Advisory Panel on Assessment of Prevention, Diagnosis, and Treatment Options Meeting Summary

October 2015

Overview

On October 9, 2015, the PCORI Advisory Panel on Assessment of Prevention, Diagnosis, and Treatment Options convened in Washington, DC, to review two previously prioritized clinical effectiveness research topics and one new clinical effectiveness research topic.

The Advisory Panel on Assessment of Prevention, Diagnosis, and Treatment Options is made up of 21 representatives of patients, caregivers, patient advocates, clinicians, researchers, industry, and policy makers. The panel was joined by PCORI leadership, staff, and research topic experts. The meeting was open to the public via teleconference, and slides and meeting materials were posted to the website in advance of the sessions.

The panel was provided with briefs for each topic prior to the meeting. After extensive discussion of each topic, panelists prioritized a subset of comparative effectiveness research questions for further consideration to be included in future PCORI Funding Announcements (PFAs).

CER Topics for Research Topic Refinement Reviewed at July 9-10, 2015 Meeting:

Topic 1: Comparative effectiveness of nonsurgical treatment for cervical disc and neck pain
Topic 2: Comparative effectiveness of narrow-spectrum antibiotics versus broad-spectrum antibiotics in the treatment of community-acquired pneumonia in adults
Topic 3: PCSK9 Inhibitors

Related Information

- About PCORI's Advisory Panels
- About the Advisory Panel on Assessment of Prevention, Diagnosis, and Treatment Options
- Orientation to PCORI's Research Prioritization
- Meeting Details and Materials

The Patient-Centered Outcomes Research Institute (PCORI) is an independent organization created to help people make informed healthcare decisions.

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Introduction

The Advisory Panel on Assessment of Prevention, Diagnosis, and Treatment Options reviewed three clinical research areas, with the input of topic experts, with the aim of formulating a subset of specific questions for further consideration as priority research areas. Two of the topics, nonsurgical treatment for cervical disc and neck pain as well as antibiotic treatment in community-acquired pneumonia in adults, had been previously highly prioritized by the panel, but further topic refinement was needed. A new topic, PCSK9 inhibitors, proposed by America's Health Insurance Plans, was discussed as well[1].

Topic Experts

- Gillian Schmidler, PhD, *Duke University*
- Amanda Brooks, PhD, *Duke University*
- Remy Coeytaux, MD, PhD, *Duke University*
- Sydney Morss Dy, MD, MSc, *Johns Hopkins University*
- Susan Hutfless, MS, PhD, *Johns Hopkins University*
- Stanley Ip, MD, *Patient-Centered Outcomes Research Institute*

Comparative Effectiveness of Nonsurgical Treatment for Cervical Disc and Neck Pain

Four Stakeholder Questions*

1. Does the presence of centralization vs. noncentralization or directional preference vs. no directional preference predict response to therapy for axial neck pain without radiculopathy?
2. Within specific patient populations of interest, what is the comparative effectiveness and safety of available nonsurgical treatments (prescription oral pharmacotherapy, over-the-counter oral pharmacotherapy, injections, or nonpharmacologic treatments) either alone or in combination for short-term symptomatic improvement of neck pain? Patient populations of interest include: (1) patients with axial neck pain with radiculopathy, and (2) patients with axial neck pain without radiculopathy?

**not ranked*

Cervical disc and neck pain is a common, bothersome, and potentially debilitating problem that results from degeneration of the structures of the cervical spine. Options for addressing neck pain depend greatly on its cause and chronicity. Conditions that can cause neck pain include cervical strain, internal disc disruption syndrome, cervical facet-mediated pain, cervical "whiplash" syndrome, and myofascial pain. With incidence rates around 150-180 per 1,000 person years, approximately 37 percent of adults worldwide experience neck pain in a given year[1].

This topic has been prioritized highly by the Advisory Panel on Assessment of Prevention, Diagnosis, and Treatment Options on two previous occasions (April 2014 and August 2014). In order to identify areas that could impact practice within the next 3-5 years, the Duke Evidence Synthesis Group appraised recent systematic reviews to identify evidence gaps, cross-check potential research questions with ongoing

[1] Topic briefs available at http://www.pcori.org/events/2015/advisory-panel-assessment-prevention-diagnosis-and-treatment-options-fall-2015-meeting

studies, and engage relevant stakeholders to identify missing questions.

Panelists agreed that the four stakeholder questions identified by the Duke Evidence Synthesis Group were on target and, while there was a fair amount of enthusiasm for this topic, panelists expressed several major concerns. One concern was the lack of patient involvement in creating the definition of the problem, especially regarding whether or not radiculopathy should be excluded. Some panelists felt that exclusion of radiculopathy would narrow down the population, thus allowing a reasonable research agenda, while other panelists felt important issues would not be addressed if radiculopathy was excluded. A second concern was about the uncertainty in clinical decision making among both providers and patients. Panelists and stakeholders noted that providers are in need of guidance due to the numerous treatment options available and the lack of heterogeneity in the population. In addition, there is general patient confusion due to the fact that they can enter the system at multiple points simultaneously.

Four Stakeholder Questions*

3. What is the comparative effectiveness of existing assessment instruments for persons with neck pain with or without radiculopathy for the purpose of prognosis or assessing the effectiveness of therapeutic interventions?
4. Are there patient characteristics, biopsychosocial and economic factors, physical examination, and imaging findings that predict which patients with new onset axial neck pain are at risk for developing chronic pain, opioid dependence, or other undesirable outcomes?

**not ranked*

In order to better identify appropriate research questions and approaches of interest for nonsurgical treatment strategies in delaying or preventing surgery for cervical disc and neck pain, PCORI staff will have a follow-up discussion with members of the neck-pain stakeholder community.

Comparative Effectiveness of Narrow-Spectrum Antibiotics versus Broad-Spectrum Antibiotics in the Treatment of Community-Acquired Pneumonia in Adults

Community-acquired pneumonia (CAP) is defined as an infection of the lung in persons who have not been hospitalized recently or exposed to other healthcare settings that markedly increase risk of contracting pneumonia. Healthcare-associated pneumonia is defined and treated differently than CAP. In 2012, 1.1 million persons were diagnosed with CAP in the United States, resulting in 327,840 hospital admissions. Characteristics of individuals at increased susceptibility to CAP include older age, comorbidities, immunosuppression, non-white race, and lower education and income. In 2013, CAP was the ninth leading cause of death in the United States with a mortality rate of 16.9 per 100,000 contributing to 53,000 deaths[2].

[2] Community-acquired pneumonia topic brief available at http://www.pcori.org/sites/default/files/PCORI-Topic-Brief-CER-Antibiotics-Community-Acquired-Peumonia.pdf

Seven Key Research Questions*

1. What is the comparative effectiveness of narrow-spectrum vs. broad-spectrum antibiotic therapy for empiric therapy and/or definitive therapy of community-acquired pneumonia in adults?
2. What is the comparative effectiveness of shorter- vs. longer-course antibiotic therapy in the treatment of community-acquired pneumonia in adults?
3. What is the comparative effectiveness of different approaches to de-escalating antibiotic therapy in the treatment of community-acquired pneumonia in adults?

**not ranked*

This topic was prioritized highly by the Advisory Panel on Assessment of Prevention, Diagnosis, and Treatment Options at its April 2015 meeting. In order to identify areas that could impact practice within the next 3-5 years, the Johns Hopkins Evidence-Based Practice Center appraised recent systematic reviews to identify evidence gaps, cross-check potential research questions with ongoing studies, and engage relevant stakeholders to identify missing questions.

Community-acquired pneumonia is a broad diagnosis in a heterogeneous population. As there is no clear definition of "narrow-spectrum" and "broad-spectrum", antibiotics used to treated community-acquired pneumonia in outpatient, emergency department, hospitalized, and intensive care unit populations often vary.. Panelists expressed concerns that a study to answer this question would be somewhat challenging and may not change practice due to all these variances. The Johns Hopkins Evidence-Based Practice Center identified seven key research questions relative to this topic. After much deliberation between panelists and stakeholders, a list of clinical areas of interest for a potential clinical effectiveness research study was created. Topics of interest included: 1) duration of antibiotic regimen, as duration has been shown to be just as important as the choice of antibiotic; 2) assessment of patient-centered outcomes such as return to work, resolution of symptoms, quality of life; 3) diagnosis options to identify causative pathogens, as the CDC EPIC study recently found that 62 percent of adults hospitalized with pneumonia had no discernible pathogen despite extensive testing etiology; 4) dosing; 5) pneumonia vaccination; and 6) severity in patient prognosis.

Seven Key Research Questions*

4. What is the comparative effectiveness of different approaches to rapidly diagnose community-acquired pneumonia?
5. What are the implications of narrow-spectrum vs. broad-spectrum antibiotic therapy on antibiotic resistance?
6. What is the comparative safety of narrow-spectrum vs. broad-spectrum antibiotic therapy for community-acquired pneumonia in adults?
7. Is the safety and effectiveness of narrow-spectrum vs. broad-spectrum antibiotic therapy different in distinct subpopulations of adults with community-acquired pneumonia?

**not ranked*

While there is a significant need for improved diagnosis strategies and there was a lot of enthusiasm and interest from the panel, it was concluded that the question was not ready for comparative effectiveness studies due to the lack of effective diagnostic tools. Panelists suggested that the most feasible and impactful study for PCORI would be one that addressed choice of antibiotics and duration of therapy while including patient-centered outcomes.

PCSK9 Inhibitors

Hypercholesterolemia affects 30 million adults and is generally asymptomatic. Yet, the condition is serious—killing 600,000 people per year. Statins are the first line of treatment after lifestyle modifications, with treatment level contingent on current risk status. PCSK9 inhibitors are new FDA-approved medications to treat high cholesterol based on efficacious results in reducing low-density lipoprotein (LDL) cholesterol levels in high-risk patients or patients who are already on maximal dosages of statins. PCSK9, or proprotein convertase subtilisin/kexin 9, is a protease that binds to LDL receptors. This binding reduces the activity of the LDL receptors, thereby decreasing the metabolism of LDL and leading toincreases in LDL cholesterol levels in the blood. By inhibiting the binding of PCSK9 to LDL receptors, the receptors can activate, metabolize LDL, and decrease levels of LDL in the blood. There are currently two PCSK9 inhibitors available on the market: Alirocumab and Evolocumab. These medications are unique, in that they are administered by injection rather than by mouth, due to the fact that PCSK9 inhibitors are human monoclonal antibodies that would be destroyed in the stomach. There currently is no evidence about the long-term tolerability and patient acceptance of the PCSK9 inhibitors. There also is little evidence about long-term side effects or harms that may occur infrequently. Comparative benefits and harms of these new medications are not known at this time[3].

This is a new topic that was brought to the Advisory Panel on Assessment of Prevention, Diagnosis, and Treatment Options by America's Health Insurance Plans (AHIP), a trade association for health plans. The stakeholder group expressed concerns about affordability because these new treatments are more expensive than existing treatments for hypercholesterolemia. There was significant interest in how and when these drugs would be used, especially considering there are many treatments for reducing cholesterol that have never shown that they've had an improved long-term outcome. On this topic, PCORI wanted to determine whether there is an opportunity for PCORI-funded research.

The panelists expressed enthusiasm for this topic and interest in future studies that better characterize population(s) that receive the most benefits from medications, adherence, comparison of new agents to non-statin treatments, safety and side effects (i.e., neurocognitive decline, injection site pain), and patient-centered outcomes. It was noted that prior studies evaluated only LDL cholesterol levels as an outcome and did not focus on any patient-centered outcomes, and most studies evaluating actual clinical outcomes (clinical events attributable to atherosclerotic cardiovascular disease) will not be completed until 2018. There were concerns that a head-to-head trial may not be feasible due to the cost of the drugs and a lack of clarity concerning whether stakeholders were interested in comparative studies. While it was suggested that PCORI partner with other research organizations in order to

[3] PCSK9 Inhibitors topic brief is available at http://www.pcori.org/sites/default/files/PCORI-Topic-Brief-PCSK9-Inhibitors.pdf

shoulder the cost of the study, it was noted that creating the arrangement could impede the ability to have results that could impact practice within the next 3-5 years.

Next Steps

- PCORI staff will review the recommendations of the panel for further consideration to be included in future PCORI Funding Announcements (PFAs).
- The panel will convene for their next meeting in March 2016. The meeting will be held in Washington, DC.