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

July 2015

## Overview

On July 9-10, 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

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 Strategies for Diabetes Prevention in Prediabetes
Topic 2: Comparative Effectiveness of Second- and Third-Line Therapies for Treatment of Type 2 Diabetes

### 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.

**1828 L St., NW, Suite 900**
**Washington, DC 20036**
**Phone: (202) 827-7700**
**Fax: (202) 355-9558**
**Email: info@pcori.org**
**Follow us on Twitter: @PCORI**

## Introduction

The Advisory Panel on Assessment of Prevention, Diagnosis, and Treatment Options reviewed two specific 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. Both topics, which focused on diabetes, had been previously highly prioritized by the panel, but further topic refinement was needed. The areas discussed were strategies for diabetes prevention in prediabetes and second- and third-line therapies for treatment of type 2 diabetes[1].

**Topic Experts**

- Gillian Schmidler, PhD, *Duke University*
- Matt Crawley, MD, *Duke University*
- David D'Allesio, MD, *Duke University*
- Robert Ratner, MD, FACP, FACE, *Chief Scientific and Medical Officer for the American Diabetes Association*
- Ronald Ackermann, MD, MPH, Northwestern University, *Diabetes Prevention Program*
- Guillermo Umpierrez, MD, *Emory University, American Association of Clinical Endocrinologists*
- Ann Albright, PhD, RD, *Director of CDC Division of Diabetes Translation*

## Comparative Effectiveness of Strategies for Diabetes Prevention in Prediabetes

Prediabetes is a condition in which blood sugar levels are elevated but are still below the threshold for diagnosis of diabetes mellitus. The primary goal of prediabetes management is type 2 diabetes prevention through lifestyle changes and/or pharmacotherapy. Diagnostic criteria for prediabetes include: 1) hemoglobin A1c of 5.7 percent to 6.4 percent; 2) fasting plasma glucose of 100 to 125 mg/dL; or 3) oral glucose tolerance test with a two-hour glucose of 140 to 199 mg/dL.[2,3] In 2012, 86 million US adults had prediabetes, which translates to 37 percent of adults aged 20 years and older and 51 percent aged 65 years or older, and this prevalence is rising.[3,4,5,6]

The Diabetes Prevention Program (DPP) was a landmark study for type 2 diabetes prevention in prediabetes. While this study has demonstrated quality evidence for diabetes prevention, adoption and delivery in real-world settings is still uncertain. The panelists and expert stakeholders provided several suggestions that may provide opportunities for progress in this research area in light of DPP. Multiple

[1] Topic briefs available at http://www.pcori.org/sites/default/files/PCORI-Assessment-Options-AP-Meeting-Topic-1-Brief-CER-Prevention-Pre-Diabetes-07-09-10-2015.pdf and http://www.pcori.org/sites/default/files/PCORI-Assessment-Options-AP-Meeting-Topic-2-Brief-CER-Type-2-Diabetes-07-09-10-2015.pdf

[2] American Diabetes Association, Professional Practice Committee. Standards of medical care in diabetes - 2015. Diabetes Care 2015.38(Suppl 1):S1-S94.

[3] Stokes A, Mehta NK. Mortality and excess risk in US adults with pre-diabetes and diabetes: a comparison of two nationally representative cohorts, 1988-2006. Population Health Metrics. 2013;11(1):3. PMID: 23448510.

[4] American Association of Clinical Endocrinologists (AACE). Common comorbidities and complications associated with prediabetes [web page]. http://outpatient.aace.com/prediabetes/common-comorbidities-and-complications-associated-with-prediabetes. Accessed June 30, 2015.

[5] Taylor LM, Spence JC, Raine K, et al. Physical activity and health-related quality of life in individuals with prediabetes. Diabetes Res Clin Pract. 2010;90(1):15-21. PMID: 20727611.

[6] Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2014. www.cdc.gov/diabetes/pubs/statsreport14/national-diabetes-report-web.pdf. Accessed June 30, 2015.

stakeholders indicated that studies were needed that assess different delivery methods (i.e., group, telemedicine, computer-based, individual, etc.), how these delivery methods impact engagement, and which method is associated with best outcomes. Another suggestion was to look at more patient-centered outcomes. While the patient population has been followed for 17 years without hiatus of involvement, no cardiovascular disease (CVD) outcomes or very long-term outcomes are being assessed in the DPP study. A third suggestion noted that much value can be gained from observational research where long-term follow-up might be present in a database that could be mined for the purpose of long-term studies, especially for renal and CVD outcomes or an observation study looking at different approaches to implementing lifestyle interventions. As part of their intervention, DPP utilized a primarily low-fat and calorie-restriction diet and, thus, panelists advised on considering low-carbohydrate and Mediterranean diets as a form of lifestyle intervention in future studies. Panelists remarked that literature evaluation could be a research agenda in and of itself, as systematic reviews and meta-analyses in other comorbid disease topic areas may be useful.

Based on stakeholder input, the Duke Evidence Synthesis Group outlined four key research priorities pertaining to diabetes prevention in the prediabetes population, listed in the table below. There was enthusiasm for Priority 1 because while there is a clear role in incorporating patient decision making and shared decision making has increasing value, there is very little research in this area with respect to diabetes prevention. There was interest in whether or not practice facilitation and office-based coaching programs make a difference in improving outcomes in diabetes prevention and adherence. Stakeholders noted that prioritizing primary care, such as leveraging communication and the ability to measure outcomes stems from relationships in the primary care physician office, was integral to this approach. Several concerns were raised, including the lack of decision aids to help determine which strategies should be utilized and the need for patients to be motivated/activated in order for this intervention to be impactful; thus, strategies are needed for informing providers about how to engage patients. Panelists agreed that this question needed further refinement. Panelists also agreed that the question posed in Priority 2 was important. Panelists suggested a study that looks at lifestyle modifications plus metformin, but they could not reach consensus on which population to target. There were concerns expressed about the feasibility of this question, and it was suggested that this question undergo further refinement. There is very little research in the area of Priority 3, and it was noted that one of the things that PCORI can offer for this is PCORnet—which provides the ability to gather bulk data in one repository and make it available to a variety of researchers across the nation. There were questions concerning the best approaches associated with high program utilization and adoption, implementation in underserved populations (i.e., leveraging of community resources to move

**Four Key Research Priorities***

Priority 1: Approaches to shared decision making for selecting a diabetes prevention strategy and treatment goals
Priority 2: Diabetes prevention strategies in different patient populations
Priority 3: Approaches for enhancing utilization and adoption of diabetes prevention strategies in real-world settings
Priority 4: Strategies for implementing lifestyle modification in real-world settings

*not ranked

prevention from specialty care to primary care), and whether there should be an investment in a behavioral modification study without behavioral modification experts. Priority 4 was a discussion topic of great interest, as lifestyle modifications have been proven to be good interventions. But there were questions concerning feasibility such as implementation (i.e. how to really engage patients), delivery, and maintenance as well as questions regarding how to measure programmatic reach and clinical gain. The CDC is currently looking at intervention strategies, such as how messages are delivered, to what populations, and at what frequency. It was also noted that the CDC is already making lifestyle interventions available to Medicaid recipients and those in low socioeconomic brackets, so it remains unclear how you encourage more engagement.

## Comparative Effectiveness of Second- and Third-Line Therapies for Treatment of Type 2 Diabetes

Type 2 diabetes generates a significant societal burden, with the prevalence, morbidity, and costs continuously increasing. While metformin is the consensus first-line treatment for type 2 diabetes, there is less certainty about the comparative effectiveness of the many second- and third-line treatment options. Many patients who initiate metformin require intensification (i.e., higher dose or additional drugs) within the first year of use and, yet, the effects on quality of life, productivity, functional capacity, mortality, and use of healthcare services for individuals who require second-line therapy are not well described. While there have been few comparative effectiveness research studies on the most common second- and third-line therapies, the Glycemia Reduction Approaches in Diabetes: A Comparative Effectiveness (GRADE) Study may provide some insight and inform choice of second- and third-line therapies. The GRADE study, which began in 2013, is a multicenter pragmatic trial designed to compare four medications commonly added to metformin with the primary outcome being treatment failure. Estimated enrollment is 5,000 subjects who have been recently diagnosed with type 2 diabetes, and study follow-up is expected to conclude in 2020. While the GRADE study will be a landmark study, there are other issues that remain unaddressed, such as other patient-centered outcomes (i.e., heart failure, recent cardiovascular events, and quality of life). Based on stakeholder input, the Duke Evidence Synthesis Group outlined four key research priorities pertaining to second- and third-line therapies for the treatment of type 2 diabetes.

**Four Key Research Priorities***

Priority 1: Different approaches to shared decision making
Priority 2: Therapies in which population
Priority 3: Different strategies for determining treatment success
Priority 4: Approaches for enhancing diabetes treatment adherence

*not ranked

While Priority 1 was an important gap, it was noted that there is little knowledge on whether decisions are patient-driven or provider-driven and, thus, there may not be universal acceptance by providers that shared decision making works or is desirable in this topic area. We also do not know patient goals related to shared decision making and other longer-term outcomes. For example, does shared decision making impact longer-term outcomes (e.g. adherence)? Little is known about how "being heard" during consultation during the

decision-making process and may impact emotional and physical well-being. The process may be more important than "sharing." The development of a mutually agreeable shared decision-making process could be one variable to examine, in terms of how it may affect longer-term outcomes. For Priority 2, there were questions regarding how to best tailor options to different populations in real-world settings. Panelists noted that tailoring drugs to populations can cause favorable results (i.e., weight loss), which could promote adherence. It was suggested that a retrospective analysis may be the best design for this topic. Priority 3 is a topic that challenges the current paradigm of relying solely on HgA1c as an indicator of treatment success. While many trials and organizations focus heavily on HgA1c, there was a question of whether there were other ways of defining treatment success that are more patient-centered and whether getting away from HgA1c-driven decision making could, in theory, lead to an increase in complications. For example, do other ways of measuring success, other outcomes, lead to polypharmacy and increased side effects? Panelists pointed out that patients may be more adherent around the time of the doctor's appointment. Priority 4 was the topic panelists were most enthusiastic about, as non-adherence is a major issue despite a substantial body of literature on how to maintain adherence. The population has many problems with polypharmacy, with complicated treatment regimens that make adherence even harder. Patients may be on other pharmaceutical interventions that are more important, and that they are more adherent to. A question was raised about what can be done, beyond education, which can holistically address the complexity of the totality of a patient's medication regimen.

## 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 October 2015 in Washington, DC.