Future Research Prioritization: Comparative Effectiveness of Strategies for Diabetes Prevention in Prediabetes

Prepared for:
Patient-Centered Outcomes Research Institute (PCORI)
1828 L St., NW, Suite 900
Washington, DC 20036
Phone: (202) 827-7700
Fax: (202) 355-9558
www.pcori.org

Prepared by:
Duke Evidence Synthesis Group
Durham, NC

Investigators:
Matthew J. Crowley, MD
Remy R. Coeytaux, MD, PhD
Evan R. Myers, MD, MPH
Jennifer M. Gierisch, PhD
Gillian D. Sanders, PhD

July 2015

ABSTRACT

Prediabetes is a condition where 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. Given the key role of diabetes prevention in enhancing patient-centered outcomes and the need to address remaining areas of uncertainty, the Patient-Centered Outcomes Research Institute (PCORI) tasked the Duke Evidence Synthesis Group (ESG) with creating a prioritized, stakeholder-informed agenda for research in this area. We solicited participation of 60 stakeholders, 21 of whom (35%) provided input related to diabetes prevention through teleconference participation, email feedback, and/or participation in the prioritization survey. Stakeholders ranked evidence gaps by importance from their perspectives using a forced-ranking prioritization method. Based on input from our stakeholder group, key research priorities pertaining to diabetes prevention in the prediabetes population include the comparative effectiveness of: 1) approaches to shared decision making for selecting a diabetes prevention strategy and treatment goals; 2) diabetes prevention strategies in different patient populations; 3) approaches for enhancing utilization and adoption of diabetes prevention strategies in real-world settings; and 4) strategies for implementing lifestyle modification in real-world settings.

INTRODUCTION

Prediabetes is a condition where blood sugar levels are elevated but are still below the threshold for diagnosis of diabetes mellitus. Prediabetes may be called "impaired fasting glucose" or "impaired glucose tolerance" depending on whether high blood sugar levels occur in the fasting state or after meals.[1,2] Diagnostic criteria for prediabetes include: 1) hemoglobin A1c of 5.7% to 6.4%; 2) fasting plasma glucose of 100 to 125 mg/dL; or 3) oral glucose tolerance test with a 2-hour glucose of 140 to 199 mg/dL.[2,3] In 2012, 86 million U.S. adults had prediabetes, which translates to 37% of adults aged 20 years and older and 51% aged 65 years or older, and this prevalence is rising.[3-6] Prediabetes is a major risk factor for developing type 2 diabetes, with 10% to 25% of people with prediabetes progressing to diabetes within 3 years, and 40% to 60% within 10 years.[2,7-9] While prediabetes prevalence does not appear to differ by race/ethnicity,[6] people of different ethnicities develop type 2 diabetes at different rates; American Indians and Alaska Natives have the highest rate of diabetes (15.9%), followed by non-Hispanic blacks (13.2%), Hispanics (12.8), and whites (7.6%).[6]

Prediabetes typically does not cause symptoms, but it is nevertheless associated with lower quality of life and a shorter lifespan. Due to elevated rates of overweight, obesity, and cardiovascular disease, people with prediabetes have higher health care service utilization.[10] When prediabetes progresses to type 2 diabetes, complications and healthcare-related costs increase dramatically;[11] for this reason, the primary goal of prediabetes management is type 2 diabetes prevention through lifestyle changes (e.g., diet, exercise, behavioral modification) or pharmacotherapy (e.g., metformin, thiazolidinediones, and other medications).

The landmark study for type 2 diabetes prevention in prediabetes was the Diabetes Prevention Program (DPP).[12] This multicenter study allocated patients with prediabetes (based on an oral glucose tolerance test) into 3 groups: 1) an intensive lifestyle intervention; 2) twice daily metformin with a standard lifestyle intervention; and 3) placebo with a standard lifestyle intervention. The DPP demonstrated that, while both study interventions reduced type 2 diabetes incidence at 3 years, intensive lifestyle modification (58% reduction versus placebo) was more effective than metformin (31% reduction). In a long-term follow-up study of the DPP population, intensive lifestyle modification remained superior to metformin at 10 years, and both were superior to placebo.[13] Other major studies have confirmed the long-term impact of lifestyle modification for diabetes prevention,[14,15] and both lifestyle modification and metformin are likely to be cost-effective.[16] Based on these data, lifestyle modification is typically recommended as the first-line treatment for diabetes prevention in prediabetes, though metformin may be recommended for individuals with a high risk for progression to diabetes (e.g., obese, gestational diabetes) or those who do not respond to lifestyle modifications.[3]

Despite efforts by the Centers for Disease Control and Prevention-led National Diabetes Prevention Program and others to translate diabetes prevention into practice, diabetes prevention in prediabetes remains a major challenge. Key areas of uncertainty, include how best to choose and implement diabetes prevention approaches for different populations and in different settings. Given the key role of diabetes prevention in enhancing patient-centered outcomes and the need to address remaining areas of uncertainty, the Patient-Centered Outcomes Research Institute (PCORI) tasked the Duke Evidence Synthesis Group (ESG) with creating a prioritized agenda

for research in this area that would: 1) incorporate the perspectives of relevant stakeholders; and 2) have a high likelihood of impacting practice within the next 3 to 5 years.

METHODS

Overview of Prioritization Approach

Our methods for prioritizing future research and developing recommendations for targeted future funding by PCORI broadly follow the steps utilized in the Agency for Healthcare Research and Quality (AHRQ)'s Evidence-based Practice Center (EPC) Program approach to identifying and prioritizing future research needs.[17] This approach involves appraisal of recent systematic reviews to identify important evidence gaps, transformation of evidence gaps into potential research questions, engagement of stakeholders to identify additional gaps and prioritize research questions, and scans of recently published and ongoing studies relevant to the list of stakeholder-prioritized research questions. We did not systematically explore study design considerations during this project.

Selection and Engagement of Stakeholders

We engaged a diverse group stakeholders, including clinical experts in diabetes prevention, researchers, representatives from federal and nongovernmental funding agencies, representatives from relevant professional societies, health care decision makers and policymakers, and representatives from related consumer and patient advocacy groups (Table 1). Within each of these categories, we sought to identify a person who was either familiar with the clinical area and its current uncertainties or brought a specific methodological expertise to the stakeholder panel.

We solicited stakeholder input during this project through teleconference-based group discussions, email communications, and web-based prioritization surveys.

Table 1. Stakeholder organizations and perspectives

Organization	Stakeholder Perspective	Purpose
American Academy of Family Physicians (AAFP)	Professional societies/researchers	AAFP and its chapters represent 120,900 family physician, resident, and medical student members. The AAFP is committed to helping family physicians improve the health of Americans by advancing the specialty of family medicine.
American Association of Clinical Endocrinologists (AACE)	Professional societies/researchers	AACE is a professional community of physicians specializing in endocrinology, diabetes, and metabolism committed to enhancing the ability of its members to provide the highest quality of patient care.
American College of Clinical Pharmacy (ACCP)	Professional societies/researchers	ACCP is a professional and scientific society that provides leadership, education, advocacy, and resources enabling clinical pharmacists to achieve excellence in practice and research. ACCP's membership is composed of practitioners, scientists, educators, administrators, students, residents, fellows, and others committed to excellence in clinical pharmacy and patient pharmacotherapy.
American Diabetes Association	Professional societies/researchers	Large professional society organization of almost 16,500 health care professionals and over 440,000 people with diabetes, with mission to prevent and cure diabetes and to improve the lives of all people affected by diabetes.
American Medical Association (AMA; Improving Health Outcomes)	Policy makers	Professional organization with goal of promoting the art and science of medicine and the betterment of public health. In 2013, AMA launched a strategic focus on cardiovascular disease and diabetes. A key part of this initiative is diabetes prevention by bridging the gap between primary care and community resources. AMA assists clinical practices in implementing new processes for identifying patients with prediabetes and referring them to the YMCA's Diabetes Prevention Program.
Centers for Disease Control and Prevention (Division of Diabetes Translation, National Center for Chronic Disease Prevention and Health Promotion)	Policy makers	The Division of Diabetes Translation is a part of the National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services. The division does not support the direct provision of services, but facilitates the efficient, fair, and effective availability of these services to all Americans affected by diabetes. One goal of this division is to implement the National Diabetes Education Program (NDEP), a joint initiative sponsored by the CDC and the National Institutes of Health. The NDEP is based on a partnership of public and private organizations that are concerned about the health status of their constituents. The NDEP is designed to improve treatment and

Organization	Stakeholder Perspective	Purpose
		outcomes for people with diabetes, to promote early diagnosis, and to prevent the onset of diabetes. Program activities are directed to these audiences: the general public; people with diabetes and their families; health care providers; and payers and purchasers of health care and policymakers.
GlaxoSmithKline (GSK)	Product makers	GSK is a British multinational pharmaceutical company. It was the world's sixth-largest pharmaceutical and was established in 2000 by a merger of Glaxo Wellcome and SmithKline Beecham. GSK has a portfolio of products for major disease areas such as asthma, cancer, infections, mental health, diabetes, and digestive conditions.
National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)	Policy makers	The mission of NIDDK is to conduct and support medical research and research training and to disseminate science-based information on diabetes and other endocrine and metabolic diseases; digestive diseases, nutritional disorders, and obesity; and kidney, urologic, and hematologic diseases, to improve people's health and quality of life.
Patient Advocate	Patient advocacy	To represent research priorities and issues from the patient's perspective.
Society for General Internal Medicine (SGIM)	Professional societies/researchers	SGIM is a national medical society of 3,000 physicians who are the primary internal medicine faculty of every medical school and major teaching hospital in the United States. SGIM's mission is to lead excellence, change, and innovation in clinical care, education, and research in general internal medicine to achieve health care delivery that is comprehensive, technologically-advanced, and individualized; instills trust within a culture of respect; is efficient in the use of time, people, and resources; is organized and financed to achieve optimal health outcomes; maximizes equity; and continually learns and adapts.
UnitedHealth Group	Payers	UnitedHealth Group is a diversified health care company in the United States and a leader worldwide in helping people live healthier lives and helping to make the health system work better for everyone. UnitedHealth Group is an active participant in the Diabetes Prevention Program.
Young Men's Christian Association (YMCA) Diabetes Prevention Program	Policy makers; Patient advocacy	As a leading nonprofit for strengthening community through youth development, healthy living, and social responsibility, the YMCA believes that all people should be able to live life to its fullest, healthiest potential. In the YMCA's Diabetes Prevention Program a trained lifestyle coach will introduce topics in a supportive, small group environment and encourage participants as they explore how healthy eating, physical activity, and behavior changes can benefit their health.

Identification of Evidence Gaps

We used an iterative process to identify evidence gaps related to prevention of type 2 diabetes in patients with prediabetes. First, we identified and appraised recent published systematic reviews, clinical practice guidelines, and future research needs documents (including a topic brief developed for PCORI by the Johns Hopkins EPC in March 2015) to develop an initial list of evidence gaps. This list was neither exhaustive nor prioritized. Next, we organized these gaps according to broad themes and transformed them into a preliminary set of research questions. We distributed these questions to our stakeholders and asked them to review, modify, and add to the list. Stakeholders participated in a teleconference discussion of the research gaps and also provided further feedback through email. Our team reviewed this stakeholder input and produced a revised list of questions reflecting gaps in the evidence supporting diabetes prevention in prediabetes. This final list was circulated to the stakeholder team for review to ensure that our edits reflected their proposed additions.

Prioritization of Future Research

After we used stakeholder feedback to refine the proposed list of research questions, stakeholders were invited to help prioritize the list. Our online survey used a forced-ranking prioritization method described by the AHRQ EPC program, whereby participants were given 3 votes to allocate to any of the 5 identified research priorities, with a maximum of 3 votes per item.[17] The stakeholders were not given specific prioritization criteria to use, but rather were told to decide, based on their perspective, which were the most important unanswered research questions in diabetes prevention. We also asked stakeholders to self-report their perspective,

recognizing that an individual stakeholder could represent more than one perspective. Possible perspectives included: patients and the public, providers, purchasers, payers, policy makers, product makers, and principal investigators. The stakeholder-prioritized research questions were then included in our horizon scan.

Horizon Scan of Studies Potentially Relevant to Prioritized Research Questions

We performed 2 database searches to identify recently published and ongoing studies relevant to the stakeholder-prioritized research questions. We searched PubMed to identify recent relevant studies published during the past 2 years and ClinicalTrials.gov for ongoing and recently completed studies. For the search of ClinicalTrials.gov, we specified the condition as "Type 2 Diabetes" OR "prediabetes" and used the keywords "diabetes prevention" OR "prevention of diabetes" OR "prevention of type" OR "primary prevention" OR "preventing diabetes" OR "preventing type." We excluded studies with unknown status and focused on ongoing Phase 3 or 4 studies. We manually added studies cited in the topic brief completed by the Johns Hopkins EPC but not included in our search findings. Appendix A provides the exact search strategy used for PubMed.

Members of our team reviewed the identified titles and abstracts. Articles were included if they met all of the following criteria: presented original data or secondary analysis of data from a randomized controlled trial (RCT), prospective or retrospective observational study, or relevant modeling study; included data related to type 2 diabetes prevention; and had a stated objective that could be categorized according to our identified list of research priorities.

For the ClinicalTrials.gov search, a member of the ESG team reviewed all study abstracts identified by the search and coded them as potentially relevant to 1 or more of the identified

research priorities. We then abstracted study type (such as observational or RCT), recruitment status, and sample size.

RESULTS

Expansion of Evidence Gaps Through Stakeholder Engagement

We solicited participation of 60 stakeholders, and 21 (35%) individuals provided input related to diabetes prevention through participation on the teleconference, through email feedback, or by participating in the prioritization survey (Appendix B). These stakeholders represented the diverse perspectives targeted in Table 1. Central themes from the stakeholders included the following:

- Definitively answering questions for which the outcome of interest is development of diabetes and its complications will require long-term studies (>5 years). Important outcomes that could be feasibly addressed in a shorter timeframe include program reach, patient engagement, treatment choices, treatment adherence/persistence, maintenance of clinical gains (e.g., hemoglobin A1c or weight change), and feasibility of use of relevant approaches in real-world settings.
- There have been studies of different approaches to delivering intensive lifestyle modification, most of which appear reasonably effective. More pressing questions are: How do different implementation strategies impact patient engagement, adherence to/persistence with programs, and maintenance of clinical gains in real-world settings? What elements of program delivery are associated with the best outcomes?

- There is a need to evaluate shared decision making approaches to ensure that the choice of initial diabetes prevention strategy (e.g., lifestyle modification versus metformin) and goals of therapy (e.g., remaining in the prediabetic range versus normalization of blood sugar) reflect patients' values, while also recognizing that external factors (e.g., medication costs, insurance) can sometimes restrict patient choice.
- There is a need to better understand the comparative effectiveness of different diabetes management strategies (and approaches to implementing those strategies) in different patient populations (e.g., based on demographics, socioeconomic factors, psychosocial factors, or risk for progression to diabetes).
- There is a need to compare strategies for enhancing uptake of diabetes prevention strategies by patients, providers, and systems in real-world settings, and also to identify elements of program delivery associated with high program adoption.
- Given emerging data regarding the effectiveness of Mediterranean and low-carbohydrate dietary approaches for weight loss and diabetes,[18] there may be value in exploring alternative dietary approaches as part of lifestyle modification for diabetes prevention.
- Metformin is known to be effective, safe, and likely cost-saving as a long-term strategy for diabetes prevention.[19] Even if other pharmacologic agents were also effective, they would be more costly with greater concern for adverse events, given expected need for long-term use, so may be unlikely to supplant metformin.

Following the stakeholder teleconference and email discussion we finalized the research questions for prioritization:

1. What is the comparative effectiveness of different strategies for implementing lifestyle modification (e.g., community-based approaches, primary care-based approaches, approaches that leverage communications technology, and others) in terms of program reach, patient engagement, treatment adherence/persistence, maintenance of clinical gains, feasibility of use in real-world settings, and other relevant outcomes? What elements of program delivery are associated with the best outcomes?
2. What is the comparative effectiveness of different approaches to shared decision making for selecting a diabetes prevention strategy and treatment goals (including versus provider-driven selection)? How does shared decision making affect treatment choices, treatment adherence/persistence, maintenance of clinical gains, feasibility of use in real-world settings, and other relevant outcomes? How can shared decision making facilitate the transition to an alternative diabetes prevention strategy should the initial choice prove insufficiently effective?
3. What is the comparative effectiveness of lifestyle modification and metformin within different patient populations in terms of patient engagement, treatment adherence/persistence, maintenance of clinical gains, and other relevant outcomes? Populations of interest could be defined by demographics (e.g., age, sex, race), socioeconomic factors (e.g., insurance status, financial stress, social support), psychosocial factors (e.g., self-efficacy, comorbid mental illness), and risk for progression to diabetes (as determined by hemoglobin A1c, body mass index, or other means).
4. What is the comparative effectiveness of different approaches (e.g., patient outreach or advertising, physician education, patient or provider incentives, and others) for enhancing

utilization and adoption of diabetes prevention strategies (including both lifestyle modification and metformin) by patients, providers, and systems in real-world settings? What elements of program delivery are associated with high program utilization and adoption?

5. What is the comparative effectiveness of alternative dietary approaches (e.g., Mediterranean diet or low-carbohydrate diet) for diabetes prevention versus established approaches (e.g., the DPP "Core Curriculum" for fat and calorie restriction)?

We had initially planned to include a sixth question, "What is the comparative effectiveness of alternative pharmacologic approaches for diabetes prevention versus established pharmacologic approaches?" However, we decided to omit this question at this stage based on 2 concerns expressed by stakeholders. First, there already exists an effective, safe, and cost-saving pharmacologic option for long-term diabetes prevention (metformin); even if other pharmacologic agents were shown to prevent diabetes, given expected need for long-term use, they would be more expensive with greater concern for long-term safety, so may be unlikely to supplant metformin. Second, in order to definitively answer comparative effectiveness questions for which the outcome of interest is the incidence of diabetes and its complications, our stakeholders felt that long-term studies (>5 years) would be needed. Because research addressing this question is unlikely to impact health care practice in the next 3 to 5 years, we concluded that this topic would be of less interest to PCORI.

Stakeholder Ranking of Research Questions

Table 2 shows the 5 final potential research topics and stakeholder ranking. Fourteen stakeholders completed the prioritization exercise. We also indicate in Table 2 the number of

stakeholders who voted for each specific research topic, and the perspectives represented by these votes. Across the 14 stakeholders, 4 self-identified as patients, 12 as providers, 1 as purchaser, 2 as payers, 2 as policy makers, and 9 as principal investigators. No stakeholders self-identified as product makers. Stakeholders prioritized question 2 (shared decision making for selecting a diabetes prevention strategy and treatment goals) most highly, followed closely by question 3 (comparative effectiveness of diabetes prevention strategies in different patient populations) and question 4 (approaches for enhancing utilization and adoption of diabetes prevention strategies in real-world settings). While question 1 (comparative effectiveness of strategies for implementing lifestyle modification in real-world settings) received 5 votes from 5 stakeholders, question 5 (comparative effectiveness of alternative dietary approaches) received votes from only 3 stakeholders. Because question 5 received votes from the fewest stakeholders, and because of stakeholder concerns about the need for long-term studies also applied to this question, we excluded it from subsequent steps of the prioritization process.

Table 2. Final ranking of future research needs for diabetes prevention in prediabetes

	Question	Score	Stakeholders, *n*	Perspectives[a]
1.	What is the comparative effectiveness of different strategies for implementing lifestyle modification (e.g., community-based approaches, primary care-based approaches, approaches that leverage communications technology, and others) in terms of program reach, patient engagement, treatment adherence/persistence, maintenance of clinical gains, feasibility of use in real-world settings, and other relevant outcomes? What elements of program delivery are associated with the best outcomes?	5	5	1 patient, 5 providers, 1 payer, 1 policy maker, 4 PIs
2.	What is the comparative effectiveness of different approaches to shared decision making for selecting a diabetes prevention strategy and treatment goals (including versus provider-driven selection)? How does shared decision making affect treatment choices, treatment adherence/persistence, maintenance of clinical gains, feasibility of use in real-world settings, and other relevant outcomes? How can shared decision making facilitate the transition to an alternative diabetes prevention strategy should the initial choice prove insufficiently effective?	11	8	1 patients, 7 providers, 1 purchaser, 1 payer1 policy maker, 4 PIs
3.	What is the comparative effectiveness of lifestyle modification and metformin within different patient populations in terms of patient engagement, treatment adherence/persistence, maintenance of clinical gains, and other relevant outcomes? Populations of interest could be defined by demographics (e.g., age, sex, race), socioeconomic factors (e.g., insurance status, financial stress, social support), psychosocial factors (e.g., self-efficacy, comorbid mental illness), and risk for progression to diabetes (as determined by hemoglobin A1c, body mass index, or other means).	10	8	2 patients, 7 providers, 1 purchaser, 2 payers, 6 PIs
4.	What is the comparative effectiveness of different approaches (e.g., patient outreach or advertising, physician education, patient or provider incentives, and others) for enhancing utilization and adoption of diabetes prevention strategies (including both lifestyle modification and metformin) by patients, providers, and systems in real-world settings? What elements of program delivery are associated with high program utilization and adoption?	9	7	2 patients, 6 providers, 1 payer, 1 policy maker, 6 PIs

	Question	Score	Stakeholders, *n*	Perspectives[a]
5.	What is the comparative effectiveness of alternative dietary approaches (e.g., Mediterranean diet or low-carbohydrate diet) for diabetes prevention versus established approaches (e.g., the DPP "Core Curriculum" for fat and calorie restriction)?	7	3	1 patient, 2 providers, 2 PIs

[a] Stakeholders could self-identify as representing more than one perspective.

Horizon Scan of Studies Potentially Relevant to Prioritized Research Questions

Our PubMed search identified 334 articles. Of these, 32 met our inclusion criteria and included 6 systematic reviews, 13 RCTs, 10 cohort studies, 0 case-control studies, and 3 other studies. Sample sizes ranged from 31 to 3060. Only 7 studies were active comparator studies; 12 studies either were placebo-controlled or used standard of care as the comparison; and 13 studies had no comparator. Sixteen studies were applicable to question 1; none were applicable to question 2; 28 were applicable to question 3; and 6 were applicable to question 4.

Our search of ClinicalTrials.gov yielded 94 studies, and 60 were added from the Johns Hopkins topic brief, bringing the total to 154. We identified 24 protocols as potentially relevant to the prioritized research questions. Sample sizes ranged from 36 to 20,000 patients.

The Tables in Appendix C detail key characteristics of the included PubMed and ClinicalTrials.gov articles separately for each of the prioritized research questions.

DISCUSSION

Prediabetes is a direct contributor to the growing diabetes epidemic in the United States. Because diabetes generates substantial morbidity and costs, preventing its development in the growing prediabetes population is crucial to improving patient-centered outcomes. Although lifestyle modification and pharmacotherapy are effective strategies for diabetes prevention, ongoing uncertainty makes diabetes prevention a high-yield area for PCORI involvement. We have worked with a diverse group of relevant stakeholders to refine and prioritize possible research questions for targeted PCORI funding initiatives.

A central theme of our stakeholder discussions was that, in order to definitively answer comparative effectiveness questions for which the outcome of interest is incidence of diabetes and its complications, long-term studies are required. This issue applies particularly to questions addressing the comparative effectiveness of pharmacologic or dietary approaches to diabetes prevention; for example, the original DPP trial was stopped due to efficacy after approximately 3 years, and outcome data covering a 10-year period have been published. Because PCORI expressed the desire to fund research that is likely to impact health care practice in the next 3 to 5 years, we used our stakeholders' input to formulate important research questions that would be answerable within this period. Rather than directly examining the incidence of diabetes and its complications, our prioritized questions address outcomes like program reach, patient engagement, treatment choices, treatment adherence/persistence, maintenance of clinical gains (e.g., hemoglobin A1c or weight change), and feasibility of use of relevant approaches under real-world conditions.

Prioritized Research Questions

Shared Decision Making for Choosing Diabetes Prevention Strategies

Our stakeholders felt that research addressing the role of shared decision making in selecting diabetes prevention strategies and treatment goals should be a high priority. Shared decision making is a process of communication, deliberation, and decision making in which: 1) the clinician shares information about relevant options with the patient, including the severity and probability of potential harms and benefits; 2) the patient explores and shares his or her preferences with the clinicians regarding these harms, benefits, and potential outcomes; and 3) the clinician and patient reach a mutual decision about the treatment plan through an interactive

process of reflection and discussion.[20] Decision aids or other tools may be utilized to facilitate the process of shared decision making.

Although there are ample data to support the use of decision aids or other shared decision making processes in other conditions,[21] there is little published evidence supporting their use in deciding between options for diabetes prevention; this is important because decision aids are disease- or condition-specific. We found one relevant published decision aid that is available for public use[22] and one ongoing trial that may inform this question. However, given the relative paucity of ongoing research, the potential value of shared decision making in enhancing the patient-centeredness of choosing diabetes prevention strategies and treatment goals, and PCORI's prior interest in promoting the use of shared decision making and decision aids,[23] this would appear to be a logical area for PCORI to fund additional research. By prospectively examining the comparative effectiveness of available strategies for shared decision making (including versus provider-driven selection) in real-world settings, and using outcomes including patient engagement, treatment choices, treatment adherence/persistence, and maintenance of clinical gains, such research could be expected to impact care in the next 3 to 5 years.

Diabetes Prevention Strategies in Different Patient Populations

Certain populations, such as American Indians, Alaska Natives, and non-Hispanic blacks are known to have higher risk than other demographic groups for developing diabetes.[6] A recent analysis of the DPP found that the effectiveness of diabetes prevention strategies may vary between populations with different levels of diabetes risk; for example, metformin appears to have a greater effect on individuals with higher hemoglobin A1c, obesity, and younger age.[24] In light of this heterogeneity, our stakeholders felt that improving our understanding of which

approaches work best for different patient populations (including those defined by demographics, socioeconomic factors, psychosocial factors, and risk for progression to diabetes) would greatly enhance diabetes prevention efforts, and should be a priority. We found little research specifically addressing this question, but we did find a large number of prior and ongoing studies comparing different lifestyle and pharmacologic approaches that could be retrospectively analyzed with population differences in mind. It is also possible that these data may warrant systematic review or meta-analysis. Alternatively, prospective research could examine patient engagement, treatment adherence/persistence, maintenance of clinical gains, and other outcomes with different diabetes prevention approaches in relevant populations under real-world conditions.

Enhancing Utilization and Adoption of Diabetes Prevention Strategies

Because prediabetes is likely underdiagnosed, and documentation of lifestyle interventions is often incomplete,[5,6] the proportion of people with prediabetes currently receiving effective diabetes prevention is unclear. However, our stakeholders believe that, given the large number of individuals with prediabetes, only a fraction of eligible individuals are currently engaged in formal diabetes prevention efforts. In order to reduce diabetes incidence and improve patient-centered outcomes, there is a clear need to increase utilization and adoption of effective diabetes prevention strategies by patients, providers, and systems. While prior and ongoing work may provide some insights,[25] we found relatively little research addressing this need. Our stakeholders felt that, given widespread underutilization of diabetes prevention strategies, research examining the comparative effectiveness of different approaches to increase utilization and adoption of effective strategies in real-world settings would likely impact care in the next 3

to 5 years, and should be a priority. Possible study designs could include prospective, comparative examinations of different patient-, provider-, and system-level approaches to increasing utilization, as well as observational explorations of program elements associated with high program utilization and adoption.

Different Strategies for Implementing Lifestyle Modification

Intensive lifestyle modification for diabetes prevention has been delivered using individual and group-based approaches in different settings, including community-based programs (e.g., churches, YMCA), primary care-based programs, and programs that leverage communications technology (e.g., telemedicine, mHealth, eHealth, etc.).[26,27] While our stakeholders saw most approaches as reasonably effective, they expressed uncertainty regarding how these different implementation strategies impact patient engagement, adherence to/persistence with programs, maintenance of clinical gains, and feasibility of use under real-world conditions. Pragmatic comparative effectiveness trials designed to evaluate these outcomes in real-world settings is likely to impact diabetes prevention practice within the next 3 to 5 years, as could observational studies examining elements of program delivery that are associated with the best outcomes. We found sufficient prior and ongoing research in this area that a systematic review could also be considered as an approach to examine features of successful programs.

Additional Research Questions

After considering our stakeholders' input, we omitted questions addressing the comparative effectiveness of alternative pharmacologic and dietary approaches for diabetes prevention versus established strategies. We did this because our stakeholders felt that definitively answering these questions would require long-term studies that are unlikely to impact health care practice in the

next 3 to 5 years. Further, in the case of alternative pharmacologic approaches, concerns relating to costs and adverse events may prevent other agents from supplanting metformin. However, if PCORI does wish to fund longer term studies examining these questions (or wishes to explore them using the shorter term outcomes of interest discussed above), these do represent important areas for future research.

Limitations

While we worked with our stakeholders to identify the most pertinent evidence gaps and research questions pertaining to diabetes prevention in the prediabetes population, the prioritized list may not reflect the full range of possible future research needs relating to this topic. Although our stakeholder group comprised renowned researchers, experienced clinicians, policy experts, and representatives of key professional organizations, payer organizations, and patient groups, it is also possible that a different group of stakeholders might prioritize future research differently. Because only 4 patients participated in the prioritization exercise, PCORI may wish to elicit additional patient perspectives on these research questions in order to ensure that all perspectives are adequately considered. Finally, because a comprehensive systematic review has not been performed for many of the identified evidence gaps, we cannot determine with certainty the degree to which prioritized future research needs have already been addressed.

CONCLUSIONS

Based on input from our stakeholder group, key research priorities pertaining to diabetes prevention in the prediabetes population include the comparative effectiveness of: 1) approaches to shared decision making for selecting a diabetes prevention strategy and treatment goals; 2)

diabetes prevention strategies in different patient populations; 3) approaches for enhancing utilization and adoption of diabetes prevention strategies in real-world settings; and 4) strategies for implementing lifestyle modification in real-world settings.

REFERENCES

1. World Health Organization. Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia : report of a WHO/IDF consultation; 2006. www.who.int/diabetes/publications/Definition%20and%20diagnosis%20of%20diabetes_new.pdf. Accessed June 30, 2015.
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.

7. de Vegt F, Dekker JM, Jager A, et al. Relation of impaired fasting and postload glucose with incident type 2 diabetes in a Dutch population: the Hoorn Study. JAMA. 2001;285(16):2109-13. PMID: 11311100.

8. Vaccaro O, Ruffa G, Imperatore G, et al. Risk of diabetes in the new diagnostic category of impaired fasting glucose: a prospective analysis. Diabetes Care. 1999;22(9):1490-3. PMID: 10480514.

9. Schottker B, Raum E, Rothenbacher D, et al. Prognostic value of haemoglobin A1c and fasting plasma glucose for incident diabetes and implications for screening. Eur J Epidemiol. 2011;26(10):779-87. PMID: 21947790.

10. Francis BH, Song X, Andrews LM, et al. Progression to type 2 diabetes, healthcare utilization, and cost among pre-diabetic patients with or without comorbid hypertension. Curr Med Res Opin. 2011;27(4):809-19. PMID: 21306287.

11. American Diabetes Association. Economic costs of diabetes in the U.S. in 2012. Diabetes Care. 2013;36(4):1033-46. PMID: 23468086.

12. Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002;346(6):393-403. PMID: 11832527.

13. Diabetes Prevention Program Research Group, Knowler WC, Fowler SE, et al. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. Lancet. 2009;374(9702):1677-86. PMID: 19878986.

14. Li G, Zhang P, Wang J, et al. The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study. Lancet. 2008;371(9626):1783-9. PMID: 18502303.

15. Lindstrom J, Ilanne-Parikka P, Peltonen M, et al. Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study. Lancet. 2006;368(9548):1673-9. PMID: 17098085.

16. Diabetes Prevention Program Research Group. The 10-year cost-effectiveness of lifestyle intervention or metformin for diabetes prevention: an intent-to-treat analysis of the DPP/DPPOS. Diabetes Care. 2012;35(4):723-30. PMID: 22442395.

17. Chang SM, Carey TS, Kato EU, et al. Identifying research needs for improving health care. Ann Intern Med. 2012;157(6):439-45. PMID: 22847017.

18. Salas-Salvado J, Bullo M, Estruch R, et al. Prevention of diabetes with Mediterranean diets: a subgroup analysis of a randomized trial. Ann Intern Med. 2014;160(1):1-10. PMID: 24573661.

19. Diabetes Prevention Program Research Group. Long-term safety, tolerability, and weight loss associated with metformin in the Diabetes Prevention Program Outcomes Study. Diabetes Care. 2012;35(4):731-7. PMID: 22442396.

20. Institute of Medicine. Shared Decision-Making Strategies for Best Care: Patient Decision Aids; September 2014. www.iom.edu/Global/Perspectives/2014/SDMforBestCare.aspx. Accessed June 30, 2015.

21. Stacey D, Legare F, Col NF, et al. Decision aids for people facing health treatment or screening decisions. Cochrane Database of Systematic Reviews. 2014;1:CD001431. PMID: 24470076.

22. Healthwise Knowledgebase. Prediabetes: Which Treatment Should I Use? www.healthwise.net/cochranedecisionaid/Content/StdDocument.aspx?DOCHWID=abp5563. Accessed June 30, 2015.

23. Gayer GC, Crowley MJ, Lawrence W, et al. PCORI's Decision Aid Portfolio: Current Status and Future Directions [In preparation].

24. Sussman JB, Kent DM, Nelson JP, et al. Improving diabetes prevention with benefit based tailored treatment: risk based reanalysis of Diabetes Prevention Program. BMJ. 2015;350:h454. PMID: 25697494.

25. Ackermann RT, Kenrik Duru O, Albu JB, et al. Evaluating diabetes health policies using natural experiments: the natural experiments for translation in diabetes study. Am J Prev Med. 2015;48(6):747-54. PMID: 25998925.

26. Ackermann RT, Finch EA, Brizendine E, et al. Translating the Diabetes Prevention Program into the community. The DEPLOY Pilot Study. Am J Prev Med. 2008;35(4):357-63. PMID: 18779029.

27. American Diabetes Association. Prevention or delay of type 2 diabetes. Diabetes Care. 2015;38(Suppl 1):S31-S32.

Appendix A. Pub Med Search Strategy

Search date: June 24, 2015

Set #	Search Terms	Results
#1	"Diabetes Mellitus, Type 2/prevention and control"[Mesh]	5268
#3	(randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR randomised[tiab] OR randomization[tiab] OR randomisation[tiab] OR placebo[tiab] OR randomly[tiab] OR trial[tiab] OR Clinical trial[pt] OR “clinical trial”[tiab] OR “clinical trials ”[tiab] OR "comparative study"[Publication Type] OR "comparative study"[tiab] OR systematic[subset] OR "meta-analysis"[Publication Type] OR "meta-analysis as topic"[MeSH Terms] OR "meta-analysis"[tiab] OR "meta-analyses"[tiab]) OR ("evaluation studies"[Publication Type] OR "evaluation studies as topic"[MeSH Terms] OR "evaluation study"[tiab] OR “evaluation studies”[tiab] OR "intervention studies"[MeSH Terms] OR "intervention study"[tiab] OR "intervention studies"[tiab] OR "case-control studies"[MeSH Terms] OR "case-control"[tiab] OR "cohort studies"[MeSH Terms] OR cohort[tiab] OR "longitudinal studies"[MeSH Terms] OR "longitudinal”[tiab] OR longitudinally[tiab] OR "prospective"[tiab] OR prospectively[tiab] OR "retrospective studies"[MeSH Terms] OR "retrospective"[tiab]) NOT (Editorial[ptyp] OR Letter[ptyp] OR Case Reports[ptyp] OR Comment[ptyp]) NOT (animals[mh] NOT humans[mh])	4,216,401
#4	#1 AND #2	2364
#5	Limits: English, Date: 2013/06/24 – present	334

Appendix B. Participating Stakeholders

Ronald Ackermann, MD, MPH
Director, Center for Community Health - Institute for Public Health and Medicine
Northwestern University
Perspective: Provider/Principal Investigator

Ann Albright PhD, RD
Director, Division of Diabetes Translation
National Center for Chronic Disease Prevention and Health Promotion
Centers for Disease Control and Prevention
Perspective: Patient/Provider/Policy maker/Principal Investigator

Kate Cornell
Perspective: Patient

Samuel Dagogo Jack, MD
President, Medicine & Science of the American Diabetes Association (ADA)
Professor of Medicine and Director, Division of Endocrinology, Diabetes and Metabolism
Director, Clinical Research Center at the University of Tennessee Health Science Center, Memphis
Perspective: Policy maker

David Dugdale, MD, MS
Treasure- Elect, Society for General Internal Medicine (SGIM)
Professor, Department of Medicine
University of Washington
Perspective: Policy maker

Judith Fradkin, MD
Director, Division of Diabetes, Endocrinology, and Metabolic Diseases
National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)
Perspective: Provider/Principal Investigator

Marion Franz, MS, RD, LD, CDE
Manager, Nutrition Concepts By Franz Inc
Perspective: Provider

Mamta Gakhar, MPH
Project Manager, Program Delivery and Technical Assistance, YMCA of the USA
Perspective: Provider

Jennifer Green, MD
Associate Profess of Medicine
Diabetes and Metabolism Specialist, Endrocrinology

Duke University
Perspective: Provider/Principal Investigator

Judith Jacobi, PharmD, FCCP, BCPS
President, American College of Clinical Pharmacy (ACCP)
Indiana University Health
Perspective: Policy maker

Ashish Joshi PhD
Senior Director, Value Evidence Leader, Metabolism
Global Value Evidence and Outcomes
RD Projects Clinical Platforms & Sciences GlaxoSmithKline (GSK)
Perspective: Product maker

Namratha Kandula, MD,MPH
Assistant Professor in Medicine
General Internal Medicine and Geriatrics
Preventive Medicine and Weinberg College of Arts and Sciences
Perspective: Principal Investigator

Kenneth Lin, MD
Palo Alto Medical Foundation
Perspective: Provider/Policy maker

Teresa Littlefield
Perspective: Patient/Provider/Purchaser/Payer

Tannaz Moin, MBA, MD, MS
Division of Endocrinology, Diabetes, and Hypertension
David Geffen School of Medicine
University of California, Los Angeles
Perspective: Provider/Principal Investigator
David Nathan, MD
Chairman, Diabetes Prevention Program
Professor of Medicine, Harvard Medical School
Chief, Diabetes Unit Medical Service
Department of Molecular Biology
Perspective: Provider/Principal Investigator

Matthew O'Brien, MD
Assistant Professor in Medicine-General Internal Medicine and Geriatrics
Center for Community Health
Institute for Public Health and Medicine
Perspective: Provider/Principal Investigator

Richard Pratley, MD
Senior Investigator, Translational Research Institute
Medical Director, Florida Hospital Diabetes Institute (FHDI)
Perspective: Provider/Principal Investigator

Jessica Trompeter, PharmD, MBA, BCPS
American College of Clinical Pharmacy (ACCP)
Division of Physician Assistant Studies
Department of Pharmacy Practice
Bernard J. Dunn School of Pharmacy
Shenandoah University
Perspective: Policy maker

Guillermo Umpierrez, MD
Professor of Medicine, Div of Endocrinology, Metabolism and Lipids
Emory University
American Academy of Endocrinologists (AACE)
Perspective: Policy maker

Deneen Vojta, MD
Senior Vice President, Business Initiatives and Clinical Affairs,
UnitedHealth Center for Health Reform & Modernization
Chief Clinical Officer and Executive Vice President,
Diabetes Prevention and Control Alliance
UnitedHealth Group
Perspective: Patient/Provider/Payer/Principal Investigator

William Yancy, MD, MPH
Associate Professor, Department of Medicine
Duke University
Perspective: Provider/Principal Investigator

Appendix C. Supplementary Tables

Appendix Table C-1. Published and ongoing studies potentially relevant to Research Question 1 *[What is the comparative effectiveness of different strategies for implementing lifestyle modification (e.g., community-based approaches, primary care-based approaches, approaches that leverage communications technology, and others) in terms of program reach, patient engagement, treatment adherence/persistence, maintenance of clinical gains, feasibility of use in real-world settings, and other relevant outcomes? What elements of program delivery are associated with the best outcomes?]*

Study	N	Objective
Systematic Reviews		
Dhippayom, 2014[1]	24 studies	To explore the extent of the use of diabetes risk assessment tools and to determine influential variables associated with the implementation of these tools
Dunkley, 2014[2]	25 studies	To summarize the evidence on effectiveness of translational diabetes prevention programs, based on promoting lifestyle change to prevent type 2 diabetes in real-world settings and to examine whether adherence to international guideline recommendations is associated with effectiveness
Merlotti, 2014[3]	71 studies	To explore the extent of the use of diabetes risk assessment tools and to determine influential variables associated with the implementation of these tools
RCTs		
Duggan, 2014[4]	320 patients	The trial compared participants in the intervention arm, who received an immediate educational curriculum (n = 166), to participants in the control arm, who received a delayed educational curriculum (n = 154).
Parker, 2014[5]	76 patients	We investigated the effect of medical nutrition therapy (MNT) compared with usual care...of a 12-week intervention in overweight or obese adults with prediabetes
Tokunaga-Nakawatase, 2014[6]	141 patients	To investigate the effect of a computer-supported indirect-form lifestyle-modification program using Lifestyle Intervention Support Software for Diabetes Prevention (LISS-DP), as a clinically feasible strategy for primary prevention, on diet and physical activity habits in adults with a family history of type 2 diabetes.
Whittemore, 2014[7]	67 patients	To describe the process of implementing a diabetes prevention program provided by homecare nurses to residents of public housing communities
Admiraal, 2013[8]	536 patients	To study 1-year effectiveness of an intensive, culturally targeted lifestyle intervention in general practice for weight status and metabolic profile of South-Asians at risk of type 2 diabetes
Ramachandran, 2013[9]	537 patients	To assess whether mobile phone messaging that encouraged lifestyle change could reduce incident type 2 diabetes in Indian Asian men with impaired glucose tolerance

Study	N	Objective
Wong, 2013[10]	54 patients	To determine the efficacy of delivering short-message service (SMS) to provide diabetes-related information in reducing the risk of developing diabetes in Chinese professional drivers with pre-diabetes
Cohort Studies		
Chen, 2014[11]	1885 patients	To develop and test an online Smart Web Aid for Preventing Type 2 Diabetes (SWAP-DM2) capable of addressing major barriers to applying proven interventions and integrating diabetes prevention into routine medical care
Kieffer, 2014[12]	278 patients	We evaluated the effectiveness of a community-based healthy lifestyle intervention in improving dietary behaviors of pregnant Latinas from 2004 to 2006 in Detroit, Michigan.
Kutob, 2014[13]	39 patients	To evaluate the feasibility and efficacy of group office visits on reducing diabetes risk in a multiethnic, primary care population
Zyriax, 2014[14]	300 patients	To assess if screening for individuals at risk and long-standing diabetes prevention is feasible in the setting of companies within the scope of the German legal health system
Agarwal, 2013[15]	588 patients	This article describes the Community Health Awareness Diabetes (CHAD) program and its feasibility
Cene, 2013[16]	104 patients	To describe the feasibility of using a community-based participatory research (CBPR) approach to implement the Power to Prevent (P2P) diabetes prevention education curriculum in rural African American (AA) settings
Case-Control Studies		
None	–	–
Ongoing Studies (ClinicalTrials.gov)		
Assessing the Effectiveness of a Weight Watchers-based Lifestyle Intervention for the Primary Prevention of Type 2 Diabetes (NCT02000024)	225 patients	Ongoing (Estimated completion April 2015). This study is a randomized pilot study to assess the applicability of the Weight Watchers model for lifestyle modification to the primary prevention of type 2 diabetes. The approach developed by Weight Watchers to achieve weight loss is based on similar nutritional principals and techniques used in the Diabetes Prevention Program (DPP) lifestyle intervention; monitoring food intake, exercising calorie control, setting modest weight loss goals and using physical activity.
Use of Mobile Technology to Promote Sustained Lifestyle Changes to Prevent Type 2 Diabetes in India and the UK (NCT01570946)	1050 patients	Ongoing (Estimated completion December 2015). The current study proposes a prevention strategy that will employ a lifestyle modification programme delivered by text messaging in both India and the UK.
(Cost-)Effectiveness of SLIMMER Diabetes Prevention Intervention (NCT02094911)	316 patients	Ongoing (Estimated completion May 2015). The overall aim of the project is to evaluate the (cost-)effectiveness of the SLIMMER diabetes prevention intervention in Dutch primary health care.

Study	N	Objective
Encourage Healthy Families (NCT01823367)	350 patients	Ongoing (Estimated completion November 2015). This study is a randomized intervention that will test two different approaches reflecting diverse levels of both intensity and cost, to achieving risk reduction of T2D.
Diabetes Prevention Using SMS Technology (NCT01795833)	2268 patients	Ongoing (Estimated completion December 2017). We propose using a mobile phone intervention for lifestyle change and will assess it in a clinical trial (study) in people with impaired glucose regulation (high risk at developing type 2 diabetes).
A Randomized Trial of Diabetes Prevention Through Lifestyle Change in India (NCT01283308)	599 patients	Ongoing (Estimated completion July 2017). The Diabetes Community Lifestyle Improvement Program (D-CLIP) will test in a randomized trial if a culturally specific, community-based lifestyle and metformin (for individuals who do not respond to lifestyle change alone) intervention for men and women living in Chennai, India can effectively prevent type 2 diabetes in high-risk individuals.
A Patient-Centered Strategy for Improving Diabetes Prevention in Urban American Indians (NCT02266576)	204 patients	Ongoing (Estimated completion April 2017). The goal of the proposed research is to identify effective patient-centered strategies to prevent diabetes in high-risk populations in real world settings.
Avoiding Diabetes After Pregnancy Trial in Moms (NCT01918345)	225 patients	Ongoing (Estimated completion January 2018). This pilot study will investigate the feasibility and effectiveness of a physical activity and diet intervention. It will also explore the relationship between behaviour change and metabolic markers of T2DM in this high-risk population.
A Pharmacist-Coordinated Implementation of the Diabetes Prevention Program (NCT02384109)	700 patients	Ongoing (Estimated completion June 2019). This proposed project will translate evidence-based strategies for diabetes prevention within the framework of an existing and highly utilized pharmacist-led diabetes care program.

Abbreviations not defined above: N=number of studies/patients; RCTs=randomized controlled trials; SMS=short message service; T2D=type 2 diabetes; T2DM=type 2 diabetes mellitus

Appendix Table C-2. Published and ongoing studies potentially relevant to Research Question 2 *[What is the comparative effectiveness of different approaches to shared decision making for selecting a diabetes prevention strategy and treatment goals (including versus provider-driven selection)? How does shared decision making affect treatment choices, treatment adherence/persistence, maintenance of clinical gains, feasibility of use in real-world settings, and other relevant outcomes? How can shared decision making facilitate the transition to an alternative diabetes prevention strategy should the initial choice prove insufficiently effective?]*

Study	N	Objective
Systematic Reviews		
None	–	–
RCTs		
None	–	–

Study	N	Objective
Cohort Studies		
None	–	–
Case-Control Studies		
None	–	–
Ongoing Studies (ClinicalTrials.gov)		
A Pharmacist-Coordinated Implementation of the Diabetes Prevention Program (NCT02384109)	700 patients	Ongoing (Estimated completion June 2019). This proposed project will translate evidence-based strategies for diabetes prevention within the framework of an existing and highly utilized pharmacist-led diabetes care program.

Abbreviations not defined above: N=number of studies/patients; RCTs=randomized controlled trials

Appendix Table C-3. Published and ongoing studies potentially relevant to Research Question 3 *[What is the comparative effectiveness of lifestyle modification and metformin within different patient populations in terms of patient engagement, treatment adherence/persistence, maintenance of clinical gains, and other relevant outcomes? Populations of interest could be defined by demographics (e.g., age, sex, race), socioeconomic factors (e.g., insurance status, financial stress, social support), psychosocial factors (e.g., self-efficacy, comorbid mental illness), and risk for progression to diabetes (as determined by hemoglobin A1c, body mass index, or other means).]*

Study	N	Objective
Systematic Reviews		
Gong, 2015[17]	NR	To determine the efficacy of lifestyle interventions in adults with IGT.
Aguiar, 2014[18]	8 studies	To systematically review and meta-analyze the evidence on multi-component (diet + aerobic exercise + resistance training) lifestyle interventions for type 2 diabetes prevention
Dunkley, 2014[2]	25 studies	To summarize the evidence on effectiveness of translational diabetes prevention programs, based on promoting lifestyle change to prevent type 2 diabetes in real-world settings and to examine whether adherence to international guideline recommendations is associated with effectiveness
Merlotti, 2014[3]	71 studies	To explore the extent of the use of diabetes risk assessment tools and to determine influential variables associated with the implementation of these tools
Schellenberg, 2013[19]	9 studies	To systematically review the effectiveness of lifestyle interventions on minimizing progression to diabetes in high-risk patients or progression to clinical outcomes (such as cardiovascular disease and death) in patients with type 2 diabetes
RCTs		
Duggan, 2014[4]	320 patients	The trial compared participants in the intervention arm, who received an immediate educational curriculum (n = 166), to participants in the control arm, who received a delayed educational curriculum (n = 154).

Study	N	Objective
Li, 2014[20]	577 patients	We assessed the long-term effect of lifestyle intervention on long-term outcomes among adults with impaired glucose tolerance who participated in the Da Qing Diabetes Prevention Study
Shek, 2014[21]	450 patients	To study whether lifestyle intervention can reduce the development of type II diabetes mellitus (DM) and metabolic syndrome (MS) among Chinese women who had gestational diabetes mellitus (GDM).
Vincent, 2014[22]	58 patients	This article reports the results of a community-based, culturally tailored diabetes prevention program for overweight Mexican American adults on weight loss, waist circumference, diet and physical activity self-efficacy, and diet behaviors
Whittemore, 2014[7]	67patients	To describe the process of implementing a diabetes prevention program provided by homecare nurses to residents of public housing communities
Admiraal, 2013[8]	536 patients	To study 1-year effectiveness of an intensive, culturally targeted lifestyle intervention in general practice for weight status and metabolic profile of South-Asians at risk of type 2 diabetes
den Boer, 2013[23]	146 patients	to determine the effects of the SLIM lifestyle intervention on the incidence and prevalence of the metabolic syndrome (MetS) during the active intervention and four years thereafter
Islam, 2013[24]	48 patients	We explore the impact and feasibility of a pilot Community Health Worker (CHW) intervention to improve health behaviors and promote diabetes prevention among Korean Americans using a randomized controlled trial
Maruthur, 2013[25]	3041 patients	To quantify the relationship between early measures of weight and glucose and subsequent diabetes in patients undergoing diabetes prevention interventions
Ramachandran, 2013[9]	537 patients	To assess whether mobile phone messaging that encouraged lifestyle change could reduce incident type 2 diabetes in Indian Asian men with impaired glucose tolerance
Cohort Studies		
Chen, 2014[11]	1885 patients	To develop and test an online Smart Web Aid for Preventing Type 2 Diabetes (SWAP-DM2) capable of addressing major barriers to applying proven interventions and integrating diabetes prevention into routine medical care
Gutierrez, 2014[26]	183 patients	To evaluate Fine, Fit, and Fabulous (FFF), a faith-based diabetes prevention program for black and Latino congregants at churches in low-income New York City neighborhoods
Islam, 2014[27]	126 patients	Using a quasi-experimental two-arm design, 126 Sikh Asian Indians living in New York City were enrolled in a six-workshop intervention led by community health workers.
Kieffer, 2014[12]	278 patients	We evaluated the effectiveness of a community-based healthy lifestyle intervention in improving dietary behaviors of pregnant Latinas from 2004 to 2006 in Detroit, Michigan.

Study	N	Objective
Kutob, 2014[13]	39 patients	To evaluate the feasibility and efficacy of group office visits on reducing diabetes risk in a multiethnic, primary care population
Rautio, 2014[28]	1661 patients	To compare cardio-metabolic risk profile and responses to a 1-year lifestyle intervention program in women with and without history of GDM
Sagarra, 2014[29]	2054 patients	Transferring the results from clinical trials on type 2 diabetes prevention is the objective of the Diabetes in Europe-Prevention using Lifestyle, Physical Activity and Nutritional intervention (DE-PLAN) project in Catalonia, whose cost-effectiveness analysis is now presented
Zyriax, 2014[14]	300 patients	To assess if screening for individuals at risk and long-standing diabetes prevention is feasible in the setting of companies within the scope of the German legal health system
Agarwal, 2013[15]	588 patients	This article describes the Community Health Awareness Diabetes (CHAD) program and its feasibility
Cene, 2013[16]	104 patients	To describe the feasibility of using a community-based participatory research (CBPR) approach to implement the Power to Prevent (P2P) diabetes prevention education curriculum in rural African American (AA) settings
Case-Control Studies		
None	–	–
Other Study Designs		
Sussman, 2015[30]	3060 patients	To determine whether some participants in the Diabetes Prevention Program were more or less likely to benefit from metformin or a structured lifestyle modification program
Png, 2014[31]	NR	Estimates the 3-year cost-effectiveness of lifestyle modification and metformin among pre-diabetic subjects from a Singapore health system and societal perspective
Lie, 2013[32]	31 patients	To explore factors influencing post-natal health behaviours following the experience of gestational diabetes, and to elicit women's views about the feasibility of lifestyle intervention to prevent diabetes during the first 2 years after childbirth
Ongoing Studies (ClinicalTrials.gov)		
Diabetes Prevention Among Post-partum Women With History of Gestational Diabetes (NCT02240420)	180 patients	Ongoing (Estimated completion December 2016). The purpose of the STAR-MAMA intervention is to develop a patient-tailored telephone-base counseling intervention for young Latino women who are at high risk of diabetes.
Diabetes Prevention in Clinical Practice (NCT01834378)	2000 patients	Ongoing (Estimated completion April 2020). The overall aim is to focus on change of physical activity and to keep other life style activities more or less unchanged (diet, smoking, etc) and the effect on metabolic variables.
Use of Mobile Technology to Promote Sustained Lifestyle Changes to Prevent Type 2 Diabetes in India and the UK (NCT01570946)	1050 patients	Ongoing (Estimated completion December 2015). The current study proposes a prevention strategy that will employ a lifestyle modification programme delivered by text messaging in both India and the UK.

Study	N	Objective
(Cost-)Effectiveness of SLIMMER Diabetes Prevention Intervention (NCT02094911)	316 patients	Ongoing (Estimated completion May 2015). The overall aim of the project is to evaluate the (cost-)effectiveness of the SLIMMER diabetes prevention intervention in Dutch primary health care.
Effect of Diet and Physical Activity on Incidence of Type 2 Diabetes (NCT01777893)	2500 patients	Ongoing (Estimated completion December 2017). Study hypothesis is that a high-protein, low-GI diet will be superior in preventing type-2 diabetes, compared with a moderate protein, moderate GI diet, and that high-intensity physical activity will be superior compared to moderate-intensity physical activity.
Local Measures to Prevent Diabetes in the Værnes Region (NCT01135901)	200 patients	Ongoing (Estimated completion September 2017). The aim is to identify adults with overweight and with an increased risk of developing diabetes mellitus type 2, then to prevent the disease to develop by the means of a behaviour change programme.
Encourage Healthy Families (NCT01823367)	350 patients	Ongoing (Estimated completion November 2015). This study is a randomized intervention that will test two different approaches reflecting diverse levels of both intensity and cost, to achieving risk reduction of T2D.
(Pakistan Diabetes Prevention Program PDPP) (NCT01530165)	20,000 patients	Ongoing (Estimated completion October 2015). The Karachi-based Pakistan Diabetes Prevention Study aims to address key issues in the prevention of type 2 diabetes. Approximately 20,000 people From four communities will be screened for diabetes risk factors using a non-invasive diabetes risk-score system. Those found to be at increased risk will be given an oral glucose tolerance test. People who, after the oral glucose tolerance test, are identified as having prediabetes will have the opportunity to take part in the Pakistan Diabetes Prevention Study lifestyle intervention. This consists of culturally adjusted preventive strategies focusing on diet and physical activity in real-life settings. Another important aspect of this trial will be to assess the impact of urban planning on the prevalence of obesity and diabetes
Diabetes Prevention Program Outcomes Study (NCT00038727)	2776 patients	Ongoing (Estimated completion January 2015). Clinically important research questions remain that focus on 1) durability of the prior DPP intervention, 2) determination of the clinical course of precisely known new onset diabetes, in particular regarding microvascular disease, CVD risk factors and atherosclerosis, 3) close examination of these topics in men vs women and in minority populations.
Individualized Lifestyle Intervention in Subjects With Prediabetes (NCT01947595)	1000 patients	Ongoing (Estimated completion not reported). The purpose of this prospective randomized multicenter intervention study is to determine whether in the prevention of Diabetes an intensified lifestyle intervention is superior to a conventional lifestyle intervention in high risk non-Responder subjects.
Diabetes Prevention Using SMS Technology (NCT01795833)	2268 patients	Ongoing (Estimated completion December 2017). We propose using a mobile phone intervention for lifestyle change and will assess it in a clinical trial(study) in people with impaired glucose regulation (high risk at developing type 2 diabetes).

Study	N	Objective
A Randomized Trial of Diabetes Prevention Through Lifestyle Change in India (NCT01283308)	599 patients	Ongoing (Estimated completion July 2017). The Diabetes Community Lifestyle Improvement Program (D-CLIP) will test in a randomized trial if a culturally specific, community-based lifestyle and metformin (for individuals who do not respond to lifestyle change alone) intervention for men and women living in Chennai, India can effectively prevent type 2 diabetes in high-risk individuals.
A Patient-Centered Strategy for Improving Diabetes Prevention in Urban American Indians (NCT02266576)	204 patients	Ongoing (Estimated completion April 2017). The goal of the proposed research is to identify effective patient-centered strategies to prevent diabetes in high-risk populations in real world settings.
Avoiding Diabetes After Pregnancy Trial in Moms (NCT01918345)	225 patients	Ongoing (Estimated completion January 2018). This pilot study will investigate the feasibility and effectiveness of a physical activity and diet intervention. It will also explore the relationship between behaviour change and metabolic markers of T2DM in this high-risk population.
Pathobiology and Reversibility of Prediabetes in a Biracial Cohort (NCT02027571)	300 patients	Ongoing (Estimated completion October 2018). In the Pathobiology and Reversibility of Prediabetes in a Biracial Cohort (PROP-ABC) study, nearly 400 African Americans and Caucasians whose parents have type 2 diabetes will undergo repeated testing to determine what factors lead to the occurrence of prediabetes, and whether race still plays a major role in a setting where everyone being studied has one or both parents with diabetes.
Effect of Saxagliptin on Pre-Diabetes Mellitus and Obesity (NCT01960205)	80 patients	Ongoing (Estimated completion December 2014). The purpose of the study is to examine the effect of Saxagliptin in the newly diagnosed people with pre-diabetes and obesity besides lifestyle intervention, there to evaluate DPP 4 inhibitors of reversing pre-diabetes curative effect to normal blood sugar, and observe its influences on the targets of obesity related metabolic abnormalities, to explore new ways for intervention on populations with pre-diabetes and obesity.
Sitagliptin + Metformin Compared to Metformin Monotherapy and Placebo in Women With a Recent GDM (NCT01856907)	36 patients	Ongoing (Estimated completion October 2016). This study will examine if combination sitagliptin (a DPP-4 inhibitor)-plus metformin is more effective than metformin alone or placebo in improving metabolic parameters, specifically the impact on β-cell function, in prior GDM women with glucose abnormalities.
Fit and Trim for Diabetes Prevention (NCT02278939)	50 patients	Ongoing (Estimated completion February 2016). This proposed pilot study is the first clinical trial to assess preliminary estimates of the short-term effect of the novel social networking diabetes prevention program lifestyle intervention for this high-risk population.
Examining the Effects of Diet on Health in Prediabetes With an Online Program (NCT02188823)	50 patients	Ongoing (Estimated completion February 2015). The present study is a clinical trial assessing a programs to help people manage prediabetes and lose weight with a low-carbohydrate diet (LC) along with information about positive affect, mindful eating strategies, exercise, and sleep.

Study	N	Objective
Dapagliflozin and Metformin,Alone and in Combination, in Overweight/Obese Prior GDM Women (NCT02338193)	72 patients	Ongoing (Estimated completion March 2018). The investigators hypothesize that combination dapagliflozin - metformin treatment over a 24-week period will have a greater positive impact on body weight, anthropometric measurements and glycemic and cardiometabolic parameters than dapagliflozin or metformin monotherapy in overweight/obese at-risk women with a history of GDM.

Abbreviations not defined above: CVD=cardiovascular disease; DPP-4=dipeptidyl peptidase 4; GDM=gestational diabetes mellitus; IGT=impaired glucose tolerance; N=number of studies/patients; NR=not reported; RCTs=randomized controlled trials; T2D=type 2 diabetes; T2DM=type 2 diabetes mellitus

Appendix Table C-4. Published and ongoing studies potentially relevant to Research Question 4 *[What is the comparative effectiveness of different approaches (e.g., patient outreach or advertising, physician education, patient or provider incentives, and others) for enhancing utilization and adoption of diabetes prevention strategies (including both lifestyle modification and metformin) by patients, providers, and systems in real-world settings? What elements of program delivery are associated with high program utilization and adoption?]*

Study	N	Objective
Systematic Reviews		
None	–	–
RCTs		
Tokunaga-Nakawatase, 2014[6]	141 patients	To investigate the effect of a computer-supported indirect-form lifestyle-modification program using Lifestyle Intervention Support Software for Diabetes Prevention (LISS-DP), as a clinically feasible strategy for primary prevention, on diet and physical activity habits in adults with a family history of type 2 diabetes.
Cohort Studies		
Chen, 2014[11]	1885 patients	To develop and test an online Smart Web Aid for Preventing Type 2 Diabetes (SWAP-DM2) capable of addressing major barriers to applying proven interventions and integrating diabetes prevention into routine medical care
Gutierrez, 2014[26]	183 patients	To evaluate Fine, Fit, and Fabulous (FFF), a faith-based diabetes prevention program for black and Latino congregants at churches in low-income New York City neighborhoods
Zyriax, 2014[14]	300 patients	To assess if screening for individuals at risk and long-standing diabetes prevention is feasible in the setting of companies within the scope of the German legal health system
Agarwal, 2013[15]	588 patients	This article describes the Community Health Awareness Diabetes (CHAD) program and its feasibility
Cene, 2013[16]	104 patients	To describe the feasibility of using a community-based participatory research (CBPR) approach to implement the Power to Prevent (P2P) diabetes prevention education curriculum in rural African American (AA) settings
Case-Control Studies		
None	–	–

Study	N	Objective
Ongoing Studies (ClinicalTrials.gov)		
Assessing the Effectiveness of a Weight Watchers-based Lifestyle Intervention for the Primary Prevention of Type 2 Diabetes (NCT02000024)	225 patients	Ongoing (Estimated completion April 2015). This study is a randomized pilot study to assess the applicability of the Weight Watchers model for lifestyle modification to the primary prevention of type 2 diabetes. The approach developed by Weight Watchers to achieve weight loss is based on similar nutritional principals and techniques used in the Diabetes Prevention Program (DPP) lifestyle intervention; monitoring food intake, exercising calorie control, setting modest weight loss goals and using physical activity.
Qingdao Diabetes Prevention Project (NCT01053195)	20,000 patients	Ongoing (Estimated completion December 2012). To evaluate the effect and the cost of the community-based prevention project. The project is community-based targeting at the entire population of 1.94 million living in four administration districts of the city of Qingdao in China. In the first phase of the project (2005-2008) the work emphasis is on health promotion, training over 2000 primary care professionals and 300 school health nurses and establishing a network consisting of 600 community clinics. In the second phase (2008-2012) lifestyle counseling sessions will be provided to about 242112 high-risk individuals identified, and the efficacy and the cost of the project will be evaluated at the end of the project in 2012.

Abbreviations not defined above: DPP=diabetes prevention program; N=number of studies/patients; RCTs=randomized controlled trials

References to Appendix C:

1. Dhippayom T, Chaiyakunapruk N, Krass I. How diabetes risk assessment tools are implemented in practice: a systematic review. Diabetes Res Clin Pract. 2014;104(3):329-42. PMID: 24485859.
2. Dunkley AJ, Bodicoat DH, Greaves CJ, et al. Diabetes prevention in the real world: effectiveness of pragmatic lifestyle interventions for the prevention of type 2 diabetes and of the impact of adherence to guideline recommendations: a systematic review and meta-analysis. Diabetes Care. 2014;37(4):922-33. PMID: 24652723.
3. Merlotti C, Morabito A, Pontiroli AE. Prevention of type 2 diabetes; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014;16(8):719-27. PMID: 24476122.
4. Duggan C, Carosso E, Mariscal N, et al. Diabetes prevention in Hispanics: report from a randomized controlled trial. Prev Chronic Dis. 2014;11:E28. PMID: 24576395.
5. Parker AR, Byham-Gray L, Denmark R, et al. The effect of medical nutrition therapy by a registered dietitian nutritionist in patients with prediabetes participating in a randomized controlled clinical research trial. J Acad Nutr Diet. 2014;114(11):1739-48. PMID: 25218597.
6. Tokunaga-Nakawatase Y, Nishigaki M, Taru C, et al. Computer-supported indirect-form lifestyle-modification support program using Lifestyle Intervention Support Software for Diabetes Prevention (LISS-DP) for people with a family history of type 2 diabetes in a medical checkup setting: a randomized controlled trial. Prim Care Diabetes. 2014;8(3):207-14. PMID: 24529485.

7. Whittemore R, Rosenberg A, Gilmore L, et al. Implementation of a diabetes prevention program in public housing communities. Public Health Nurs. 2014;31(4):317-26. PMID: 24251677.

8. Admiraal WM, Vlaar EM, Nierkens V, et al. Intensive lifestyle intervention in general practice to prevent type 2 diabetes among 18 to 60-year-old South Asians: 1-year effects on the weight status and metabolic profile of participants in a randomized controlled trial. PLoS One. 2013;8(7):e68605. PMID: 23894322.

9. Ramachandran A, Snehalatha C, Ram J, et al. Effectiveness of mobile phone messaging in prevention of type 2 diabetes by lifestyle modification in men in India: a prospective, parallel-group, randomised controlled trial. Lancet Diabetes Endocrinol. 2013;1(3):191-8. PMID: 24622367.

10. Wong CK, Fung CS, Siu SC, et al. A short message service (SMS) intervention to prevent diabetes in Chinese professional drivers with pre-diabetes: a pilot single-blinded randomized controlled trial. Diabetes Res Clin Pract. 2013;102(3):158-66. PMID: 24466598.

11. Chen P, Chai J, Cheng J, et al. A smart web aid for preventing diabetes in rural China: preliminary findings and lessons. J Med Internet Res. 2014;16(4):e98. PMID: 24691410.

12. Kieffer EC, Welmerink DB, Sinco BR, et al. Dietary outcomes in a Spanish-language randomized controlled diabetes prevention trial with pregnant Latinas. Am J Public Health. 2014;104(3):526-33. PMID: 23763411.

13. Kutob RM, Siwik VP, Aickin M, et al. Families United/Familias Unidas: family group office visits to reduce risk factors for type 2 diabetes. Diabetes Educ. 2014;40(2):191-201. PMID: 24464087.

14. Zyriax BC, Letsch B, Stock S, et al. DELIGHT (delay of impaired glucose tolerance by a healthy lifestyle trial) - a feasibility study on implementing a program of sustainable diabetes prevention in German companies. Exp Clin Endocrinol Diabetes. 2014;122(1):20-6. PMID: 24132568.

15. Agarwal G, Kaczorowski J, Hanna S. Community health awareness of diabetes (CHAD): description of a community-wide diabetes awareness demonstration program and its feasibility. Can J Diabetes. 2013;37(5):294-300. PMID: 24500554.

16. Cene CW, Haymore LB, Ellis D, et al. Implementation of the power to prevent diabetes prevention educational curriculum into rural African American communities: a feasibility study. Diabetes Educ. 2013;39(6):776-85. PMID: 24129595.

17. Gong QH, Kang JF, Ying YY, et al. Lifestyle interventions for adults with impaired glucose tolerance: a systematic review and meta-analysis of the effects on glycemic control. Intern Med. 2015;54(3):303-10. PMID: 25748739.

18. Aguiar EJ, Morgan PJ, Collins CE, et al. Efficacy of interventions that include diet, aerobic and resistance training components for type 2 diabetes prevention: a systematic review with meta-analysis. Int J Behav Nutr Phys Act. 2014;11:2. PMID: 24423095.

19. Schellenberg ES, Dryden DM, Vandermeer B, et al. Lifestyle interventions for patients with and at risk for type 2 diabetes: a systematic review and meta-analysis. Ann Intern Med. 2013;159(8):543-51. PMID: 24126648.

20. Li G, Zhang P, Wang J, et al. Cardiovascular mortality, all-cause mortality, and diabetes incidence after lifestyle intervention for people with impaired glucose tolerance in the Da Qing Diabetes Prevention Study: a 23-year follow-up study. Lancet Diabetes Endocrinol. 2014;2(6):474-80. PMID: 24731674.

21. Shek NW, Ngai CS, Lee CP, et al. Lifestyle modifications in the development of diabetes mellitus and metabolic syndrome in Chinese women who had gestational diabetes mellitus: a randomized interventional trial. Arch Gynecol Obstet. 2014;289(2):319-27. PMID: 23897066.

22. Vincent D, McEwen MM, Hepworth JT, et al. The effects of a community-based,

culturally tailored diabetes prevention intervention for high-risk adults of Mexican descent. Diabetes Educ. 2014;40(2):202-13. PMID: 24510942.

23. den Boer AT, Herraets IJ, Stegen J, et al. Prevention of the metabolic syndrome in IGT subjects in a lifestyle intervention: results from the SLIM study. Nutr Metab Cardiovasc Dis. 2013;23(11):1147-53. PMID: 23462149.

24. Islam NS, Zanowiak JM, Wyatt LC, et al. A randomized-controlled, pilot intervention on diabetes prevention and healthy lifestyles in the New York City Korean community. J Community Health. 2013;38(6):1030-41. PMID: 23813322.

25. Maruthur NM, Ma Y, Delahanty LM, et al. Early response to preventive strategies in the Diabetes Prevention Program. J Gen Intern Med. 2013;28(12):1629-36. PMID: 23860722.

26. Gutierrez J, Devia C, Weiss L, et al. Health, community, and spirituality: evaluation of a multicultural faith-based diabetes prevention program. Diabetes Educ. 2014;40(2):214-22. PMID: 24518138.

27. Islam NS, Zanowiak JM, Wyatt LC, et al. Diabetes prevention in the New York City Sikh Asian Indian community: a pilot study. Int J Environ Res Public Health. 2014;11(5):5462-86. PMID: 24852392.

28. Rautio N, Jokelainen J, Korpi-Hyovalti E, et al. Lifestyle intervention in prevention of type 2 diabetes in women with a history of gestational diabetes mellitus: one-year results of the FIN-D2D project. J Womens Health (Larchmt). 2014;23(6):506-12. PMID: 24787505.

29. Sagarra R, Costa B, Cabre JJ, et al. Lifestyle interventions for diabetes mellitus type 2 prevention. Rev Clin Esp (Barc). 2014;214(2):59-68. PMID: 24267869.

30. Sussman JB, Kent DM, Nelson JP, et al. Improving diabetes prevention with benefit based tailored treatment: risk based reanalysis of Diabetes Prevention Program. Bmj. 2015;350:h454. PMID: 25697494.

31. Png ME, Yoong JS. Evaluating the cost-effectiveness of lifestyle modification versus metformin therapy for the prevention of diabetes in Singapore. PLoS One. 2014;9(9):e107225. PMID: 25203633.

32. Lie ML, Hayes L, Lewis-Barned NJ, et al. Preventing type 2 diabetes after gestational diabetes: women's experiences and implications for diabetes prevention interventions. Diabet Med. 2013;30(8):986-93. PMID: 23534548.