



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

April/May 2015

## Overview

On April 28, 2015 and May 1, 2015, the PCORI Advisory Panel on Assessment of Prevention, Diagnosis, and Treatment Options convened via webinar to review nine new clinical effectiveness research topics.

The panel is made up of 21 representatives of patients, caregivers, patient advocates, clinicians, researchers, industry, and policy makers. The meetings were open to the public via teleconference, with slides and meeting materials 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 the comparative effectiveness research questions.

The highest-ranked topics include: narrow-spectrum antibiotics versus broad-spectrum antibiotics for pneumonia in adults, second-line drug therapies after failed metformin use in type 2 diabetes, and long-term outcomes for drug treatment vs. non-drug treatment in prediabetes.

In order to help formulate a subset of comparative effectiveness research questions for further consideration to be included in future PCORI Funding Announcements (PFAs), panelists will convene with topic experts in July 2015 for further topic refinement.

## 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](#)
- [How PCORI Assesses and Selects Topics for Potential Research Funding](#)
- [April 28, 2015 Meeting Details and Materials](#)
- [May 1, 2015 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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### **CER Topics for Research Topic Refinement Reviewed at April 28, 2015 and May 1, 2015 Webinars:**

Topic 1: Comparative effectiveness of drug treatment versus non-drug treatments in the treatment of patients with prediabetes.

Topic 2: Comparative effectiveness of early treatment (prediabetes stage) strategies versus treatment initiated after type 2 diabetes has been diagnosed on long-term patient outcomes

Topic 4: Comparative effectiveness of high-intensity statin versus low-intensity statin in the prevention of CVD

Topic 5: Comparative effectiveness of antiretroviral drugs in the treatment of HIV infection

Topic 6: Comparative effectiveness of stem cell transplantation versus immunosuppressive therapy for acquired severe aplastic anemia among children and young adults

Topic 7: Comparative effectiveness of early therapy versus observation for monoclonal gammopathy of undetermined significance in the prevention of multiple myeloma

Topic 8: Comparative effectiveness of second-line drug therapies after failed metformin use in type 2 diabetes treatment

Topic 9: Comparative effectiveness of optimal timing (early versus late) for reduced-intensity conditioning allogeneic hematopoietic stem cell transplantation for older patients in reducing mortality risk and increasing survival in patients with MDS

Topic 10: Comparative effectiveness of narrow-spectrum antibiotics versus broad-spectrum antibiotics in the treatment of community-acquired pneumonia

## **Introduction**

The Advisory Panel on Assessment of Prevention, Diagnosis, and Treatment Options reviewed nine specific clinical research areas, with the aim of prioritizing a subset of specific questions for further consideration as priority research areas. The clinical effectiveness research team originally reviewed 10 clinical research topic nominations. PCORI's [Science Oversight Committee](#) (SOC) reviewed the nominations to determine whether the questions fit PCORI's research strategy. Upon review, nine topics were approved and moved forward for deliberation by the Advisory Panel on Assessment of Prevention, Diagnosis, and Treatment Options. The panelists reviewed five topics on April 28, 2015 and four topics on May 1, 2015. The areas discussed include prediabetes, diabetes, statin therapy, pneumonia, stem cell transplantation, multiple myeloma, and HIV.<sup>1</sup> Upon completion of both webinars, panelists prioritized all nine topics using SurveyGizmo.

## **Long-Term Outcomes for Drug Treatment vs. Non-Drug Treatment in Prediabetes**

Prediabetes is a condition in which blood sugar is higher than normal but not enough to be called type 2 diabetes. While estimates of

progression from prediabetes to type 2 diabetes vary, one fact that is agreed upon is that diabetes is a large public health population issue that is often comorbid with several other chronic diseases. Researchers continue to work on new interventions to address this health issue, and there are many new lifestyle and medication interventions on the horizon. Panelists commented on the importance of progression from prediabetes to type 2 diabetes and noted there is a need, if thinking about application of new interventions, to improve ways of determining patient characteristics that would be useful to

<sup>1</sup> Topic briefs available at <http://www.pcori.org/sites/default/files/PCORI-Advisory-Panel-Assessment-Of-Options-Webinar-Topic-Briefs-042815.pdf> and <http://www.pcori.org/sites/default/files/PCORI-Advisory-Panel-Assessment-Of-Options-Webinar-Topic-Briefs-050115.pdf>

predict who is likely to progress. If there are new drugs that hold promise, it is likely that they would be evaluated by pharmaceutical companies, not PCORI. Compelling questions for this topic included who should be the focus of the intervention and when the intervention should be initiated.

### **Long-Term Outcomes for Early Treatment vs. Treatment Initiated after Type 2 Diabetes Diagnosis**

The panel agreed that both prediabetes and diabetes are important topics due to their adverse effects on organs such as the heart, kidney, eyes, and nerves. Prediabetes, because of its high prevalence, raises the question concerning the need to be proactive in order to prevent the disease. The panel agreed that if PCORI were to consider comparative effectiveness clinical trials or observational studies on medications, they may be concentrating on a domain that is not approved by the FDA, thus raising the question of whether PCORI should and can be engaged in evaluation of drugs for non-approved indications. Panelists surmised that perhaps the right topic to highlight is the need for more studies of lifestyle intervention and new ways of promoting lifestyle intervention (i.e., the use of newer apps or technology in assisting individuals in making lifestyle changes), but they noted that the focus of these studies could not only be on prediabetes but on other conditions such as hypertension and obesity.

### **High-Intensity Statin vs. Low-Intensity Statin in Prevention of Cardiovascular Disease (CVD)**

Cardiovascular disease (CVD) refers to conditions of the heart and blood vessels. Two of the most serious and most common types of CVD are heart attack and stroke, both of which can be caused by narrowed or blocked blood vessels. Research suggests that statins lower cholesterol and can prevent cardiovascular events and may play a role in an immunomodulatory and anti-inflammatory function that can reduce susceptibility to the formation of blood clots in arteries. This topic is similar to two previously mentioned diabetes topics, in that it highlights the need for preventing a risk factor from progressing into a disease. Newer drugs are being created, and there is a question regarding whether they are better than statins, and panelists were interested in the possibility of incorporating them into the research agenda for this topic. If PCORI were going to be involved, it would either have to develop a large-scale randomized controlled trial, including the new agents, or include high/low intensity for the current treatment group, and enroll a large number of patients and have long follow-up to show effectiveness in the primary prevention group. That kind of question could be looked at through observational design, but it would require a large database with significant variability in clinical practice. There would be significant methodological issues with both study types. A point was raised regarding PCORI refining risk predictions, and thereby providing guidance in choosing individuals for therapies.

### **Antiretroviral Drugs (3TC/FTC + boosted PI vs 2NRTI + boosted PI) in the Treatment of HIV Infection**

HIV, or human immunodeficiency virus, is the virus that can lead to acquired immunodeficiency syndrome (AIDS). HIV attacks the host immune system, especially the T cells (CD4) that defend against infections. As CD4 numbers drop and viral burden (viral load) goes up, the immune system weakens, and

the patient develops infections and other complications. AIDS is diagnosed when HIV infection is associated with one or more infections, certain cancers, or a very low number of CD4 cells. While HIV is now considered a chronic disease and not a deadly acute disease, one of the big issues, from the treatment perspective, is that the population often has difficulties in terms of tolerance and adherence to multi-drug therapies. The panel views HIV and HIV infection as important topics that present opportunities for PCORI, due to the importance of patient-centered outcomes. Some panelists had questions about whether the interventions in the brief are the best choices for a PCORI-initiated research agenda.

### **Stem Cell Transplantation vs. Immunosuppressive Therapy for Severe Aplastic Anemia in Children and Young Adults**

Aplastic anemia is a serious rare disease in which the stem cells in the bone marrow fail to produce new blood. There was a lengthy discussion on how the proposed clinical research questions could address the relative risks and benefits of immunosuppressive therapy versus non-matched donors. It was noted that there are currently no studies considering or analyzing the quality of life in this population. There is also the possibility that results from this study could benefit other populations experiencing bone marrow conditions, which enhances the importance of this topic. Questions of concern include feasibility, and the ability to mount a large representative sample size for research.

### **Early Therapy vs. Observation for Monoclonal Gammopathy in the Prevention of Multiple Myeloma**

Monoclonal gammopathy of undetermined significance (MGUS) is a disease that involves plasma cells and primarily affects the elderly. The disease can be symptomatic or asymptomatic, and there are very specific criteria and definitions used in order to place a single patient in one of these criteria. In addition, multiple myeloma develops at the rate of about 1–2 percent a year for patients with MGUS. This topic focuses on prevention by comparing early therapy versus observation. Questions of concern included risks versus benefit of interventions and feasibility of recruitment. Panelists discussed whether the correct group was being targeted for this multiple myeloma prevention topic (i.e., should the question look at smoldering myeloma studies versus MGUS?). Panelists expressed concern about the ability and willingness to recruit, especially since MGUS patients are treated in primary care settings.

### **Second-Line Drug Therapies after Failed Metformin Use in Type 2 Diabetes**

Treatment for type 2 diabetes usually begins with metformin, but requires intensification. However, there are few clinical guidelines on how to do this. There seem to be differences in the presentation across different population in terms of ethnic background and demographics, with many individuals not knowing they have the disease. There were concerns that a comparative research study may be duplicative of the GRADE study—which has about 6,000 patients and looks at four classes of drugs but doesn't include other alternatives to care—and, thus, screening trials may be something to consider. There were questions about the durability of the findings regarding these new drugs, given the speed of

development and the fact that pharmaceutical companies do not focus on head-to-head studies. There is room for research that would address side-effect profiles as well as adherence. Lifestyle is a reasonable comparator to include in the study; however, panelists pointed out that it does take a long time to see lifestyle changes.

## **Optimal Timing for Reduced-Intensity Conditioning Allogeneic Hematopoietic Stem Cell Transplantation for Older Patients**

Myelodysplastic syndromes (MDS) are a group of hematologic stem disorders in which the bone marrow fails to produce blood cells, resulting in pancytopenia; the disorders are characterized by inefficient hematopoiesis and increased apoptosis. A key current gap in the evidence is the optimal timing of stem cell transplantation with RIC (early versus late). Since older patients have a high risk of progression to leukemia, there is an increasing trend toward early transplantation, but because of the rarity of MDS, there are no data from large randomized clinical trials. Panelists noted that there is currently a clinical research MDS consortium that is building cohorts for Phase I and II clinical trials, with quality of life as one of their main outcomes.

## **Narrow-Spectrum Antibiotics vs. Broad-Spectrum Antibiotics for Pneumonia in Adults**

Community-acquired pneumonia (CAP) is the acute infection of the lung in persons who have not been hospitalized recently and have not been regularly exposed to the healthcare system. A wide range of microorganisms can cause CAP, including bacteria (20–50 percent) and viruses (15–23 percent). There is a general trend toward broader and longer-duration antibiotic therapy for CAP. Public health experts are concerned about the use of antibiotics in patients who do not really have pneumonia, especially because excess use of broad-spectrum antibiotics can lead to emergence of multidrug-resistant bacteria. Using narrow-spectrum antibiotics is one of several ways to reduce bacteria resistance. One of the major issues in this population does not seem to be about broad-spectrum antibiotics versus narrow-spectrum antibiotics but more on appropriate use of antibiotics. There are issues of over-use and under-use (in elderly populations who experience CAP) in the healthcare system, and hospitals are concerned and have antibiotic stewardship problems in place. Tension seems to arise concerning “appropriate” use of antibiotics—narrow vs. broad *and* over-use vs. under-use *and* drug resistant vs. rapid use. Panelists have called for pragmatic clinical trials or perhaps a system wide inquiry concerning why physicians aren’t using current guidelines. This would be a feasible trial with quick turnaround of results.

## **Next Steps**

- The panel will next convene for an in-person meeting in July 2015 to discuss the highly prioritized topics from this discussion. The meeting will be held in Washington, DC.