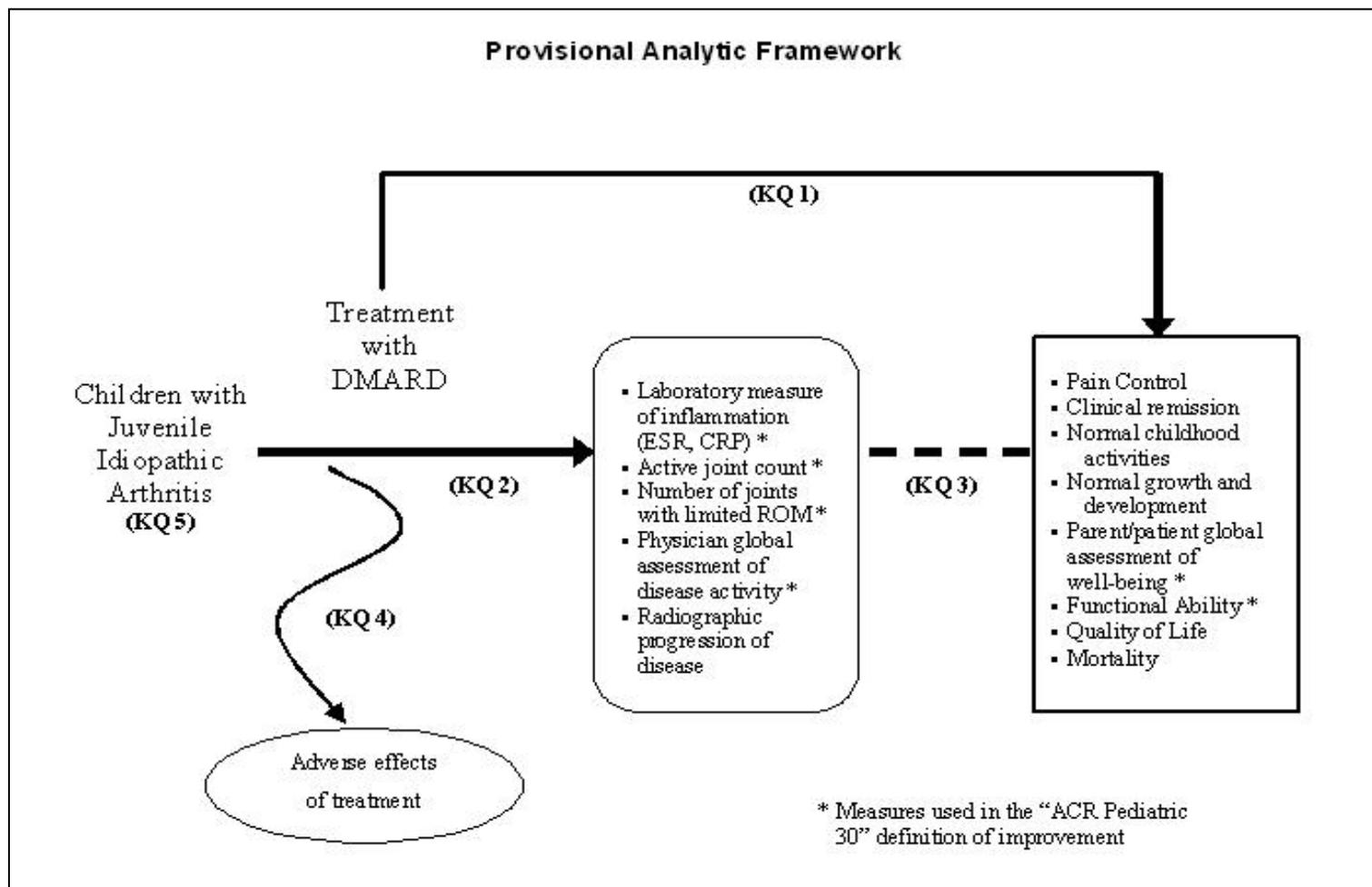
Note: DMARD= disease-modifying anti-rheumatic drug, JIA=juvenile idiopathic arthritis, KQ=key question, NSAID=nonsteroidal anti-inflammatory drug, PICO=population, intervention, comparator, outcome.

**Table B1. Changes to elements of the nominated topic with rationale for refinements**

Original Element	Source of input	Comment	Decision	Change	Rationale
Nominated KQ	Local expert, literature scan	There are at least six sub-types of JIA, with distinct clinical characteristics and different treatment approaches. The amount of published literature for each subtype varies substantially.	Specify in the KQ that subtypes of JIA exist and that the population of interest will include children with any subtype.	-No change in PICO. -KQ 3 was added about possible variations in effectiveness and safety of DMARDs between subtypes.	Added detail about subtypes makes the key questions more specific, and improves the accuracy and researchability of the SR. Inclusion and analysis by JIA subtypes might expand the scope and heterogeneity of the SR; however the literature predominately addresses two subtypes and reduces this concern.
PICO (Intervention): Corticosteroids; Synthetic disease-modifying anti-rheumatic drugs (DMARDs); Biologic DMARDs	Literature scan, Key Informant	Corticosteroids are commonly used as first-line treatment for most cases of JIA.	Remove as a intervention, and include as a comparator	Intervention: DMARDs	This change reflects the standard of care and the literature. This does not significantly compromise fidelity to the original nomination. The principal dilemma relates to DMARDs and not corticosteroids; this makes them better suited as a comparator for DMARDs.
PICO (Outcome): Outcomes include looking at potential harms and benefits of various treatments	Literature scan, Key Informants, Local Experts	Specific outcomes are not included	Include relevant outcomes, and specify them in the key questions and PICO	-See refined KQs -Outcome: Patient-centered outcomes (such as pain control, clinical remission, and quality of life); intermediate outcomes (laboratory measure of inflammation, number of joints with limited range of motion); and adverse effects of treatment.	Distinguishing between patient-centered outcomes and intermediate outcomes elucidates the underlying relationship of the outcomes and the logic of the SR
Nominated KQ	Literature scan, key informant, local experts	The outcomes listed do not reflect the clinical logic typically seen in AFs and refined KQs. The nominated topic places patient-centered outcomes (e.g., patient functioning) and intermediate outcomes (e.g., radiographic joint damage) in the same key question.	Formulate key questions specific to the outcome categories (patient-centered outcome; intermediate outcome).	-KQ: See refined KQ 1 (patient-centered outcomes) and KQ 2 (intermediate outcomes). -AF: The relationship of the outcome categories is represented in the AF	Accuracy and researchability are improved by including specific outcomes in the KQ.  Distinguishing patient-centered outcomes from intermediate outcomes elucidates the underlying relationship of the outcomes and the logic of the SR.

Original Element	Source of input	Comment	Decision	Change	Rationale
Nominated KQ	Literature scan	Many studies use ACR Pediatric 30, a validated composite measure of improvement of JIA. It includes patient – centered outcomes and intermediate measures. Some measures of the Peds 30 were included in the nominated materials.	Include mention of Peds 30 measure in the AF.	In the AF, asterisks (*) have been added to the outcomes that are constituents of the Peds 30 measure.	The literature scan provided added detail about relevant outcomes, including that part of the ACR Pediatric 30. This improves the accuracy and researchability of the review.

Figure B2. Example analytic framework



Note: CRP=C-reactive protein, DMARD= disease-modifying anti-rheumatic drug, ESR = erythrocyte sedimentation rate, KQ = key question, ROM=.range of motion

## Key Questions

**KQ1:** Does treatment with any of a variety of disease-modifying anti-rheumatic drugs (DMARDs), alone or in combination, improve health outcomes (i.e. pain control; clinical remission; quality of life; parent/patient global assessment; mortality; function; or growth and development) compared with placebo, NSAIDs and/or corticosteroids, or other DMARDs?

**KQ2:** Does treatment with any of a variety of DMARDs, alone or in combination, improve other outcomes (i.e. active joint count; number of joints with limited ROM; laboratory measures of inflammation; physician global assessment; or radiographic change) compared with placebo, nonsteroidal anti-inflammatory drugs (NSAIDs) and/or corticosteroids, or other DMARDs?

**KQ3:** Is improvement with other outcomes associated with improvement in health outcomes?

**KQ4:** Does treatment with any of a variety of DMARDs, alone or in combination, result in additional troublesome or serious harms compared with placebo, NSAIDs and/or corticosteroids, or other DMARDs?

**KQ5:** How do the efficacy, effectiveness, safety or adverse effects of treatment with DMARDs differ between each of the various subtypes of juvenile idiopathic arthritis (JIA)?

## Appendix A References

1. Kemper A, Coeytaux R, Sanders G, et al. Disease-Modifying Antirheumatic Drugs (DMARDs) in Children With Juvenile Idiopathic Arthritis (JIA). Comparative Effectiveness Review No. 28. (Prepared by the Duke Evidence-based Practice Center under Contract No. HHS A 290 2007 10066-I.) AHRQ Publication No. 11-EHC039-EF. Rockville, MD: Agency for Healthcare Research and Quality. September 2011. Available at: [www.effectivehealthcare.ahrq.gov/reports/final.cfm](http://www.effectivehealthcare.ahrq.gov/reports/final.cfm).