Objective: This article discusses the identification, selection, and refinement of topics for comparative effectiveness systematic reviews within the Agency for Healthcare Research and Quality’s (AHRQ) Effective Health Care (EHC) program.

Study Design and Setting: The EHC program seeks to align its research topic selection with the overall goals of the program, impartially and consistently apply predefined criteria to potential topics, involve stakeholders to identify high-priority topics, be transparent and accountable, and continually evaluate and improve processes.

Results: A topic prioritization group representing stakeholder and scientific perspectives evaluates topic nominations that fit within the EHC program (are “appropriate”) to determine how “important” topics are as considered against seven criteria. The group then judges whether a new comparative effectiveness systematic review would be a duplication of existing research syntheses, and if not duplicative, if there is adequate type and volume of research to conduct a new systematic review. Finally, the group considers the “potential value and impact” of a comparative effectiveness systematic review.

Conclusion: As the EHC program develops, ongoing challenges include ensuring the program addresses truly unmet needs for synthesized research because national and international efforts in this arena are uncoordinated, as well as engaging a range of stakeholders in program decisions while also achieving efficiency and timeliness.

Keywords: Comparative effectiveness; Evidence-based practice; Systematic review; Priority setting; Methods; Decision making

1. Introduction

Globally, people are struggling with the reality of limited resources to address the breadth of health and health care needs. Evidence has been recognized as the “new anchor for medical decisions” [1], and many consider systematic reviews to be the best source of information for making clinical and health policy decisions [2]. These translational research products rigorously summarize existing research studies so that health and health care decisions by practitioners, policy makers, and patients are more evidence based. Yet, dollars for research—whether for systematic reviews, trials, or observational studies—are constrained, and are likely to be into the future. Effective prioritization is clearly necessary to identify the most important topics for synthesized research investment that may help the US health care system realize powerful and meaningful improvements in health status.

This article discusses the identification, selection, and refinement of topics for comparative effectiveness systematic reviews within the Agency for Healthcare Research and Quality’s (AHRQ) Effective Health Care (EHC) program, which has been described in more detail elsewhere [3]. Briefly, AHRQ’s EHC program was authorized in 2003 by the US Congress to conduct and support research on outcomes, comparative clinical effectiveness, and appropriateness of pharmaceuticals, devices, and health care services. This program uses the AHRQ Evidence-based Practice Center (EPC) program, with 14 designated centers throughout North America that conduct comparative effectiveness systematic reviews, among other research products of the program. AHRQ has designated a Scientific Resource Center (SRC) currently housed at the Oregon EPC to support the EHC program as
Selecting and developing good topics for research is not a simple process. Researchers’ success depends, in large part, on their ability to identify meaningful questions, whereas funding agencies continually seek to maximize the return on their investment by funding research on important, answerable questions relevant to significant portions of priority populations. Although some have criticized how well funders have actually achieved these results [4], there is little guidance for successfully developing a research program that generates the type of evidence necessary to improve the public’s health.

2. Guiding principles for identifying and selecting comparative effectiveness research topics in AHRQ’s EHC program

To derive guiding principles for selecting important comparative effectiveness systematic review topics, we considered what others have done when trying to select priority topics for any health care–related activity. Over the last 18 years, the Institute of Medicine (IOM) and selected others have explored priority setting models and approaches [5–10]. Across a diverse set of international health- and health care–related activities, including the development of guidelines by professional societies; clinical service and quality improvement priorities within health care organizations; and national health service guidance for health technologies, clinical practice, and public health, experts have tried to define clear-cut processes and criteria [9,11–13]. Although most of this existing work has not focused on specific priority setting for comparative effectiveness systematic reviews, the lessons learned from this process are relevant. These experts have found that there is no obviously superior approach to setting priorities and little objective analysis to compare the relative strengths and shortcomings of various approaches [10,14].

However, across these activities, we found five consistent principles for selecting the highest priority topics (Table 1). The first of these principles is to clearly identify the overall goals/strategic purpose of the activity to align

<table>
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<tr>
<th>Table 1: Guiding principles for selecting important comparative effectiveness systematic review topics in AHRQ’s EHC program</th>
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<tr>
<td><strong>Principle</strong></td>
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<tr>
<td>1. Align goals/strategic purpose</td>
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<td>2. Identify meaningful questions</td>
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<td>3. Align with funding priorities</td>
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<td>4. Align with current literature</td>
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<td>5. Tailor to local contexts</td>
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Fig. 1. Effective Health Care program lifecycle of a topic nomination for research.
the goals for priority setting within the strategic purpose of the sponsoring program. In the instance of the EHC program, because no single entity can undertake activities to address all health or health care research needs, priority-setting decisions must flow from the overall mission and strategic purposes of the program.

The second principle is to clearly define and apply criteria for prioritization among potential program activities. Although a relatively consistent set of criteria has been used across health-related priority setting activities in the US, UK, and Canada (Table 2), specific criteria will vary with the overall goals and the purpose of any given activity. For example, to determine the national and regional estimates of health care utilization and expenditures, the Medical Expenditure Panel Survey prioritized data collected by considering the prevalence of medical conditions and also how accurately households could report on data related to these [9]. Similarly, to identify priority conditions for quality improvement research, the Veterans Administration’s Quality Enhancement Research Initiative focused on prevalent disease but further prioritized prevalent diseases with evidence for both best practices and practice variation that could be improved to enhance quality [9]. Thus, for comparative effectiveness systematic review prioritization, we have considered additional criteria promulgated by the National Institute for Health and Clinical Excellence (NICE) when considering topics for evidence-based guidance. These criteria have pointed out the importance of considering whether proposed topics are subject to influence by the program [13]. Additional NICE criteria consider whether new evidence-based products could be produced in a timely manner and the risk of inappropriate treatment in the absence of evidence-based guidance [13]. This could also be considered as the opportunity cost associated with inaction [5,13]. The process of decision making in health-related priority setting activities is complex, context dependent, and involves social processes; therefore, priority setting processes should be guided by ethical principles, including careful attention to conflicts of interest [14]. A good priority setting process that is fair and publicly accountable within a system that is capable of scrutiny, feedback, evaluation, and improvement is viewed as the best approach to gaining desirable outcomes [14].

The third principle for priority setting addresses the need to involve stakeholders in the identification and/or prioritization process. Engaging stakeholders as key informants provides credibility and avoids prioritizing topics that have no relevance to real-world issues. Organizations engaged in health care—related priority setting indicate that stakeholders must be made familiar with and understand the criteria by which topics will be prioritized [11]. A recent report from the IOM on identifying highly effective evidence-based clinical services calls attention to the fact that different audiences have different needs from systematic reviews [10]. Health care payers may be most interested in the comparative effectiveness of a treatment or intervention. Regulatory agencies may be interested in questions of safety and effectiveness. Clinicians and patients may be particularly interested in the applicability of research to their specific populations. The priorities for research topics and the questions these topics should answer clearly vary by audience.

The fourth principle is the need for transparency. Because priority setting is actually an allocation of limited resources among many desirable but competing programs or people [16], it is highly political and can be controversial. Some have asserted that priority setting in health care represents one of the most significant international health care policy questions of the 21st century [14]. Battista and Hodge point out that documentation of the process leading to a particular topic being selected (e.g., for a clinical practice guideline) should be explicit and made available to stakeholders [5]. The documentation should include the rationale that relates specific priority-setting decisions to priority-setting criteria, the evidence used when making these decisions, and any programmatic constraints that had a bearing on the process [11]. Transparency requires not only that documentation be kept, but also that program decisions and their rationales be actively communicated to stakeholders.

The fifth principle is the need for any prioritization approach to undertake process evaluation and improvement measures. Because priority setting at present is inherently a subjective process based on ideals (e.g., fairness) and decisions are made by considering clusters of factors rather than simple trade-offs [14], there is a great need for ongoing process evaluation and improvement. As Battista and Hodge point out, process documentation forms the basis for process evaluation and improvement [5].

These general principles provide a good framework for selecting topics for comparative effectiveness systematic reviews; however, more specific additional criteria for clinical and comparative effectiveness research were recently articulated in a 2008 IOM report [10]. This report calls on us to consider how well potential comparative effectiveness research topics reflect the clinical questions of patients and clinicians and whether selected topics truly represent a potentially large impact on clinical or other outcomes that matter most to patients. The IOM also emphasizes that topics for comparative effectiveness systematic reviews should be identified and prioritized using a system that aims to be “open, transparent, efficient, and timely” with sufficient input from key end-users [10].

3. Processes for identifying and selecting comparative effectiveness systematic reviews in AHRQ’s EHC program

As illustrated in Fig. 2, the current EHC program processes aim to allow the consistent, broadly focused development of a portfolio of relevant comparative effectiveness systematic reviews. These processes are more heavily focused now on engaging stakeholders than in the initial years
Under the direction of the US Secretary of Health and Human Services priority health conditions are identified to guide the focus of research (see Table 5). These health conditions are being updated throughout the life of the program.

Table 1: EHC program: principles and processes for research topic selection

<table>
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<tr>
<th>Principles for priority setting in health-related programs</th>
<th>Applied principles for comparative effectiveness systematic review topic selection in the EHC program</th>
<th>Guidelines and processes used during comparative effectiveness systematic review topic selection in the EHC program</th>
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<tr>
<td>Alignment of priority setting with the overall strategic purpose of the program</td>
<td>• As mandated by the US Congress, the EHC program conducts research regarding “the outcomes, comparative clinical effectiveness, and appropriateness of health care items and services” on topics that are of broad interest and applicability, with an emphasis on topics of special importance to Medicare, Medicaid, and the State Children’s Health Insurance program (SCHIP) [15]. • Recent work by the IOM calls on us to focus these aims further by particularly considering how well potential research topics reflect the clinical questions of patients and clinicians, and whether selected topics truly represent a potentially large impact on clinical or other outcomes that matter most to patients [10].</td>
<td>• Under the direction of the US Secretary of Health and Human Services priority health conditions are identified to guide the focus of research (see Table 5). These health conditions are being updated throughout the life of the program. • For the EHC program, robust research topics are those that represent an important decisional dilemma for consumers or for one or more participant groups in the US health care system—including patients, clinicians, health system leaders, purchasers, payers, and policy makers—with a strong potential for significant improvements in health outcomes and/or reductions in unnecessary health care–related burdens or costs. • In aligning the EHC process with the desired outcomes for research topic selection, we have set an overarching goal to create a research agenda that is clearly stakeholder driven by first engaging with and then faithfully representing stakeholder interests in the products of the EHC program.</td>
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<tr>
<td>Apply clear and consistent criteria for prioritization of potential program activities</td>
<td>• To be ethically justifiable, prioritized topics must be relevant to the context of the program; this relevance is supported by specific rationales for prioritization that rest on reasons (evidence and principles) that could be agreed on by “fair-minded” people [14]. • We have adopted a set of specific criteria for use in prioritizing all nominated topics for systematic review (see Table 4).</td>
<td>• A topic prioritization group composed to represent scientific, stakeholder, and programmatic perspectives reviews, reasonably considers, and recommends disposition for all research topic nominations. • Topic prioritization criteria applied by this group can be loosely grouped into a hierarchy of criteria to: o First, determine the appropriateness of the topic for inclusion in the EHC program; o Second, establish the overall importance of a potential topic as representing a health or health care issue that matters; o Third, determine the feasibility and desirability of conducting a new evidence synthesis; o Fourth, estimate the potential value by considering the probable impact on health from commissioning a new evidence synthesis.</td>
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<tr>
<td>Involve stakeholders</td>
<td>• Engaging a range of stakeholders across various sectors in the US (see Table 3) increases the likelihood of identifying ideal EHC research topics. • Ideal EHC research topics are those that can clearly lead to evidence-based practice and policies that support the public’s health and that help better the nation’s health care system by reflecting the important needs of stakeholders. • A major source of potential topics should come through regularly engaging stakeholders as active participants to generate topics. • This enhanced involvement of stakeholders and more robust incorporation of their input will make the EHC program research more relevant with a higher propensity for effective dissemination and uptake.</td>
<td>• As the constituencies of the EHC program, stakeholders are key participants throughout the process (see Fig. 2). • We have convened an EHC program National Stakeholder Panel representing leaders in various health and health care–related sectors of the US. • We have developed a variety of means to engage outside experts and program partners at key points throughout the topic identification and development process. These include: o an open forum, supplemented by ongoing regular engagement with key stakeholder groups, to generate topic nominations; o soliciting stakeholder consultation during topic refinement; o soliciting participation in the technical expert groups advising the EPCs conducting the systematic reviews in key question and research protocol refinement; o opportunities for public feedback during key question development. • Stakeholder groups are also engaged in key aspects of report finalization and the creation of dissemination products, as described in future parts of this series.</td>
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</table>
Updates on program activities and priorities are available at www.effectivehealthcare.ahrq.gov.

The topic selection and refinement aspects of the EHC program are striving to achieve a level of transparency that not only allows stakeholders to be a meaningful part of the process, but also tracks progress and decisions for specific nominations. Engage in ongoing self-evaluation/evaluation. Ethical principles require that there be an opportunity for challenge and re-vision in light of considerations raised by stakeholders and the environment. The culture of the program must incentivize timely and high-quality input from key end-users. A transparent system that aims to be open, transparent, efficient, and timely with sufficient input from key end-users is required. The IOM also emphasizes that topics for evidence syntheses that will underpin highly effective clinical services should be publicly accessible. The EHC program prioritization criteria (Table 3) are designed to allow public accountability.

We will continually review and evaluate the topic selection and refinement activities of the EHC program to assess:

- how effectively we are engaging outside experts and program partners in the EHC program (Table 3), while continuing to involve stakeholders that represent the broad-based constituencies of the EHC program (Table 3), while continuing to involve stakeholders that represent the broad-based constituencies of the EHC program.
- whether the overall research portfolio represents a valuable set of critical evaluations for clinical and comparative effectiveness questions across a broad range of health and health care topics.
- whether the research products meet the needs of stakeholders.
- whether we are engaging outside experts and program partners in the EHC program.

The topic is then evaluated for its appropriateness to the US population and health care system. The available research basis on which a topic would build, including consideration of research of the EHC program, particularly during topic identification, but throughout the processes of research development and dissemination within the EHC program. We are using new and existing publicity avenues to encourage nominations and engage in discussions with internal and external stakeholders interested in health care decision making.

Although our initial mechanisms for topic identification included all of those recently cited by the IOM [10]: such as an open ongoing process for public engagement; topic solicitation; internal processes (e.g., engaging federal agencies, such as the Center for Medicare and Medicaid Services); and mandates—we found that these approaches did not always produce products that met the needs of stakeholders. Nominations were often received through the Web site, although some of these nominations were insufficiently documented for consideration by the program. In addition, initial approaches to topic identification did not always identify important topics that had not previously been systematically reviewed, and even when new, important systematic review topics were identified through topic nominations, these were not always developed into concise topics ideally suited for decision makers.

Thus, we are currently implementing a revised system that has two important changes. First, the initial topic identification process involves more direct, focused conversations with stakeholders that represent the broad-based constituencies of the EHC program (Table 3), while continuing to involve stakeholders in other aspects of the program as described below and elsewhere. This direct interaction helps the EHC program to better identify the populations, interventions, comparators, outcomes, timing, and settings of interest to the stakeholder, and to understand the current practice or health policy context underlying the need for synthesized research. A similar approach has been successfully undertaken by others [17]. Second, we are making more explicit attempts to reduce potential duplication through consultation with experts and the literature to ensure that nominated topics have not already been adequately systematically reviewed. Unlike setting priorities for primary research, where replication of existing research can be desirable, conducting duplicate systematic reviews is not clearly advantageous when existing reviews are current and of high quality.

All fully articulated nominations are supported by issue briefs that provide data and contextual details addressing the EHC program prioritization criteria (see Table 4). Topic briefs are circulated in advance and presented during monthly or more frequent meetings of a topic prioritization group that represents stakeholder perspectives, scientific perspectives, and the programmatic authority vested in AHRQ. The topic prioritization group first considers objective information on the appropriateness of a topic and its fit within the mandate and priority conditions of the EHC program. The priority conditions (Table 5) were determined through an open and transparent process and approved by the Secretary of Health and Human Services. The topic is then evaluated for its importance to the US population and health care system. The available research basis on which a topic would build, including consideration of research...
activities already undertaken or underway by others, frames considerations of both the feasibility and desirability of a new systematic review for a nominated topic. Based on these objective data, we engage in the more subjective discussions of the potential and relative value of commissioning a new systematic review for nominated topics. The topic prioritization group can request that final decisions regarding a topic nomination be deferred until further investigation is completed. Such investigations may involve outreach to nominators or other stakeholders, or further background research to determine answers to questions raised during presentation of the topic brief. At the end of the final topic prioritization discussion, the topic prioritization group can recommend that topics be sent for further refinement as a comparative effectiveness systematic review, be eliminated as outside the purview of the program, or be tabled because of other factors that affect their immediate priority. These recommendations are not binding but are highly weighted in the final decision by AHRQ as to which research topics are selected for comparative effectiveness systematic reviews.

4. Principles and processes for refining selected topics for comparative effectiveness systematic review in AHRQ’s EHC program

Once topics are selected for comparative effectiveness systematic review, they are further focused into research questions for systematic review. This process is designed to ensure that the research review results in a product that meets the needs of stakeholders. Key questions should reflect the uncertainty that decision makers, patients, clinicians, and others may have about the topic. Key questions guide the entire systematic review process, from the formulation of comprehensive search strategies and the selection of admissible evidence to the types of data abstracted, synthesized, and reported in the final evidence report. Developing clear, unambiguous, and precise key questions is an early and essential step in the development of a meaningful and relevant systematic review.

For a fully formulated comparative effectiveness systematic review topic, key questions in their final form concretely specify the patient populations, interventions, comparators, outcome measures of interest, timing, and settings (PICOTS) to be addressed in the review [18]. Although the elements of the PICOTS construct are outlined in a general form at the topic identification phase, further focus and refinement of these parameters are generally required for a clear and transparent systematic review process to occur (Tables 6 and 7). The processes to fully develop key questions are designed to carry forward the overall principles of the EHC program of being relevant and timely, objective and scientifically rigorous, and transparent with public participation [3].

The EHC program’s current approach to key question development is largely based on past experiences from AHRQ’s Evidence-based Practice Center (EPC) program

Table 2
Definitions of commonly used priority criteria for health-related topic selection*

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Disease burden</td>
<td>• Extent of disability, morbidity, or mortality imposed by a condition, including effects on patients, families, communities, and society overall [10].</td>
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<td></td>
<td>• Number of people/proportion of population affected; prevalence and burden of illness (quality-of-life years lost) [5].</td>
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<tr>
<td></td>
<td>• A condition associated with significant morbidity or mortality in the population as a whole or specific subgroups [13].</td>
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<tr>
<td>Public or provider interest</td>
<td>• Consumers, patients, clinicians, payers, and others want an assessment to inform decision making [10].</td>
</tr>
<tr>
<td></td>
<td>• Of interest to primary stakeholder [5].</td>
</tr>
<tr>
<td>Controversy</td>
<td>• Controversy or uncertainty around the topic and supporting data [10].</td>
</tr>
<tr>
<td>Variation in care</td>
<td>• Potential to reduce unexplained variations in prevention, diagnosis, or treatment; the current use is outside the parameters of clinical evidence [10].</td>
</tr>
<tr>
<td></td>
<td>• In the absence of guidance, there could be inappropriate variation in access or in clinical care [13].</td>
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<tr>
<td>Cost</td>
<td>• Economic cost associated with the condition, procedure, treatment, or technology related to the number of people needing care, unit cost of care, or indirect costs [10].</td>
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<tr>
<td></td>
<td>• High costs of care (unit or aggregate); economic importance of technology [5].</td>
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<tr>
<td></td>
<td>• An area of action where better evidence of cost effectiveness would be expected to lead to substantive cost efficiencies or might significantly impact on the National Health Service (or other societal) resources (financial or other) [13].</td>
</tr>
<tr>
<td>Sufficient evidence</td>
<td>• The available research literature provides adequate evidence to support an assessment [10].</td>
</tr>
<tr>
<td></td>
<td>• Adequacy of data [5].</td>
</tr>
<tr>
<td>New evidence</td>
<td>• There is a substantive or developing body of research or related evidence [13].</td>
</tr>
<tr>
<td>Potential impact</td>
<td>• New evidence with the potential to change conclusions from prior assessments [10].</td>
</tr>
<tr>
<td></td>
<td>• Potential to improve health outcomes (morbidity, mortality) and quality of life; improve decision making for patient or provider [10].</td>
</tr>
<tr>
<td></td>
<td>• No other assessment available; potential of assessment to impact health and economic outcomes of population [5].</td>
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</table>
|                 | • Would guidance promote the best possible improvement in public health or wellbeing and/or patient care? Does the proposed guidance address interventions or practices that could significantly improve quality of life (for patients or carers), reduce avoidable morbidity, reduce avoidable premature mortality, or reduce inequalities in health relative to current standard practice [13]?

*Bolded criteria are those identified by the Institute of Medicine as most consistently used.
and from other experts in systematic review. Since the inception of the EPC program in 1997, AHRQ has emphasized the importance of input from key stakeholder informants, technical experts, and patients to elucidate the important concerns and clinical logic or reasoning underlying potential questions for systematic reviews [20]. A perfunctory set of questions or an incomplete problem formulation that outlines the general comparisons but does not specify the circumstances that are of most interest to decision makers clearly reduces the usability of the resulting review [18,20–23]. Formulating questions that address dilemmas in real-world situations, coupled with an understanding of the context around these dilemmas, prevents the production of irrelevant systematic reviews that can result from key questions that focus only on interests pertinent to researchers without much (if any) public input [2].

The EHC program has extended the original EPC concept of involving key stakeholder informants by developing additional mechanisms for public input. Key informants representing key stakeholder groups may be consulted as part of the topic selection process or, once selected, as part of the topic refinement process. The EHC program also convenes a group of key stakeholder informants (including patients) and technical experts to provide additional input to the EPC in finalizing key questions for the research review. The SRC, AHRQ, and the EPC conducting the research review work together with this group to refine the key questions for a given topic. Obtaining input from stakeholders on patients’ preferences is essential to identifying pertinent clinical concerns that even expert health professionals may overlook [24].

Incorporating a broad range of perspectives contributes to the objectivity and scientific rigor of a review by assisting

Fig. 2. Effective Health Care program activities to engage stakeholders in developing and disseminating systematic reviews.

Table 3
Stakeholder categories for the Effective Health Care program

- Clinicians
- Consumers/patients, including consumer/patient organizations
- Employers and business groups
- Federal and state partners
- Healthcare industry representatives
- Payers, health plans, policy makers
- Researchers
EPC researchers in understanding the health care context and clarifying the parameters of greatest interest when planning the research review (Table 6). These parameters are the basis for formulating good key questions and include focused determination of the most relevant PICOTS. In focusing on outcomes that matter most to patients, key questions need to identify the overarching, long-range goals of interventions. It is insufficient for key questions to focus only on what is assumed to be true or what is presently studied in the literature; they must include the populations, comparisons, and outcomes that are important to patients, providers, and policy makers using health information in their decision making.

Furthermore, beliefs about the advantages or disadvantages of various alternative treatments are an important target for exploration. Many beliefs about the advantages and disadvantages of a treatment are based on direct evidence about health outcomes from long-term comparative trials. However, some beliefs about comparative effectiveness are based on clinical theories that invoke understanding of the pathophysiology of a disease, assumptions about its course, or expectations about the health benefits associated with improvements in a surrogate measure of outcome. Often, experts and stakeholders can bring attention to the issues that underlie uncertainty about the comparative effectiveness of alternative tests or therapies.

Stakeholders and other technical experts also provide important insight to direct the search for evidence that is most relevant to current practice. First, they can clarify specific (sub)populations or interventions of greatest clinical or policy interest. Second, interviewing those with knowledge of current (clinical) practices can identify areas in which studies differ in ways that may reduce their applicability.

Consistent with the principle of transparency and public participation, the EHC program solicits public commentary on proposed key questions before finalization of the scope of a new systematic review. These public comments are reviewed by AHRQ, the SRC, and the EPC, and all parties agree on changes to be made to the existing key questions to reflect this public input. Final key questions that reflect public input, as well as key stakeholder and expert input, are posted on the AHRQ EHC Web site after a review begins.

Through the processes outlined for topic identification, selection, and refinement, the EHC program attempts to develop a considerable number of important topics for comparative effectiveness systematic reviews consistent with the principles that have been outlined above. Each topic
must have appropriately focused key questions to adequately frame the systematic review while also faithfully incorporating public feedback and perspectives. The EHC processes have been developed to reduce the amount of bias that individual investigators working in isolation could potentially introduce into a topic for systematic review. However, given the complexities of the process, those involved throughout must keep foremost in their minds the overall goal for EHC topic development—producing critically important research that positively impacts the decision making of audiences at all levels of health and health care decision making to improve the health of the public.

5. Challenges in identifying, selecting, and refining topics for comparative effectiveness systematic reviews in AHRQ’s EHC program

One of the main challenges we face as we move forward is to ensure that we have engaged the most important perspectives since, due to issues of timeliness and cost, we cannot engage all types of stakeholders at each step for every topic. Our goal is to continue to develop a system that fairly represents the range of interests of all stakeholders across all aspects of the program (Fig. 2), yet that results in timely and clear reports that are useful to decision makers and other audiences. For topic identification and refinement, this process is complicated by the large range of potential stakeholder perspectives for any given topic, by the wide-reaching clinical breadth of potential topics for the EHC program, and by very short timeframes that are inherent in a program seeking to be publicly responsive and accountable. This tension between maintaining the relevance and rigor of research while being responsive to questions in a timely manner is an ongoing challenge.

A related challenge is gaining sufficient detail from nominators and stakeholders to allow topics to be adequately defined in order to be prioritized. We have recently revised our web-based nomination system (http://effectivehealthcare.ahrq.gov/), but have found it necessary to define a minimum set of information necessary to understand a topic nomination sufficiently to develop it for explicit prioritization activities. This minimum set of information includes the populations, interventions, comparators, and outcomes of interest to the nominator, as well as the policy and/or clinical context. If any of these components is not clear in the nomination, we must have the ability to contact the nominator for more information. Because many web-based nominations occur anonymously and resource constraints prevent us from contacting every nominator to clarify all unclear topics, some good nominations may be missed simply because they are unclear.

Another challenging area is the relatively subjective nature of decision making around topic prioritization and the sometimes highly political ramifications of these decisions. When one ventures into the realm of relative value or worth, considerations are particularly less objective and more subject to bias. To address this challenge, we have structured our topic prioritization process to consistently consider the same program criteria for every potential topic in the same hierarchical order. We consider objective evidence and use that as a basis for the more subjective aspects of our prioritization process. However, only process evaluation will enable us to determine if this approach assists us in fairly selecting topics for research among viable and valuable candidates.

Further experience in making this process and its results more transparent will undoubtedly raise unforeseen challenges as we seek to balance the range of perspectives that are likely to be expressed, and to do so while minimizing conflicts of interest.

Prioritization of research is a necessity from a practical and a societal perception standpoint. We must make a commitment to target scarce research dollars and efforts to those areas where there will be the greatest impact and where there is a gap in needed research. Given the level of interest in evidence-based policy and practice and the volume of uncoordinated effort internationally, we are also working to more closely track the systematic review and policy-related activities of other programs, federal agencies, and researchers. Enhanced coordination with others involved in setting topic priorities or in conducting analogous research is intended to reduce the opportunities for duplication. Such efforts would be greatly assisted by international registries of
Table 7
Issues that technical expert groups address during topic development

1. Focusing research questions for systematic review
   - Who are the populations and clinical subgroups of interest?
   - Why might clinical variation exist, especially if evidence-based guidelines are readily available?
   - What specific patient characteristics may affect outcomes?
   - Which interventions should be compared (leading to an understanding of why)?
   - What is the potential impact of intervention on patients?
   - What are the therapeutic aims of treatment?
   - Which outcomes (intended and unintended effects) are relevant, including timing?

2. Clarifying clinical theories and beliefs underlying practice variation
   “...Every review, just like every intervention, is based on a theory... Systematic reviews gather evidence to assess whether the expected effect of an intervention does indeed occur.” (Cochrane Manual) [19]

Understanding the clinical logic underlying claims about comparative effectiveness is an important goal of topic development. Interviews with technical experts aim to answer questions such as:
   - Why do proponents of one or another treatment believe it is better?
   - When and for whom?
   - What characteristics of the alternative treatments are likely to drive choices?

The following examples illustrate how beliefs are linked to clinical theories:

**Belief:** Newer antiserotonergic drugs are likely to be better for glycemic control of diabetes than are sulfonylureas.

**Theory:** Sulfonylureas have been disappointing, and their use has not brought about a meaningful reduction in the risk of macrovascular complications. They may, in fact, be implicated in progression of diabetes, and they make it difficult to lose weight. Newer classes of drugs may result in better long-term outcomes because they have a better metabolic profile.

**Context:** Proponents of the new drugs do not base their claim of superiority on evidence about short-term glycemic control. The belief that the new drug will have an advantage is based on the understanding of how diabetes progresses; how the new drug works; and evidence from short-term efficacy trials about effects on lipid levels, weight gain, and other metabolic markers.

**Belief:** A new long-acting opioid drug for relief of pain is likely to play an important role in chronic pain treatment.

**Theory:** Because of tolerance and individual differences in response, chronic pain patients may have more consistent and prolonged symptom relief when several long-acting opioid medications are used in rotation.

**Context:** The belief that the new drug has an advantage is based on the fact that it has a long half-life, rather than on how the likelihood and degree of pain relief and the frequency and severity of side effects compare with alternatives. The review may want to focus on evidence about how this drug performs as a part of an opioid rotation regimen rather than as the sole or initial treatment for chronic pain.

planned, in process, and completed comparative effectiveness and other systematic reviews.

Although still not a precise science, attempting to standardize and evaluate a structured process of setting research priorities for comparative effectiveness systematic reviews will further the goal of linking research to the actual needs of health care decision makers. Finding innovative and effective ways to increase the participation of health care decision makers in priority setting and the research process is required to bring real-world perspective and the hope of greater relevancy of findings to the needs of decision makers.

References


