

Continuous Patient Engagement in Comparative Effectiveness Research

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THE GOAL OF COMPARATIVE EFFECTIVENESS RESEARCH (CER) is to provide patients, their advocates and caregivers, health care professionals, federal officials, policy makers, and payers with evidence-based information to make informed health care decisions.^{1,2} Previously, CER studies were designed by researchers and had relatively little input from patients. Patient engagement has rapidly gained acceptance as crucial to the successful translation of CER for all interested parties.³ Experiences with patient engagement in research, including community-based participatory research,⁴ suggest that success hinges on patients being interested and emotionally involved in the research question and understanding their role in the CER process.

Evaluation of information from the Agency for Healthcare Research and Quality and the Patient-Centered Outcomes Research Institute suggests that CER may be enhanced through continuous patient engagement. The framework for doing so, as proposed in this Viewpoint, reflects pragmatic experiences and observations in which patient engagement has helped to shape and translate CER for patients and health care professionals; however, the framework needs to be tested empirically (FIGURE). This proposed 10-step process for CER describes how patient engagement might guide CER toward patient-centered outcomes research and offers suggestions for the process and purpose of patient engagement across the 10 steps. Each step has different purposes, advantages and disadvantages, and implications for time and resources. The proposed framework is intended to span the entire “life cycle” of a CER project.

At the first step, patients could help identify understudied CER topics. By soliciting input from diverse patients, the process could generate a broad array of topics, from which a more narrow focus could be achieved by framing specific research questions. When designing a potential framework for a specific CER question, patients would provide a “reality check,” indicating the extent to which the proposed framework reflects their personal experiences.

When CER involves primary data collection, patient input could help determine the best practices for data collection, provide input about the proposed content of the data

collection tool, and participate in pilot testing survey items. Traditionally, patient feedback is infrequently used during the development of the analysis plan. However, this framework proposes that patients could assist in helping to define or categorize variables even if they do not have training in research methods. When reviewing and interpreting results, patients could reflect on whether results are plausible and believable, what other factors should be considered, and how results may vary across subgroups of patients.

In the translation phase, patients could identify which results are easy or difficult to understand. If the results do not affect patients or are counterintuitive, CER findings will not be translated into medical practice. Patients could also offer suggestions for how best to explain study findings to other patients. Patients could help determine the best dissemination strategies, provide dissemination channels, and craft specific messages targeted to patients who will benefit most.

Thoughtful consideration should be given to determining which approach would best elicit the patient’s perspective at each particular step. For example, during the early stages of research, it may be most beneficial to engage patients through patient forums or telephone conversations to solicit potential topics of importance. As research progresses to protocol development, involving patients in stakeholder meetings could provide an opportunity for robust discussion regarding which outcomes to assess, populations to include, and treatment options to compare.⁵ Input on the patient experience also could be obtained from indirect means of engagement. For example, using online patient forums in which groups of patients talk about their disease may be a source of valuable information provided the process adheres to ethical standards of protection of human research participants.^{6,7}

When creating the conceptual framework, collecting data, and specifying the analysis plan, more in-depth information and patient input may be required. Methods of engagement such as in-person meetings, focus groups, and individual patient interviews could allow patients to give more detailed input. Patients could assist in framing the message, creating plain language summaries, targeting audi-

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Figure. Enhancement of Comparative Effectiveness Research (CER) Through Continuous Patient Engagement

Step in CER Process	Purpose of Patient Engagement
Topic solicitation	<ul style="list-style-type: none"> Identify topics that are important to patients, caregivers, and the community Propose topics to be investigated
Prioritization	<ul style="list-style-type: none"> Solicit feedback on relevance and priority of topics Discuss the urgency of addressing topics
Framing the question	<ul style="list-style-type: none"> Ascertain questions' relevance and usefulness Assess "real-world" applicability
Selection of comparators and outcomes	<ul style="list-style-type: none"> Identify comparator treatments of interest Identify outcomes of interest Incorporate other aspects of treatment
Creation of conceptual framework	<ul style="list-style-type: none"> Provide a "reality check" Verify logic of conceptual framework Supplement with additional factors not documented in the literature
Analysis plan	<ul style="list-style-type: none"> Verify importance of factors and variables Ascertain whether there is a good proxy for a specific concept Inquire about potential confounding factors
Data collection	<ul style="list-style-type: none"> Determine best approaches for data collection (eg, trial, registry, medical charts) Assist with selection of data sources
Reviewing and interpreting results	<ul style="list-style-type: none"> Assess believability of results Suggest alternative explanations or approaches Provide input for sensitivity analysis
Translation	<ul style="list-style-type: none"> Interpret results to be meaningful Document which results are easy or difficult to understand Indicate which results are counterintuitive
Dissemination	<ul style="list-style-type: none"> Facilitate engagement of other patients Help other patients to understand findings

ences for dissemination efforts, and critiquing draft materials (eg, patient guides). However, these encounters should be supplemented by targeting patient advocacy organizations, media, social media, and patient navigators (peer counselors who help patients navigate through the complex health care system) to link patients with appropriate resources.⁸ It would be important to communicate how patient input will be used so that patients remain engaged even when CER results do not answer all their questions.

Involving patients' perspectives would most likely make CER more meaningful and, therefore, potentially more useful. Nonetheless, including patients could pose substantial challenges. For example, in prioritizing research questions or selecting outcomes, different patients will want different questions answered and different outcomes to be measured. One solution could be to select patient representatives who are connected with a greater patient community (eg, through advocacy organizations) and able to discuss broad concerns of interest to diverse patients, not just for themselves or their special interests. It also is important to address real and potential conflicts of interest. Ultimately, principal investigators would be wise to develop partner-

ships with patients and their physicians, advocates, and caregivers, but should maintain authority in developing protocols to ensure scientific rigor. Patient engagement is a dynamic process and the relative amounts of time spent and costs incurred will depend on several factors, including the techniques, duration, and intensity of patient engagement. Despite the potential advantages and that there likely will be efficiencies over time as researchers learn how to engage patients in CER, patient engagement is likely to increase the cost and length of time to plan and conduct CER. As such, complete and meaningful patient engagement may be affected by the availability of funding and resources.

Best practices for patient engagement in CER will continue to evolve. A systematic approach for eliciting patient input could serve to promote a more patient-centered approach to CER despite many challenges. Incorporating input from a variety of patients would help provide insights for producing CER results that go beyond "average treatment effects" and produce results that are applicable to specific patient subgroups.⁹ Engaging patients in CER will require additional effort compared with the traditional research process; however, if done well, engaging patients in this process could provide patient-centered outcomes research evidence that is useful and informative at the level of clinical practice and decision making.

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SPECIAL REPORT

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Stakeholder engagement for comparative effectiveness research in cancer care: experience of the DEcIDE Cancer Consortium

Stakeholder input is a critical component of comparative effectiveness research. To ensure that the research activities of the Developing Evidence to Inform Decisions about Effectiveness (DEcIDE) Network, supported by the Agency for Healthcare Research and Quality, translate into the greatest impact for everyday practice and policy-making in cancer, we were tasked with soliciting stakeholder input regarding priority areas in cancer-related comparative effectiveness research for the DEcIDE Cancer Consortium. Given the increasing emphasis on stakeholder engagement in research, many investigators are facing a similar task, yet there is limited literature to guide such efforts, particularly in cancer care. To help fill this gap, we present our approach to operationalizing stakeholder engagement and discuss it in the context of other recent developments in the area. We describe challenges encountered in convening stakeholders from multiple vantage points to prioritize topics and strategies used to mitigate these barriers. We offer several recommendations regarding how to best solicit stakeholder input to inform comparative effectiveness research in cancer care. These recommendations can inform other initiatives currently facing the challenges of engaging stakeholders in priority setting for cancer.

KEYWORDS: cancer ■ CER ■ comparative effectiveness research ■ stakeholder

The 2009 Federal Coordinating Council's Report to the President and Congress on comparative effectiveness research (CER) outlined stakeholder engagement as a core component [101]. A stakeholder can be defined as: "an individual or group who is responsible for, or affected by, health- and healthcare-related decisions that can be informed by research evidence" [1]. Stakeholder groups with an interest in the success of CER broadly include patients, providers, payers and policy-makers. By allowing these frontline actors in the American healthcare system to drive the research agenda, the hope is that valuable resources will be allocated to those research questions with the greatest potential to impact clinical practice and health policy. Stakeholder engagement has quickly become a major component of the health services research enterprise, with little practical experience on which to base such activities.

The mission of the Agency for Healthcare Research and Quality (AHRQ) is to improve the quality, safety, efficiency and effectiveness of healthcare for all Americans by supporting research that helps people make more informed decisions and improves the quality of healthcare services [102]. To that end, AHRQ created the Developing Evidence to Inform Decisions about Effectiveness (DEcIDE) Research Network to conduct patient-centered outcomes research including studies on comparative clinical effectiveness in four major disease areas: cancer, diabetes, cardiovascular health and mental health. As the coordinating center for the DEcIDE Cancer Consortium (Can-DEcIDE), we were charged with engaging stakeholders



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to help set the agenda for high-quality cancer research that contributes to the evidence base and informs decision-making.

This is one of the first federally funded initiatives to operationalize stakeholder engagement as a core tenet of the research program. Given the apparent critical role that stakeholder engagement will play in the future of comparative effectiveness and other patient-centered outcomes research, we describe our initial approach to stakeholder engagement, as well as the limitations that were identified and the refinements that were implemented in future years. The lessons from our experience can inform the development of stakeholder engagement initiatives throughout the cancer research community.

At the inception of our initiative, there was little published on stakeholder engagement in health services research. Previously used stakeholder engagement methods and techniques include identifying stakeholders based on their interests and influence, developing a strategy that allows each stakeholder to actively participate, and establishing a clear, continuous communication plan [2,3,103]. While stakeholder engagement is well documented in fields, such as environmental science [4,104], the role of the stakeholders in CER [5], and cancer-related CER in particular [105,106], remained largely undefined. Since that time, the Patient-Centered Outcome Research Institute (PCORI) and several other groups have published recommendations for stakeholder engagement [1,5,6,105,107]. While none offer specific recommendations on how to operationalize stakeholder engagement, each proposes core principles and advocates for adaptation to individual disciplines, programs or projects. The PCORI Methodology Report in particular acknowledges that stakeholder engagement is novel and encourages individuals to publish their experiences, recognizing that there is no one-size-fits-all approach [107].

Initial stakeholder engagement

■ Participants

In 2010, the first annual Can-DEcIDE Stakeholder Meeting was held at AHRQ headquarters. Stakeholder representatives from the National Cancer Institute (NCI), Centers for Medicare and Medicaid Services (CMS), New York State Department of Health (state Department of Health representation), District of Columbia Department of Healthcare Finance (Medicaid representation), American Society of Clinical

Oncology, American Cancer Society, American College of Surgeons, Oncology Nursing Society, American Society for Radiation Oncology, and the National Coalition for Cancer Survivorship were present for the meeting. While the stakeholders were the key participants, representatives from AHRQ and Can-DEcIDE were present to facilitate the meeting and provide scientific content, support and expertise.

■ Orientation & context

Background reading on CER was distributed to attendees in advance of the meeting, but no potential topics in cancer-related CER were distributed or solicited prior to the meeting. The stakeholder meeting started with formal presentations to orientate the stakeholders and provide context for the discussion by: introducing the AHRQ Effective Healthcare Program [108], and the Can-DEcIDE and its ongoing initiatives; providing a definition of the term ‘comparative effectiveness research’; and giving an overview of CER as a national priority by introducing both the Institute of Medicine [109] and Federal Coordinating Council’s Report [101]. During this introduction, the Population, Intervention, Comparator and Outcome (PICO) framework [7] was introduced with several hypothetical illustrative examples developed by the Can-DEcIDE team.

■ Topic generation & prioritization

The stakeholders were divided into working groups to brainstorm new CER topics in cancer using the PICO format. The entire stakeholder panel then participated in a number of ranking exercises that took place based on the following metrics: potential impact on mortality, morbidity and suffering; potential impact on quality of care (based on Institute of Medicine definition [109]); potential impact on specific stakeholder group; degree of uncertainty; and feasibility. This framework includes many of the research prioritization factors later offered in the PCORI Methodology Report [107]. These include: disease incidence, prevalence and burden; gaps in evidence in terms of clinical outcomes, practice variation and health disparities; potential for new evidence to improve health, wellbeing and the quality of care; effect on national expenditures associated with a healthcare treatment, strategy or health conditions; patient needs, outcomes and preferences; relevance to patients and

clinicians in making informed health decisions; and priorities in the National Strategy for Quality Care.

■ Continued engagement

Topics identified as a result of the 2010 stakeholder meeting were developed into one-page project proposals and presented to the stakeholders for final prioritization and feedback via an email survey. Ultimately, two topics were deemed highest priority in cancer-related CER by stakeholders (Box 1).

Limitations with the initial approach

While the 2010 stakeholder engagement activities were successful in meeting our goal of identifying specific priority areas in cancer-related CER, we encountered several challenges.

■ Spectrum of cancer not well represented

We were focused on ensuring that all categories of stakeholders and professional disciplines were at the table, but did not recognize the importance of ensuring adequate clinical representation based on cancer disease sites (e.g., lung and breast) and time points across the cancer continuum (e.g., diagnosis, active treatment, surveillance and end-of-life). Clinical expertise was limited to those cancers for which representatives were in the room by virtue of their representation of a specialty society or federal partner. This was also true of the patient advocate involvement. It became apparent that we needed a larger group than could be managed at one meeting.

■ Task not matched to appropriate stakeholder

By holding only one all-inclusive meeting, we did not aptly match each task to the appropriate stakeholder group [106]. For example, while all stakeholder groups offer great insights into the identification and prioritization of topics, practicing caregivers and researchers are in the best position to operationalize these research topics. As a result, we left the 2010 meeting with overly broad topics that could not be feasibly addressed in a single protocol.

The need to expand our stakeholder list to include researchers was also recognized by Concannon and colleagues in a 2012 publication proposing a taxonomy for stakeholder engagement [1]. They identified seven stakeholder groups that should be considered for CER, termed the 7Ps: patients, providers, purchasers, payers, policy-makers, product makers and principal investigators (or researchers).

■ Biases & conflicts of interest

Some inherent difficulties arise when attempting to convene the 7Ps [1]. In addition to the challenges of balancing varying levels of expertise, there are complex issues related to conflicts of interest brought into these processes. While each stakeholder is inherently biased toward research that will benefit his or her stakeholder groups, we felt that this could be managed by broadening our inclusion of patients and clinicians representing a variety of clinical scenarios. While we remained cognizant

Box 1. Priority areas identified during 2010 stakeholder engagement activities.

Initial topics/areas identified

- Compare the effectiveness of continued care by an oncologist versus transfer to a PCP for surveillance and subsequent care of cancer survivors
- Compare the effectiveness of provider education versus preoperative tumor board conference on receipt of surgery and surgical outcomes for stage I pancreatic cancer
- Compare the effectiveness of radiation (IMRT, proton and brachytherapy) versus surgery (robotic and open) for the treatment of localized prostate cancer
- Compare the effectiveness of 'high-intensity care' provided at a comprehensive cancer center versus local hospital
- Compare the effectiveness of decision support tools for treatment or supportive cancer care in complex or elderly patients
- Compare the effectiveness of intensive radiologic surveillance versus symptom-driven follow-up for cancer survivors s/p curative treatment

Highest priority topics

- Compare the effectiveness of preoperative MRI to usual care in early-stage breast cancer
- Compare the effectiveness of routine versus symptom-driven surveillance in colorectal cancer

Topics operationalized

- None

IMRT: Intensity-modulated radiation therapy; PCP: Primary care physician; s/p: Status post.

of the importance of including ‘purchasers’ and ‘product makers’ in the process, we remained unclear on the best approach to do so [1].

■ The scope of meeting is too broad

We tried to combine too many tasks into one meeting. We asked stakeholders to identify, discuss, prioritize and operationalize cancer-related CER topics during a single, 1-day meeting. As a result, we were unable to adequately address the development of specific research projects from the topic proposals.

■ Identified topics difficult to operationalize

During the meeting, many of the topics focused on system-related issues that cut across cancer disease sites. This was consistent with the Institute of Medicine report ‘Initial National Priorities for Comparative Effectiveness Research’, where 50% of the topics were system-related issues [109]. This reflects the popular belief highlighted in the Institute of Medicine report that in the healthcare system, the ‘how’ and ‘where’ of treatment need to be discussed before the ‘what’. Additionally, there was significant discussion on the need to focus on the logistics and infrastructure required for CER in cancer, rather than on specific clinical problems, consistent with the Federal Coordinating Council’s report [101]. While these broad topics are clearly of great national priority and the need for infrastructure is apparent, our goal was to identify and prioritize feasible and discrete research projects.

■ Poor stakeholder engagement via email

The feedback loop is extremely important. Following-up with stakeholders via an email survey was only moderately effective, as the response rate was 50%. In 2010, Hoffman and colleagues proposed several principles for stakeholder engagement in CER, including the need to get participants to ‘buy in’ to the process and keep participants engaged throughout the research process [8]. Our attempt at electronic communication failed to meet these objectives.

Refined stakeholder engagement mechanism

In order to address these issues, in the following year we convened a three-part stakeholder meeting series by utilizing two separate forums – one focused on clinicians and researchers and one that included federal partners and payers. Given the critical role of patients, we included patient advocacy groups in both forums.

■ Meeting one out of three: topic identification

In order to engage the full array of clinicians, patient advocates and professional society stakeholders, we utilized the already established infrastructure of the Cancer and Leukemia Group B (CALGB; now The Alliance for Clinical Trials in Oncology, a collaborative effort of CALGB and two other cancer cooperative groups), a national clinical research cooperative group sponsored by the NCI [110]. We held the first meeting at the Spring CALGB Meeting, where clinicians, patient advocates and researchers from all cancer disciplines were already in attendance, allowing us to have a broader representation of the multidisciplinary continuum of cancer care and avoid additional travel for stakeholders.

All CALGB members (including medical oncology, nursing, surgery, radiation oncology, radiology, pathology and patient advocacy) were invited to participate in 2011 stakeholder activities aimed at identifying and prioritizing cancer-related CER topics important to their discipline. The primary goal of the first meeting was to identify topics for CER in cancer. This meeting resulted in the identification of ten critical cancer-related CER areas (Box 2).

■ Meeting two out of three: topic prioritization

Several weeks later, we gathered payer, federal partner and patient advocate stakeholders at a hotel conference center near AHRQ headquarters. Stakeholders representing Aetna, TRICARE®, Kaiser Permanente, CMS, DC Department of Healthcare Finance, NCI, Patient Advocates In Research (PAIR) and the US FDA attended the meeting.

After a brief introduction and orientation, we presented the ten topics identified during the first stakeholder meeting and opened the floor for discussion, inviting feedback and the introduction of additional topics in cancer-related CER, leading to the identification of 11 additional topic areas (Box 2).

In order to prioritize topics, we performed three different ranking exercises:

- Group discussion: an independent, third-party moderator (also identified by Hoffman *et al.*) [8] led a group discussion aimed at eliminating the topics of lowest priority and highlighting the topics of greatest priority;
- Scoring metrics: each stakeholder was given a worksheet and asked to score the topics on a

scale of 1 (least) to 5 (most) in the same five categories utilized in 2010 – potential impact on mortality, morbidity and suffering; on quality of care; on specific stakeholder group; degree of uncertainty about approach; and on feasibility;

- Final ranking: each stakeholder was asked to list his/her top six cancer-related CER topics in order from highest priority to lowest priority based on the viewpoint of his/her respective stakeholder constituency. This process resulted in the prioritization of seven key cancer-related CER areas as presented in **Box 2**.

■ Meeting three out of three: operationalization

These seven most-highly ranked key cancer-related CER areas were brought back to the next CALGB meeting for final prioritization and assessment of feasibility as a specific research project. Stakeholder representatives from surgery, medical oncology, radiation oncology, geriatrics, pharmacy, epidemiology and patient advocacy participated in group discussions, scoring metrics, operationalization and a final ranking, yielding the following topic of highest priority: surveillance approaches following active treatment for cancer – a critical target for CER.

Conclusion & future perspective

In an attempt to overcome the challenges faced during our initial stakeholder engagement activities, we made several improvements (**Box 3**). First, we held a three-part meeting series in which we solicited the input of those stakeholders involved in the front-line care of cancer patients (clinicians, cancer researchers and patients) separately from the input of those involved on the policy and payment side (payers, federal partners and patient advocacy). We also assigned each task to the appropriate stakeholder group. Priority topic areas were identified by those stakeholders with the most intimate knowledge of the dilemmas faced in the everyday care of cancer patients. Payer, federal partner and patient advocate stakeholders reacted to these previously identified topics and identified additional areas critical from their viewpoint. Clinician, patient advocate and research stakeholders completed a final prioritization of topics in cancer-related CER and discussed ways to operationalize these high-priority topics. By utilizing the three-part stakeholder mechanism feedback loop, we increased overall communication

Box 2. Priority areas identified during 2011 stakeholder engagement activities.

Initial topics/areas identified

- Meeting one out of three
 - CER of follow-up regimens/surveillance/scanning intervals across various cancer types
 - AIs versus tamoxifen
 - New drugs versus standard-of-care drugs
 - Metastases resection versus chemotherapy
 - Management of pleural effusion
 - Health disparities among the elderly
 - Off-label drug use
 - First-line lymphoma therapies
 - Various brain tumor therapies
 - Generics versus name-brand medications
- Meeting two out of three
 - Environmental exposure
 - Compressed treatments to return to regular activity level
 - Head-to-head comparison of drugs
 - Ethnic differences in drug response
 - Physical activity after diagnosis
 - Develop data capacity for CER in cancer care
 - Quality of life
 - Comorbidity impact on cancer care
 - Long-term survival issues
 - Comorbidities and relaxed eligibility criteria in clinical trials
 - Supportive palliative care
- Meeting three out of three
 - N/A

Highest-priority topics

- Meeting one out of three
 - N/A
- Meeting two out of three
 - Surveillance
 - Treatment that leads to full function most effectively
 - Off-label drug use
 - Long-term outcomes in cancer care
 - End-of-life
 - Ethnic and biological disparities
 - Cancer care for children in Medicaid
- Meeting three out of three
 - Post-treatment surveillance
 - Cancer care for the elderly/disabled
 - End-of-life cancer care/symptom intervention

Topics operationalized

- Meeting one out of three
 - N/A
- Meeting two out of three
 - N/A
- Meeting three out of three
 - Post-treatment surveillance (specifically, the need to address gaps in treatment guidelines)

AI: Aromatase inhibitor; CER: Comparative effectiveness research; N/A: Not applicable.

with stakeholders and minimized the need for email communication without increasing travel requirements.

Box 3. Evolution of the DEcIDE Cancer Consortium stakeholder engagement model over time.

Goals

- 2010 model
 - Set cancer-related CER agenda
 - Identify topics
 - Prioritize topics
 - Develop two specific research protocols
- 2011 model
 - Set cancer-related CER agenda
 - Identify topics
 - Prioritize topics
 - Operationalize topics and ensure feasibility
- Future model
 - Set cancer-related CER agenda
 - Identify topics
 - Prioritize topics
 - Operationalize topics and ensure feasibility

Attendees

- 2010 model
 - National Cancer Institute
 - Centers for Medicare and Medicaid Services
 - New York State Department of Health
 - District of Columbia Department of Healthcare Finance
 - American Society of Clinical Oncology
 - American Cancer Society
 - American College of Surgeons
 - Oncology Nursing Society
 - American Society for Radiation Oncology
 - National Coalition for Cancer Survivorship
- 2011 model
 - Meeting one: clinicians (nurses, medical oncologists, pathologists, radiologists and surgeons), patient advocates and professional societies
 - Meeting two: payers, federal partners and patient advocates
 - Meeting three: clinicians, patient advocates and professional societies
- Future model
 - Include 'product makers' [1]
 - Demarcate professional societies more clearly
 - Include noncancer patients and/or 'healthy volunteer' stakeholders in addition to patient advocates who are already represented

Activities to engage

- 2010 model
 - Small group discussions
 - Priority ranking activity
- 2011 model
 - Large group discussions
 - Worksheets (responses anonymous)
- Future model
 - Large group discussions
 - Worksheets (responses anonymous)

Setting

- 2010 model
 - One master meeting (all stakeholder types together)
 - Follow-up email

AHRQ: Agency for Healthcare Research and Quality; CER: Comparative effectiveness research.

Box 3. Evolution of the DEcIDE Cancer Consortium stakeholder engagement model over time (cont.).**Setting (cont.)**

- 2011 model
 - Three part meeting series
- Future model
 - Three part meeting series

Logistics

- 2010 model
 - No third-party moderator/facilitator
 - In-person meeting at AHRQ
 - Follow-up via email
- 2011 model
 - Used third party moderator/facilitator
 - Series of in-person meetings at hotels
 - Utilized existing infrastructure of cancer cooperative groups
- Future model
 - Use third-party moderator/facilitator
 - Supplement with webinar or email communications
 - Utilize existing infrastructure of cancer cooperative groups

AHRQ: Agency for Healthcare Research and Quality; CER: Comparative effectiveness research.

To ease the logistical and cost-related barriers to three meetings per year and to ensure broad representation of the many facets of cancer care, we utilized the already established infrastructure of CALGB (now the Alliance for Clinical Trials in Oncology [110]). The Alliance for Clinical Trials in Oncology is an NCI-sponsored cooperative group. Clinician leaders from a consortium of major academic medical centers, as well as members from community practice and minority-focused community-based practice, gather at least two-times per year to plan clinical trials. Patient advocates are represented on all committees. To overcome the logistical challenges inherent in convening multidisciplinary stakeholders for the specific purpose of generating topics in cancer-related CER, we integrated CER topic prioritization into clinical trial planning meetings. Accordingly, the first and third meetings of our stakeholder engagement series were held at the multiannual Alliance conferences, offering us the unique opportunity to engage stakeholders from all disciplines across the continuum of cancer care. Patient and clinician stakeholders were familiar with the task since the processes used to generate, vet and review ideas for efficacy studies are not fundamentally dissimilar to the approach we outline for effectiveness studies. Moreover, the practical advantages of leveraging a preassembled and organized group enabled efficient use of time and resources.

Partnering with the NCI Clinical Trials Cooperative Groups offers many advantages. While the infrastructure of the cooperative groups was built to support large, multi-institutional efficacy trials, it can also be leveraged to facilitate stakeholder engagement, as well as retrospective and prospective CER with the potential for a profound impact on cancer care. This infrastructure facilitates the collaboration of patients, providers, policy-makers, researchers and federal partners throughout the scientific process, which is required for truly stakeholder-driven research. Finding similar ways to leverage existing research infrastructure for CER in other disease areas can help to mitigate the costs associated with this type of research.

Based on our experiences and a review of the literature, we offer the following recommendations when attempting to solicit stakeholder input for CER in cancer:

- Patients and frontline providers are in the best position to identify the most pressing clinical questions faced in everyday practice;
- Given the vast array of disciplines, cancer sites and points across the cancer continuum that require representation, separate forums for clinicians/researchers and payers/policy-makers offer the opportunity to ensure all stakeholders are represented, while keeping the groups small enough to facilitate meaningful discussion and

participation. Patient stakeholders should be present at both meetings;

- The most important component of successful stakeholder engagement is maintaining an ongoing dialogue via recurring meetings supplemented by email updates;
- It is beneficial to come to the table with some specific potential priority topics already in hand. This will facilitate the discussion and optimize productivity.

Challenges that still need to be addressed include how to best incorporate the stakeholder input of ‘product makers’ [1]. Furthermore, including noncancer patients and/or ‘healthy volunteer’ stakeholders in future meetings, in addition to patient advocates who are already represented, may contribute to an unbiased view and add value, particularly related to topics such as cancer screening. With time, cost and travel restrictions, a webinar-based stakeholder engagement mechanism may prove to be beneficial in the future but must be weighed against the loss of face-to-face communication. Partnering with existing organizations, as we did with the CALGB, offers a unique opportunity that may benefit both parties. Finally, while we acknowledge that stakeholder input on the conduct of cost–effectiveness research is important, discussion of cost–effectiveness was outside the scope of the stakeholder engagement activities at hand, which focus on comparative clinical effectiveness. The relationship between CER and cost–effectiveness is nonetheless an important, but politically charged, issue that will need to be addressed [9].

The focus of this initiative was to identify priority topics for AHRQ as it continues to

set its cancer-specific agenda in CER. As such, the content of the discussion is focused on stakeholder engagement in topic generation and prioritization. We do, however, want to emphasize the philosophy that stakeholder involvement is an ongoing process that spans research topic conception, prioritization, operationalization, completion and beyond to dissemination of results and implementation of practice and policy change. Much work needs to be carried out to fully integrate stakeholders into the scientific process, but we believe that we have made important first steps. We suggest that coordination of federal efforts by integrating clinical trial networks charged with designing efficacy studies and those focused on effectiveness research is especially strategic. Leveraging this existing infrastructure should help to engage a broad panel of informed stakeholders with representation from patients and clinicians from diverse practice settings across the USA. In addition, we suggest that this integration of topic generation and prioritization could be adapted outside of cancer.

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Executive summary

- Stakeholder input is a critical component of comparative effectiveness research.
- The primary aim was to engage stakeholders to help set the agenda for high-quality cancer research that contributes to the evidence base and informs decision-making.
- Our 2010 single-stakeholder engagement meeting presented several challenges: the spectrum of cancer was not well represented; tasks were not matched to appropriate stakeholders; biases and conflicts of interest were challenging to manage; the scope of the meeting was too broad; the identified topics were difficult to operationalize; and the stakeholder engagement via email was poor.
- In 2011, we conducted a three-part meeting series in which we solicited the input of those stakeholders involved in the frontline care of cancer patients (clinicians, cancer researchers and patients) separately from the input of those involved on the policy and payment side (payers, federal partners and patient advocacy), and partnered with the Cancer and Leukemia Group B (now the Alliance) to ease logistical and cost barriers.
- In the future, one may want to consider including ‘healthy volunteer’ stakeholders or conducting webinar-based stakeholder meetings.

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The authors of the report are responsible for its content. Statements in the report should not be construed as endorsement by the Agency for Healthcare Research and Quality or the US Department of Health and Human Services.

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Continuous Patient Engagement in Comparative Effectiveness Research

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THE GOAL OF COMPARATIVE EFFECTIVENESS RESEARCH (CER) is to provide patients, their advocates and caregivers, health care professionals, federal officials, policy makers, and payers with evidence-based information to make informed health care decisions.^{1,2} Previously, CER studies were designed by researchers and had relatively little input from patients. Patient engagement has rapidly gained acceptance as crucial to the successful translation of CER for all interested parties.³ Experiences with patient engagement in research, including community-based participatory research,⁴ suggest that success hinges on patients being interested and emotionally involved in the research question and understanding their role in the CER process.

Evaluation of information from the Agency for Healthcare Research and Quality and the Patient-Centered Outcomes Research Institute suggests that CER may be enhanced through continuous patient engagement. The framework for doing so, as proposed in this Viewpoint, reflects pragmatic experiences and observations in which patient engagement has helped to shape and translate CER for patients and health care professionals; however, the framework needs to be tested empirically (FIGURE). This proposed 10-step process for CER describes how patient engagement might guide CER toward patient-centered outcomes research and offers suggestions for the process and purpose of patient engagement across the 10 steps. Each step has different purposes, advantages and disadvantages, and implications for time and resources. The proposed framework is intended to span the entire “life cycle” of a CER project.

At the first step, patients could help identify understudied CER topics. By soliciting input from diverse patients, the process could generate a broad array of topics, from which a more narrow focus could be achieved by framing specific research questions. When designing a potential framework for a specific CER question, patients would provide a “reality check,” indicating the extent to which the proposed framework reflects their personal experiences.

When CER involves primary data collection, patient input could help determine the best practices for data collection, provide input about the proposed content of the data

collection tool, and participate in pilot testing survey items. Traditionally, patient feedback is infrequently used during the development of the analysis plan. However, this framework proposes that patients could assist in helping to define or categorize variables even if they do not have training in research methods. When reviewing and interpreting results, patients could reflect on whether results are plausible and believable, what other factors should be considered, and how results may vary across subgroups of patients.

In the translation phase, patients could identify which results are easy or difficult to understand. If the results do not affect patients or are counterintuitive, CER findings will not be translated into medical practice. Patients could also offer suggestions for how best to explain study findings to other patients. Patients could help determine the best dissemination strategies, provide dissemination channels, and craft specific messages targeted to patients who will benefit most.

Thoughtful consideration should be given to determining which approach would best elicit the patient's perspective at each particular step. For example, during the early stages of research, it may be most beneficial to engage patients through patient forums or telephone conversations to solicit potential topics of importance. As research progresses to protocol development, involving patients in stakeholder meetings could provide an opportunity for robust discussion regarding which outcomes to assess, populations to include, and treatment options to compare.⁵ Input on the patient experience also could be obtained from indirect means of engagement. For example, using online patient forums in which groups of patients talk about their disease may be a source of valuable information provided the process adheres to ethical standards of protection of human research participants.^{6,7}

When creating the conceptual framework, collecting data, and specifying the analysis plan, more in-depth information and patient input may be required. Methods of engagement such as in-person meetings, focus groups, and individual patient interviews could allow patients to give more detailed input. Patients could assist in framing the message, creating plain language summaries, targeting audi-

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Figure. Enhancement of Comparative Effectiveness Research (CER) Through Continuous Patient Engagement

Step in CER Process	Purpose of Patient Engagement
Topic solicitation	<ul style="list-style-type: none"> ■ Identify topics that are important to patients, caregivers, and the community ■ Propose topics to be investigated
Prioritization	<ul style="list-style-type: none"> ■ Solicit feedback on relevance and priority of topics ■ Discuss the urgency of addressing topics
Framing the question	<ul style="list-style-type: none"> ■ Ascertain questions' relevance and usefulness ■ Assess "real-world" applicability
Selection of comparators and outcomes	<ul style="list-style-type: none"> ■ Identify comparator treatments of interest ■ Identify outcomes of interest ■ Incorporate other aspects of treatment
Creation of conceptual framework	<ul style="list-style-type: none"> ■ Provide a "reality check" ■ Verify logic of conceptual framework ■ Supplement with additional factors not documented in the literature
Analysis plan	<ul style="list-style-type: none"> ■ Verify importance of factors and variables ■ Ascertain whether there is a good proxy for a specific concept ■ Inquire about potential confounding factors
Data collection	<ul style="list-style-type: none"> ■ Determine best approaches for data collection (eg, trial, registry, medical charts) ■ Assist with selection of data sources
Reviewing and interpreting results	<ul style="list-style-type: none"> ■ Assess believability of results ■ Suggest alternative explanations or approaches ■ Provide input for sensitivity analysis
Translation	<ul style="list-style-type: none"> ■ Interpret results to be meaningful ■ Document which results are easy or difficult to understand ■ Indicate which results are counterintuitive
Dissemination	<ul style="list-style-type: none"> ■ Facilitate engagement of other patients ■ Help other patients to understand findings

ences for dissemination efforts, and critiquing draft materials (eg, patient guides). However, these encounters should be supplemented by targeting patient advocacy organizations, media, social media, and patient navigators (peer counselors who help patients navigate through the complex health care system) to link patients with appropriate resources.⁸ It would be important to communicate how patient input will be used so that patients remain engaged even when CER results do not answer all their questions.

Involving patients' perspectives would most likely make CER more meaningful and, therefore, potentially more useful. Nonetheless, including patients could pose substantial challenges. For example, in prioritizing research questions or selecting outcomes, different patients will want different questions answered and different outcomes to be measured. One solution could be to select patient representatives who are connected with a greater patient community (eg, through advocacy organizations) and able to discuss broad concerns of interest to diverse patients, not just for themselves or their special interests. It also is important to address real and potential conflicts of interest. Ultimately, principal investigators would be wise to develop partner-

ships with patients and their physicians, advocates, and caregivers, but should maintain authority in developing protocols to ensure scientific rigor. Patient engagement is a dynamic process and the relative amounts of time spent and costs incurred will depend on several factors, including the techniques, duration, and intensity of patient engagement. Despite the potential advantages and that there likely will be efficiencies over time as researchers learn how to engage patients in CER, patient engagement is likely to increase the cost and length of time to plan and conduct CER. As such, complete and meaningful patient engagement may be affected by the availability of funding and resources.

Best practices for patient engagement in CER will continue to evolve. A systematic approach for eliciting patient input could serve to promote a more patient-centered approach to CER despite many challenges. Incorporating input from a variety of patients would help provide insights for producing CER results that go beyond "average treatment effects" and produce results that are applicable to specific patient subgroups.⁹ Engaging patients in CER will require additional effort compared with the traditional research process; however, if done well, engaging patients in this process could provide patient-centered outcomes research evidence that is useful and informative at the level of clinical practice and decision making.

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Methodological Standards and Patient-Centeredness in Comparative Effectiveness Research

The PCORI Perspective

Methodology Committee of the Patient-Centered Outcomes Research Institute (PCORI)

METHODOLOGICAL STANDARDS AND PATIENT-CENTEREDNESS

Methodological standards can help ensure that comparative effectiveness research (CER) produces information that is meaningful, unbiased, timely, and actionable. This applies across the continuum of research design, implementation, analysis, and dissemination. Large investments are too often made in studies that provide poor-quality evidence,¹ are overtly biased,² are not applicable to most patients,³ or yield results that do not address the real concerns of individuals facing clinical decisions.^{4,5}

The central role of methodological standards in CER is reflected in the Patient Protection and Affordable Care Act signed into law in 2010, which created the Patient-Centered Outcomes Research Institute (PCORI). This legislation stipulates that PCORI include both a board of governors and a Methodology Committee.⁶ Although funding agencies have traditionally supported research in methodological standards, it has not been a discrete focus of any agency until the establishment of PCORI and its Methodology Committee.

 CME available online at www.jamaarchivescme.com and questions on p 1650.

Rigorous methodological standards help to ensure that medical research produces information that is valid and generalizable, and are essential in patient-centered outcomes research (PCOR). Patient-centeredness refers to the extent to which the preferences, decision-making needs, and characteristics of patients are addressed, and is the key characteristic differentiating PCOR from comparative effectiveness research. The Patient Protection and Affordable Care Act signed into law in 2010 created the Patient-Centered Outcomes Research Institute (PCORI), which includes an independent, federally appointed Methodology Committee. The Methodology Committee is charged to develop methodological standards for PCOR. The 4 general areas identified by the committee in which standards will be developed are (1) prioritizing research questions, (2) using appropriate study designs and analyses, (3) incorporating patient perspectives throughout the research continuum, and (4) fostering efficient dissemination and implementation of results. A Congressionally mandated PCORI methodology report (to be issued in its first iteration in May 2012) will begin to provide standards in each of these areas, and will inform future PCORI funding announcements and review criteria. The work of the Methodology Committee is intended to enable generation of information that is relevant and trustworthy for patients, and to enable decisions that improve patient-centered outcomes.

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The Methodology Committee is charged with developing methodological standards for patient-centered outcomes research (PCOR). These standards will be detailed in a Congressionally mandated methodology report to be issued in its first iteration in May 2012, and will inform PCORI's funding announcements and review criteria. Patient-centered outcomes research is distinguished from CER by its focus on patient-centeredness, which is determined by the extent to

which the decision-making needs, preferences, and characteristics of patients are addressed in diverse settings of health care.⁷ Engagement of patients at every step of the research process is viewed as essential, including in the selection of research ques-

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tions, study design, conduct, analysis, and implementation of findings. As such, the Methodology Committee is engaged in developing standards to support the validity and generalizability of research, as well as patient-centeredness.

WHERE METHODOLOGICAL STANDARDS ARE NEEDED

Two patient case studies are presented to illustrate disconnects between existing research and the preferences, needs, and characteristics of patients that can be addressed in the development of methodological standards for PCOR.

Mr B is a 78-year-old man with heart failure, diabetes, and renal failure (BOX 1). Although Mr B values his independence most, much of the existing research on care for patients with heart failure focuses on reductions in all-cause mortality and heart failure hospitalizations in highly selected patient populations. This care is now guideline-driven and represents the standard against which quality is judged.⁸ There is limited evidence about the best care for patients with multiple comorbidities or about care processes that facilitate out of hospital management with patient-centered goals.⁹ How can patient perspectives and preferences be integrated into the evidence-base and care processes? How confident can physicians be about the mortality benefits of current guideline-based care for patients with Mr B's complement of comorbidities?

Mr B's case demonstrates the importance of generating evidence that informs complex decisions. For example, multidisciplinary team models include physicians, nurses, pharmacists, psychologists, social workers, and nutritionists. Are these models or components of them capable of improving outcomes that matter to patients? Should approaches differ in urban vs rural areas like where Mr B lives, and if so, how?

Which study designs are both rigorous and feasible to address the challenges presented by a particular clinical

Box 1. A 78-Year-Old Man With Heart Failure, Diabetes, and Renal Failure

Mr B was admitted to his local hospital for the fourth time this year. Mr B experienced symptoms of shortness of breath and weight gain that led him to contact his physician, who recommended another hospitalization. He lives with his wife in a 2-story house located 30 miles from the hospital. He has recently been unable to climb the stairs to his bedroom. Mr B requires outpatient hemodialysis 3 times per week, but missed his last dialysis treatment because he felt too tired to go. This is his second hospital admission after missing a dialysis appointment. After each admission, Mr B received standard discharge instructions on how to care for himself at home. Mr B's highest priority is his independence, including the ability to drive and to remain in his own home.

scenario? Randomized controlled trials, cluster randomized trials, and quasi-experimental designs may be considered. How much can each type of design be trusted to yield a reliable answer for each aspect of a health care decision that may be applied to Mr B's case?¹⁰

Ms M is a 45-year-old woman with depression (BOX 2), whose situation similarly highlights the gap between existing research and the characteristics and concerns of patients. Little evidence exists about which sequence of treatments is optimal for Ms M's constellation of symptoms, adverse effects, or initial response. Despite more than 1000 trials on antidepressants and related treatments, most studies include patients with narrowly defined characteristics who are followed up for short periods, do not take place in settings in which care is routinely delivered, and include a limited spectrum of comparators, including drugs and other therapeutic approaches.¹¹ How can clinical research focusing on much larger, long-term issues yield more personalized guidance for patients like Ms M?¹²

An additional methodological issue raised by Ms M's case involves reporting bias, which can lead to erroneous conclusions about treatment success or failure.¹³ Commonly cited estimates of antidepressant remission based solely on published studies are discordant with estimates that include the results of unreported studies.¹⁴ Efforts to syn-

thesize evidence on multiple treatment options through network meta-analyses have yielded divergent conclusions, likely due to differences in eligibility criteria, outcome selection, and variable effects of biases in this field.^{15,16} What methods and standards can be developed to monitor and aggregate published and unreported study results?¹⁷

METHODS TO ENHANCE PCOR

The 4 general areas identified by the Methodology Committee in which standards for PCOR will be developed are (1) prioritizing research questions, (2) using appropriate study designs and analyses, (3) incorporating patient perspectives throughout the research continuum, and (4) fostering efficient dissemination and implementation of results (TABLE). These 4 areas are considered critical to address the types of limitations highlighted in the cases of Mr B and Ms M regardless of whether a topic involves prevention, diagnosis, treatment, or health care delivery systems. The directions envisioned by the Methodology Committee in these 4 areas are summarized herein, and serve as the basis of the methodology report.

Prioritizing Research Questions

Patients like Mr B and Ms M demonstrate the challenge of addressing the range of patient-level characteristics and preferences. The number of research questions that can be asked is im-

Box 2. A 45-Year-Old Woman With Depression

For several months Ms M has experienced feelings of unhappiness, hopelessness, and pessimism, as well as low self-esteem, worthlessness, and guilt. She no longer enjoys hobbies and work. She recently developed insomnia, early morning awakening, and difficulties with concentrating, remembering, and making decisions. After initially prescribing an antidepressant for Ms M, her primary care physician switched her to a different medication after 1 week because of adverse effects. After 4 weeks, Ms M reported that she was no better, and her physician discussed options including switching to another antidepressant in the same or in a different drug class, stopping medication entirely and trying cognitive behavioral therapy or a different psychotherapy technique, and complementary approaches such as yoga and mindfulness meditation.

Table. Areas for Development of Methodological Standards in Patient-Centered Outcomes Research

Area for Standards Development	Description
Prioritizing research questions	Use a systematic approach that incorporates decision-making needs, potential health benefits of decisions, and prevalence and burden of illness
Using appropriate study designs and analyses	Select an approach with consideration of the type of clinical questions of interest, previous evidence, strengths and weaknesses of alternative designs and corresponding analyses, and efficient use of resources
Incorporating patient perspectives	Engage patients throughout the research continuum to inform selection of research questions, design, conduct, and analysis, as well as dissemination and implementation of findings
Fostering efficient dissemination and implementation of results	Design research with actionable results and a plan for disseminating results to inform decision making

mense. Therefore, prioritizing among them is essential to identify and address the most pressing evidence gaps. Initial steps involve generation of topics and identification of methods to productively engage patients and other key stakeholders. Systematic reviews of the literature to identify benefits and harms and gaps in the evidence are required before launching any new studies.^{18,19}

Once the constellation of questions has been generated, which knowledge gaps are the most pressing to fill? Techniques like value of information analysis are of interest to predict how best to spend limited research funds to improve population health, accounting for issues such as the prevalence and burden of an illness, the likelihood that research on a topic will produce changes in care decisions made by patients and other stakeholders, and the potential health benefits of those changes in de-

terminations.²⁰ Challenges associated with such an approach include adequately reflecting the variation among patients in preferences and other attributes that can affect the value of research, and making optimal use of existing evidence in the design of new research.²¹

Using Appropriate Study Designs and Analyses

Comparative effectiveness research and hence PCOR entail an array of randomized and nonrandomized study designs that exploit exposure variation within patients (eg, self-controlled designs, crossover trials), between individual patients (eg, parallel-group randomized trials and cohort studies using case-control, case-cohort, 2-stage sampling, or other observational designs), and between population groups (eg, cluster randomized trials, instrumen-

tal variable analyses, and time-trend analyses). The choice among these options is directed by the study question, the type of evidence required by stakeholders, feasibility, existing and ongoing research, and ethical considerations—and in PCOR specifically, as described in the next section, by patient-centeredness. The broader context of ongoing and planned research must be considered to avoid duplication and ensure the complementarity of information, as well as to anticipate ultimate synthesis with other sources for literature reviews or clinical practice guidelines.

The Methodology Committee will produce a Congressionally mandated translation table in the methodology report to assist investigators and grant reviewers in determining the range of appropriate study designs for addressing particular research questions in PCOR. Some key evidence characteristics in design selection include the level of validity and precision desired, generalizability to routine care, the urgency with which the evidence is needed, sufficiency of clinical granularity of data sources, ethical issues related to clinical equipoise, practical constraints, and whether studies of similar or different design are ongoing or planned. Transparency of these evidence characteristics helps to guide the challenging but necessary trade-off between compromising some design features (eg, precision, generalizability) to optimize others (eg, baseline randomization and complex outcome measurement).

Methodological advances have been made in conducting randomized trials efficiently through adaptive designs and simplification of recruitment, follow-up, and outcome assessment, highlighting the pragmatic aspects of trials in attempt to make findings more generalizable to routine care.²² When nonrandomized designs are indicated, progress has been made in adjustment techniques for the selection of patients to treatments, and the resulting imbalances of risk factors in the comparison groups. Propensity scores allow adjustment for many

variables, including proxies for unobservable confounders in health care databases.²³⁻²⁵ Instrumental variable analyses have been promoted in health care evaluation over the last 2 decades, although their value remains unclear.^{26,27} More empirical evidence is required to determine how nonrandomized approaches compare with or add to randomized trials in diverse fields and settings.²⁸

The increasing complexity of treatment regimens after initial randomization requires novel approaches that address time-varying exposures and adjustment for confounding.²⁹ Studies based on health care databases benefit from their large size, permitting evaluation of treatment effects shortly after market availability of a product³⁰ or in a larger number of patient subgroups. Bundling patient baseline risks for a study end point into risk scores may improve estimation precision when exploring many patient subgroups.³¹ Because subgroup analyses can be misleading even in randomized designs,³² empirical evaluation of newer methods with larger-scale evidence will be required.

Incorporating Patient Perspectives Throughout the Research Continuum

To be truly patient-centered, PCOR faces the challenge of how to best incorporate the patient and caregiver perspective at every step in the selection of research questions, design, conduct, and analyses of studies, as well as dissemination and implementation of findings. Although patient involvement is essential to improve the value of PCOR, there are knowledge gaps regarding how best to do this and how to trade off this perspective with other perspectives or priorities. The Methodology Committee envisions a PCOR lens through which research questions and design components may be viewed to ensure adequate patient-centeredness. Toward this end, methodological standards for capturing information about people’s perspectives at various steps are required, which in-

variably will include qualitative and quantitative approaches; strategies for including difficult-to-reach individuals; consideration of perspectives of caregivers and surrogates; guidelines for the development, validation, and use of patient-reported outcomes and for patient-centered non-patient-reported outcomes (ie, outcomes that matter to patients that are not reported directly by patients); and approaches for addressing heterogeneity of perspectives across a given population.³³ Some existing methods are applicable, but work is required to refine them and to develop new approaches appropriate to PCOR.^{34,35}

Fostering Efficient Dissemination and Implementation of Results

Achieving appropriate, timely implementation and routine use of research represents the critical last step in the CER process. Study designs should consider implementation issues at the time of inception.³⁶ Research examining implementation processes, barriers, and facilitators, and evaluating effectiveness of innovative implementation strategies has revealed considerable heterogeneity in implementation settings, processes, and mechanisms.³⁷ These findings have motivated the development of standards to ensure that studies reflect and report external validity,³⁸ measure contextual influences and other effect moderators,^{39,40} and examine key mediators and mechanisms of impact.⁴¹⁻⁴³

Good evidence often exists but it is not integrated into practice, illustrating the challenges of beneficially modifying patient and clinician behavior, and the importance of implementation science research in PCOR.^{44,45} Implementation barriers must be addressed once effectiveness has been demonstrated, or even concurrently with research assessing effectiveness.⁴⁶

CONCLUSIONS

The Methodology Committee recognizes the unique opportunity afforded by the Patient Protection and Affordable Care Act to enhance and expand

methodological approaches for designing and implementing high-quality medical research. Methods for prioritizing research questions, using appropriate study designs and analyses, incorporating patient perspectives, and fostering efficient dissemination and implementation of results will drive future Methodology Committee activities and guide PCORI’s funding announcements.

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