The Effectiveness of Diabetes Prevention Programs in Community Settings

MARCH 2015

PREPARED BY:

Chia-Hung Chou, Ph.D.

Deborah L. Burnet, M.D., M.A.

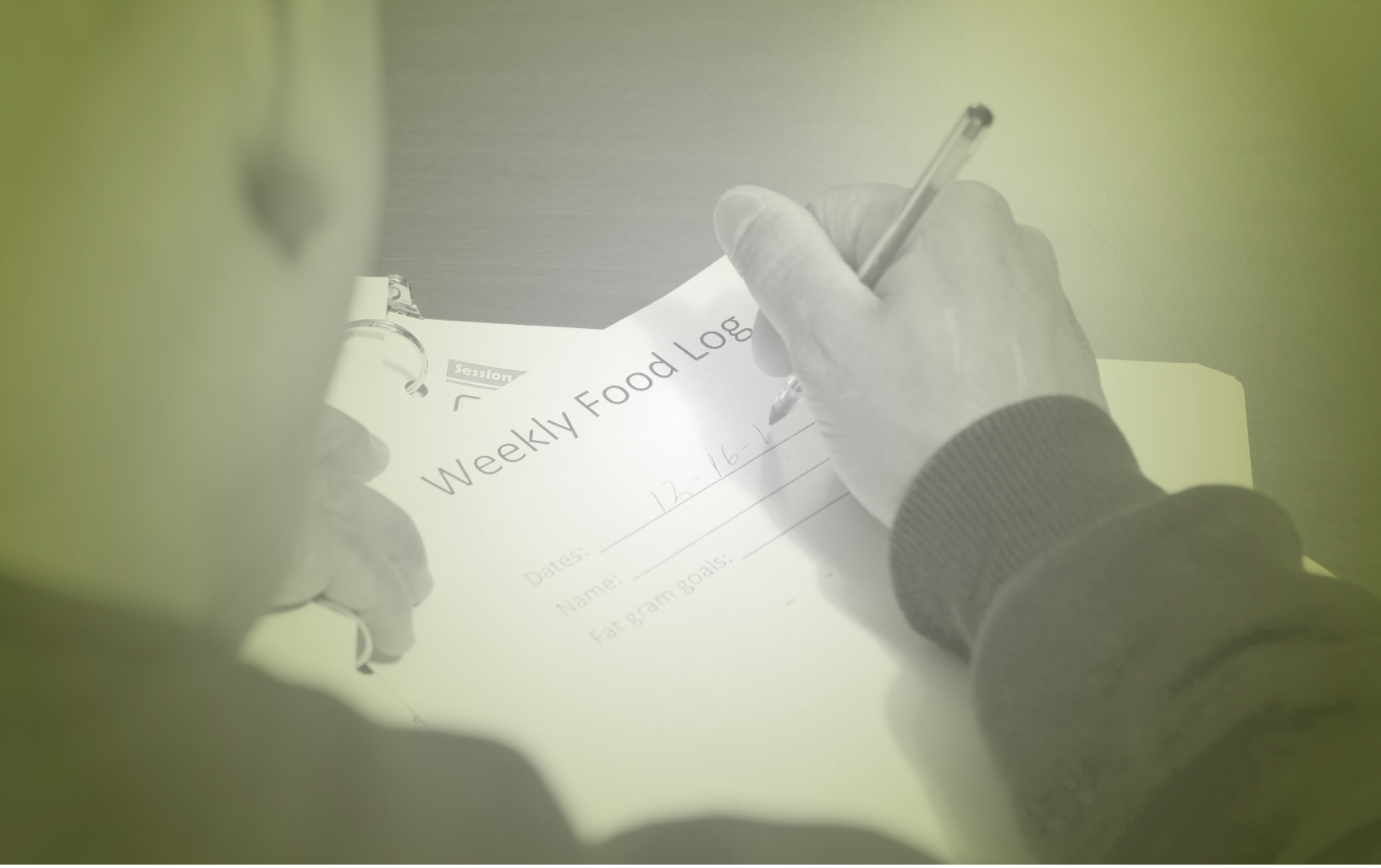
David O. Meltzer, M.D., Ph.D.

Elbert S. Huang, M.D., M.P.H., F.A.C.P.

University of Chicago

NYS HEALTH FOUNDATION

Improving the state of New York's health



Contents

Acknowledgments

Support for this work was provided by the New York State Health Foundation (NYSHealth). The mission of NYSHealth is to expand health insurance coverage, increase access to high-quality health care services, and improve public and community health. The views presented here are those of the authors and not necessarily those of the New York State Health Foundation or its directors, officers, or staff.

Funding for this project also was provided by the Robert Wood Johnson Foundation. For more than 40 years the Robert Wood Johnson Foundation has worked to improve health and health care. We are striving to build a national Culture of Health that will enable all to live longer, healthier lives now and for generations to come. For more information, visit www.rwjf.org.

PROJECT CONTACTS

PAMELA G. RUSSO, M.D., M.P.H.
Robert Wood Johnson Foundation

KELLY A. HUNT, M.P.P.
New York State Health Foundation

ADVISORY GROUP

MARILYN AGUIRRE-MOLINA, M.S., Ed.D.
CUNY School of Public Health/Lehman

SHADI CHAMANY, M.D., M.P.H.
New York City Department of Health and Mental Hygiene

SHERRY GLIED, Ph.D.
New York University

JOHN W. ROWE, M.D.
Columbia University

ELIZABETH A. WALKER, Ph.D., R.N.
Albert Einstein College of Medicine

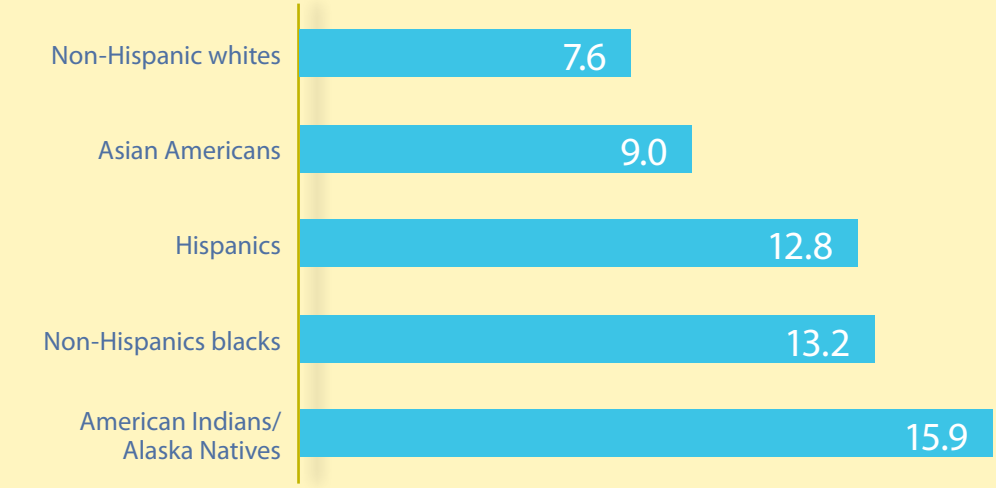
Introduction

WHY IS THIS ISSUE IMPORTANT TO POLICYMAKERS?

Type 2 diabetes is a preventable disease. It is the most common form of diabetes, which develops when the body no longer uses insulin properly and is unable to keep blood glucose at normal levels.[1] The prevalence of Type 2 diabetes (referred to hereafter as diabetes) has reached epidemic levels and is expected to worsen in the coming decades if effective means of prevention are not implemented. Diabetes already affects approximately 29 million Americans—almost 1 in 10—based on 2012 data.[2] The Centers for Disease Control and Prevention (CDC) projects total diabetes prevalence (diagnosed and undiagnosed) of the U.S. population to increase to 21% by 2050—more than 1 in 5 American adults.[3] In 2008, almost one in five patients admitted to hospitals in New York State had a primary or secondary diagnosis of diabetes.[4]

The prevalence of diabetes is particularly high among racial and ethnic minorities, contributing to the overall challenge of health disparities in the United States. The American Indian/Alaska Native population has a rate of diabetes that is double that of non-Hispanic whites, whereas blacks and Hispanics are 1.7 times as likely to have a diabetes diagnosis as non-Hispanic whites (Figure 1).[2]

FIGURE 1: Age-adjusted percentage of people aged 20 years or older with diagnosed diabetes by race/ethnicity, United States, 2010–2012

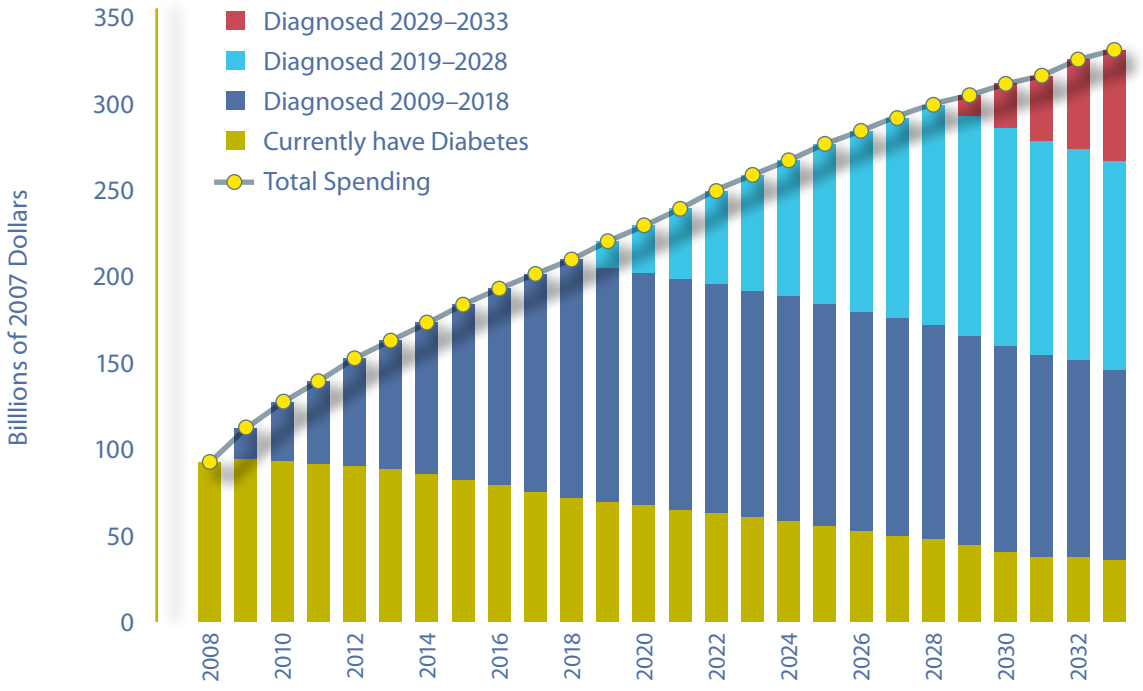


Source: National Diabetes Statistics Report: Estimates of Diabetes and Its Burden in the United States, 2014. Centers for Disease Control and Prevention.

In addition to the number of diagnosed cases of diabetes, estimates suggest that as many as 86 million people in the United States—more than 1 out of 3 adults—have prediabetes (people at higher risk of developing diabetes as indicated by moderately elevated blood sugar levels, namely, HbA1c 5.7%–6.4%).[2] The annual incidence of Type 2 diabetes is 5%–10% in people with prediabetes compared with about 1% per year in the general adult population.[5] Still others are at risk for developing diabetes based on one or more risk factors. Some risk factors cannot be changed, including age,[6] race or ethnicity,[7] gender,[8] and family history,[9] but many others, including weight (overweight and obesity),[10] physical inactivity,[11] and smoking,[12] can be modified. If these major modifiable risk factors for diabetes were reduced or eliminated, a large proportion of diabetes cases could be prevented.

The epidemic of diabetes and prediabetes has serious implications for health care costs. Multiple forecasting studies have predicted that costs related to diabetes will rise exponentially in the next several decades. Huang, Basu, O'Grady, and Capretta (2009) projected that annual U.S. diabetes-related health care costs will triple from $113 billion in 2009 to $336 billion in 2034 (in 2007 dollars) (Figure 2).[13] Individuals with diagnosed diabetes currently incur average

FIGURE 2: Projected direct spending on diabetes and its complications for different cohorts, 2009–2034



Source: Copyright 2009 American Diabetes Association. From *Diabetes Care*®, Vol. 32, 2009; 2225–2229. Reprinted with permission from The American Diabetes Association.

medical expenditures of approximately $13,700 which is about 2.3 times the average medical expenditures for those without diabetes.[14] Most of the costs for treating people with diabetes in the United States (62.4%) are borne by government insurance, including Medicare, Medicaid, and the military.[14] Beyond health care costs, the economic burden of diabetes also includes indirect costs such as increased absenteeism ($5 billion), reduced productivity for those in the workforce ($20.8 billion), inability to work as a result of disease-related disability ($21.6 billion), and lost productive capacity resulting from early mortality ($18.5 billion).[14]

Strong empirical evidence from clinical trials suggests that preventing or delaying the onset of diabetes can be achieved through lifestyle interventions.[15,16,17] Hundreds of distinct programs have been developed to move the success of clinically based interventions to community settings across the country to help people change their eating and exercise patterns to lose weight and prevent or delay the onset of diabetes. This synthesis aimed to identify the full range of studies of community-based diabetes prevention programs, assess the strength of their research methodologies, and weigh the evidence available from this literature to answer the following questions:

1	What types of community-based diabetes prevention strategies have been evaluated in the peer-reviewed literature?
2	How effective are community-based prevention interventions in reducing the risk or delaying the onset of diabetes?
3	What are the costs of community-based diabetes prevention programs?
4	What are the limitations and gaps of the existing literature for diabetes prevention programs?

Given that real lives and dollars are at stake, policymakers need answers to these fundamental questions to make policy decisions that use investments wisely to implement the most effective, efficient, and sustainable interventions for their communities.

Methodology Overview

To conduct this synthesis report, we defined a diabetes prevention program as an intervention for adult participants who are at risk for diabetes or diagnosed with prediabetes. We defined at risk for diabetes to mean an individual who is overweight or obese and has at least one other risk factor (e.g., physical inactivity, smoking) for developing diabetes.[i] These risk factors are listed in more detail in Table I-1 of Appendix I. We defined prediabetes to mean individuals with glucose levels consistent with impaired fasting glucose (100–125 mg/dL) or impaired glucose tolerance (140–199 mg/dL, 2 hours after a 75-gram oral glucose tolerance test). This synthesis is limited to U.S. studies of adults aged 18 years or older. A comprehensive and systematic search was conducted using multiple electronic databases for evaluation studies of interventions. This synthesis reviewed the literature for all programs designed to reduce the risk of diabetes in adults diagnosed with prediabetes or at risk for developing diabetes. Literature prior to 2002 was excluded, as were the three original clinical trials (NIH-DPP, Da Qing, Finnish Diabetes Prevention),[15–17] because the focus of the synthesis was on translational studies of community-based diabetes prevention programs. The primary focus of the search was lifestyle change studies and evaluations that have been published in the peer-reviewed literature. More details on the literature search are available in Appendix I.

Findings from randomized controlled trials (RCTs) offer the highest degree of confidence that the outcomes are a result of the interventions being studied rather than other factors. This synthesis includes both studies with true experimental designs and studies with other designs, however, for two reasons. First, although RCTs rank high in terms of strength of evidence, they are less likely to be easily replicated in real-world settings. Second, many community-based diabetes prevention studies did not use RCTs because their primary intent was to assess the feasibility of modifying a clinical trial (i.e., the NIH-DPP intervention[17]) for use outside of research settings. Nonetheless, we relied more on evidence from RCTs compared with non-RCT studies for our conclusions.

THE NIH-DPP

The Diabetes Prevention Program, sponsored by the National Institutes of Health (NIH-DPP), is the gold standard in the United States for a well-designed clinical trial to determine whether diet, exercise, or drugs can prevent or delay the onset of Type 2 diabetes in people who are at risk. The study included more than 3,200 participants—nearly half of whom represented minority groups. Participants who received intensive, one-on-one counseling on lifestyle interventions, including diet and exercise, cut their risk of developing diabetes by more than half. Participants who used the oral drug, metformin, reduced their risk of developing diabetes by almost one-third. This was the first large-scale study in the United States to successfully show that interventions can prevent, or at least delay, the onset of Type 2 diabetes.

[i] The definition of at risk for diabetes was finalized based on the current state of knowledge and discussion with and input from the Advisory Group for New York State Health Foundation and Robert Wood Johnson Foundation.

EVALUATING QUALITY AND STRENGTH OF EVIDENCE

To evaluate the quality of individual RCTs, we relied on criteria established by West et al. (2002) in an evidence report from the Agency for Healthcare Research and Quality (AHRQ) for assessing study quality and overall strength of evidence from RCTs.[18] According to this AHRQ report, the critical domains in the criteria to rate the quality of RCTs are study population, randomization, blinding, interventions, outcomes, statistical analysis, and funding or sponsorship. Studies were assessed a score from one to seven based on these criteria.

To our knowledge, there are no settled evaluation criteria or guidelines available to assess the quality of studies using non-randomized controlled design. As a result, we assessed the quality of individual non-RCT studies based on study population; participant recruitment; sample size and attrition; development and implementation of an intervention; outcomes; statistical analysis; and limitations.

When assessing the strength of bodies of evidence after evaluating the quality of individual studies, we considered three criteria in the evidence report from AHRQ: quality, quantity, and consistency.[18] Quality refers to "the aggregate of quality ratings for individual studies, predicated on the extent to which bias was minimized." Quantity considers the "magnitude of effect, numbers of studies, and sample size or power." Consistency means "for any given topic, the extent to which similar findings are reported using similar and different study designs."[18]

ORGANIZATION OF INTERVENTION CATEGORIES

In light of significant variation in programs designed to reduce the risk of diabetes in adults, we classified interventions into three categories. The first type, lifestyle studies, were those using an intervention modeled after the NIH-DPP lifestyle intervention and included both components of healthy diet and physical activity. The second type used an intervention that focused on either healthy diet or physical activity, but not both. The third type were pharmacological interventions that used medications as the main intervention to prevent diabetes.

COMPARING OUTCOMES ACROSS STUDIES

Although all studies aimed to evaluate the effectiveness of diabetes prevention programs, they targeted various outcome measures, including weight change, hemoglobin A1c (blood sugar), fasting glucose level, lipid profile (cholesterol), blood pressure, and insulin resistance. The heterogeneity in reported outcome measures makes it challenging to perform a head-to-head comparison between different studies. We adopted a multivariate prediction model of diabetes risk to address this problem.[19] The San Antonio Diabetes Prediction Model (SADPM)

calculates the likelihood of being diagnosed with diabetes over a 7½-year period based on age, gender, ethnicity, fasting blood glucose, systolic blood pressure, high-density lipoprotein (HDL) cholesterol, body mass index (BMI), and family history of diabetes. The main advantage of using this validated, peer-reviewed prediction model is that it enables us to compare the most important outcome measure—the reduction in risk of developing diabetes—across all diabetes prevention programs. This model has been applied and cited in more than 70 papers, including many from the NIH-DPP.

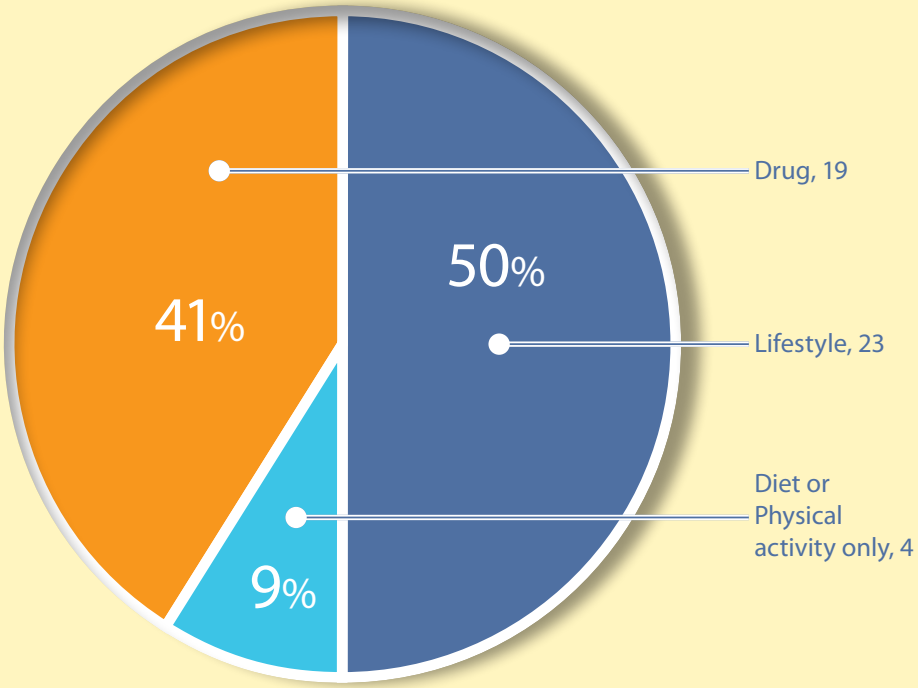
After estimating risks of developing diabetes from the model, we calculated the relative risk reduction (RRR) for each identified study—that is, how likely the intervention was to reduce the risk of developing diabetes compared with other studies. RRR is a standardized risk reduction measure that can be used to compare the relative effectiveness of each diabetes prevention program.

Findings

WHAT TYPES OF COMMUNITY-BASED DIABETES PREVENTION PROGRAMS HAVE BEEN EVALUATED IN THE PEER-REVIEWED LITERATURE?

We identified 46 studies that met both our inclusion criteria and our methodological criteria. Among these studies, we found 23 lifestyle studies that included both components of healthy diet and physical activity, 4 studies that used an intervention focused on either healthy diet or physical activity, and 19 pharmacological intervention studies (Figure 3). Detailed information about each study is tabulated in Appendices III–V.

FIGURE 3: Types of diabetes prevention programs (N=46)



HOW EFFECTIVE ARE COMMUNITY-BASED PREVENTION INTERVENTIONS IN REDUCING THE RISK OR DELAYING THE ONSET OF DIABETES?

There is modest evidence that full lifestyle interventions implemented in community settings can reduce the risk of diabetes, but the effect of the interventions is highly variable across studies. For full lifestyle interventions (interventions that included both diet and exercise) we found 9 RCTs and 14 non-RCT studies that met our inclusion criteria.[20–28, 29–41] Among the RCTs, 2 of 9 trials (Ma et al. and Katula et al.) had relatively large RRRs (-24% and -19%), whereas

the remaining 7 trials had very small RRRs (-5% or less) (Table 1).[20, 21] Participants in the Ma study were randomized to a coach-led group intervention, a self-directed DVD intervention, or usual care. Thirty-seven percent of participants in the coach-led group achieved the weight-loss goal compared with 36% in the self-directed group and 14% in the usual care group.[20] Katula et al. (2011) evaluated the community-based translation of the NIH-DPP lifestyle intervention with overweight and obese participants with prediabetes via a local diabetes education program overseen by registered dietitians and community health workers. The study found that participants in the intervention group experienced statistically significant decreases in blood glucose, insulin, insulin resistance, weight, BMI, and waist circumference compared with usual care participants.[21]

Among large non-RCT studies, only one study had a large RRR (Vanderwood, Hall, Harwell, Butcher, and Helgerson, 2010), whereas the other four studies had modest RRRs of -13% or less (Table 2).[29–33] Vanderwood et al. (2010) evaluated an adapted group-based NIH-DPP lifestyle intervention with 1,003 participants and 8 health care facilities.[29] Among participants who completed the core curriculum, 45% achieved the weight-loss goal and 66% achieved the physical activity goal. Among those who also completed 6 group booster sessions after the core curriculum, 49% achieved the weight-loss goal and 70% achieved the physical activity goal. Studies by Davis-Smith and Boltri had large RRRs (46% and 40%), but these two studies had 10 or fewer patients.[34, 35] Several other non-RCT studies had relatively large RRR scores (ranging from -18% to -29%), but again the small sample size (ranging from 8–84) makes it hard to generalize from their conclusions.[34–41]

Evidence indicates lifestyle interventions can work outside of a research setting and be modified to take place in groups. All full lifestyle studies included in this synthesis implemented diabetes prevention programs in nonresearch settings such as primary care facilities, YMCAs, churches, homes, and neighborhoods. In addition, almost the entire body of literature on community-based diabetes prevention programs used group-based lifestyle interventions. Group settings make the intervention less resource intensive, so it becomes easier for communities with modest resources to adopt the intervention. Both results make diabetes prevention programs more feasible compared with clinically based prevention programs.

Despite the high prevalence of diabetes and prediabetes in blacks and Hispanics, we know little about successful community-based interventions for racial and ethnic minorities. Although the participants in the NIH-DPP were racially and ethnically diverse, the majority of participants in nearly all the community-based studies in this synthesis were white, non-Hispanic, and primarily female. The lack of minority participants was common across all types of studies (full lifestyle interventions, diet- or exercise-only interventions, and pharmacological interventions) with a few exceptions. We identified four studies with a small group of participants entirely consisting of either Hispanics or blacks.[27, 34–36] A study by Davis-Smith et al.

TABLE 1: RCTs of Full Lifestyle Interventions

Study	Quality score	Group (G) or individual (I)	Personal (P) or virtual (V)	Main setting	Prediabetes (PD) or at risk (AR)	Sample size	Findings	Relative Risk Reduction (RRR)
Ma et al. (personal)[20]	7	G	P	Outpatient	PD	241	BMI decrease from baseline in the diabetes prevention-led group vs. that in the usual care group (-2.2 vs. -0.9, p<0.001). The percentage of participants who achieved the 7% DPP-based weight-loss goal was 37.0% in the diabetes prevention-led group vs. 14.4% in the usual care group (p=0.03). The intervention also achieved greater net improvements in waist circumference and fasting plasma glucose level.	-31% (-24% compared to control)
Katula et al.[21]	6	G	P	Community	PD	301	After 12 months, compared with usual care participants, intervention participants experienced significantly greater decreases in blood glucose (-4.3 vs. -0.4 mg/dL; p<0.001), insulin (-6.5 vs. -2.7 µU/mL; p<0.001), homeostasis model assessment of insulin resistance (-1.9 vs. -0.8; p<0.001), weight (7.1 vs. 1.4 kg; p<0.001), BMI (2.1 vs. 0.3 kg/m2; p<0.001), and waist circumference (-5.9 vs. -0.8 cm; p<0.001).	-31% (-19% compared to control)
Tate et al.[22]	5	I	V	Home	PD	92	Behavioral e-counseling group lost more mean weight at 12 months than the basic Internet group (p=0.04).	-10% (-5% compared to control)
Ackermann et al.[23]	6	G	P	YMCA	PD	92	After 6 months, body weight decreased by 6.0% in intervention participants and 2.0% in controls (p<0.001; difference between groups). Intervention participants also had greater changes in total cholesterol (-22 mg/dL vs. 6 mg/dL controls; p<0.001). These differences were sustained after 12 months.	-8% (-6% compared to control)
Ackermann et al.[24]	6	G	P	YMCA	PD	66	At 28 months, after both arms were offered the same 8-month lifestyle maintenance intervention, both arms had statistically significant weight losses compared to baseline (brief advice controls: 3.6%; 95% CI: 5.8 to 1.4; intensive lifestyle: 6.0%; 95% CI: 8.8 to 3.2). Participants initially assigned to the DPP also experienced significant improvements in blood pressure and total cholesterol.	-6% (-4% compared to control)
Parikh et al.[25]	6	G	P	Community	PD	99	The intervention group lost significantly more weight than the control group and maintained weight loss at 12 months (7.2 vs. 2.4 lbs; p<0.01). Limited behavioral changes from both groups. No changes in fat intake and physical activity.	-6% (-4% compared to control)
Liao et al.[26]	6	G/I	P	Community	PD	64	The treatment group showed significantly greater reduction in percentage of body fat; BMI; subcutaneous fat by computed tomography at the abdomen, thigh, and thorax; and skinfold thickness at the bicep and triceps, which continued despite moving to home-based exercise for the last 18 months.	-4% (-5% compared to control)
Ockene et al.[27]	6	G/I	P	Community	AR	312	Compared with the control group, the intervention group had significant weight reduction (-2.5 vs. 0.63 lb; p=.04), reduction in hemoglobin A1c (-0.10% vs. -0.04%; p=0.009), insulin resistance improvement, and greater reductions in percentage of calories from total and saturated fat. No significant difference in physical activity or fasting blood glucose between the two groups.	-1% (-1% compared to control)
Whittemore et al.[28]	6	I	P	Outpatient	AR	58	25% of lifestyle participants met treatment goals of 5% weight loss compared with 11% of standard care participants at 6 months. No significant difference was observed in other clinical outcomes from baseline between the two groups.	—

Note: Quality score is based on the criteria established by AHRQ for evaluating quality in RCTs (see Methodology Overview). A point is given based on each criteria for measuring quality with 7 being the highest score.

(2007) and two studies by Boltri et al. (2008, 2011) evaluated full lifestyle interventions that took place in black churches. These studies modified the NIH-DPP intervention for use in a church setting and found modest weight loss among participants, but all three studies had sample sizes of 10 or less. More studies, each with a greater sample size of minority populations, are needed to provide adequate evidence regarding how a diabetes prevention program could work in these high-risk populations and whether barriers exist to their participation.

The variability of the study designs makes it difficult to conclude what made some programs more effective than others. One of the challenges of comparing studies of diabetes prevention programs is that they vary in design, intervention, setting, eligibility criteria, duration, and health outcomes studied. Studies also varied in how they measured the effect of the intervention. Without uniform outcome measures, making comparisons among studies is challenging. Many studies lack the most important and direct outcome measure for evaluating the effectiveness of diabetes prevention programs: reduction in risk of developing diabetes. Future studies should include, at a minimum, change in weight, change in HbA1c, change in blood pressure, and change in cholesterol.

The long-term effects of community-based lifestyle interventions have not been evaluated extensively. The original clinical trial-style diabetes prevention programs have had long-term monitoring to determine the duration of effect following the conclusion of the active intervention period, but similar follow-up has been limited in diabetes prevention programs at the community level. Although community-setting studies have shown that their interventions were effective during and immediately after the interventions, very few studies have had the resources to track the effect beyond one year of follow-up. Evidence remains limited as to whether a community-setting lifestyle intervention that has short-term effectiveness will have lasting effects on outcome measures or how well it will measure up to the level of success of the NIH-DPP long-term outcomes.

Programs that focus on either healthy diet or increased physical activity—but not both—do not show much promise for reducing the risk of diabetes. We identified three RCTs that focused on either diet or increased physical activity, and none showed significant reductions in risk factors in the intervention group versus the control group (Table 3).[42–44] The only study in this group that reduced the risk of diabetes was by Swartz, Strath, and Basset (2003), but that study had no control group and a small sample size.[45]

Full lifestyle interventions were more successful than pharmacological interventions at reducing the risk of diabetes on average. The studies of pharmacological interventions evaluated a variety of drugs (e.g., thiazolidinediones, meglitinides, angiotensive receptor blockers, ACE inhibitors) and nutritional supplements (e.g., cholecalciferol, vitamins, chromium picolinate), making it hard to generalize across pharmacological interventions.[56–74] Some pharmacological interventions did reduce the risk of diabetes. Using the RRR model, the studies

Findings *(continued)*

TABLE 2: Non-RCT studies of Full Lifestyle Interventions

Study	Group (G) or individual (I)	Personal (P) or virtual (V)	Main setting	Prediabetes (PD) or at risk (AR)	Sample size	Findings	Relative Risk Reduction (RRR)
LIFESTYLE INTERVENTION — LARGE STUDIES							
Vanderwood et al.[29]	G	P	Outpatient	AR/PD	1,003	45% core participants and 49% core plus after-core session participants achieved the 7% weight-loss goal. There were significant improvements in blood pressure, fasting glucose, and LDL cholesterol among participants completing the intervention.	-0%
Swanson et al.[30]	G	P	Outpatient	PD	221	At the end of the intervention, 59% had significantly lower fasting glucose concentrations, 59% had improvement in 2-hour glucose levels, and 61% had weight loss.	-13%
Amundson et al.[31]	G	P	Outpatient	AR/PD	355	45% of the participants achieved the 7% weight-loss goal; 70% achieved the physical activity goal of 150 minutes or more per week.	-10%
Almeida et al.[32]	G	P	Outpatient	PD	1,520	A significantly higher proportion of small-group participants lost at least 5% of their body weight compared with controls (22% vs. 15%, p=0.001)	-2%
Smith-Ray et al.[33]	G	P	Outpatient	PD	292	Participants significantly increased reported minutes of moderate ($p < 0.001$) and vigorous ($p = 0.028$) physical activity and their daily servings of fruits and vegetables ($p < 0.001$).	N/A
LIFESTYLE INTERVENTION — SMALL STUDIES							
Davis-Smith[34]	G	P	Church	PD	10	Mean weight loss of 8.8, 6.5, and 10.6 lbs. right after the intervention, after 6 months, and after 12 months, respectively.	-46%
Boltri et al.[35]	G	P	Church	PD	8	Following the intervention, weight, systolic and diastolic BP, and FG decreased by 7.5 lb (3.6%), 16 mm Hg (11.7%), 12 mm Hg (14.0%), and 5 mg/dL (4.8%), respectively ($p < 0.05$).	-40%
Boltri et al.[36]	G	P	Church	PD	37	Overall, interventions were associated with decreased fasting glucose (108 to 101.7 mg/dL; p=0.037) and weight loss (-1.7 kg) post intervention; 16-session intervention had similar results with minimum improvement from 6-session.	-29%
Kramer et al.[37]	I; G	1 V; 1 P	Home	PD	48	Significant physical activities increase and weight loss were observed in both groups. GLB-DVD with remote support may provide an effective alternative for GLB-group delivery.	-28%
Kramer et al.[38]	G	P	Community	PD	81	Significant decreases were noted in weight (-5.1%, p<0.001), fasting plasma glucose, low-density lipoprotein cholesterol, triglycerides, and blood pressure.	-23%
Vadheim et al.[39]	G	P	Outpatient	AR/PD	84	52% achieved the 7% weight-loss goal and 78% achieved at least a 5% weight loss during the core program.	-18%
Vadheim et al. (tele-health)[40]	G	V	Home	PD	16	50% of telehealth participants achieved the 7% weight-loss goal.	-12%
Vadheim et al. (on-site)[40]	G	P	Community	PD	13	46% of onsite participants achieved the 7% weight-loss goal.	-11%
Seidel et al.[41]	G	P	Community	AR/PD	88	Weight loss (46.4% lost ≥5% and 26.1% lost ≥7%) was observed after completion of the intervention. Of these subjects, 87.5% (n=28) and 66.7% (n=12) sustained the 5% and 7% reduction, respectively, at the 6-month reassessment.	N/A

conducted by Saremi et al. (2012), evaluating pioglitazone, and by Buchanan et al. (2002),[54] evaluating troglitazone—both types of thiazolidinediones—had the largest reduction in risk of developing diabetes among all RCTs (-21 and -22%, respectively), similar to the studies with the largest risk reduction in the full lifestyle interventions. The remaining RCTs had estimates of risk reduction that were between -12% and 4%. On average, the effectiveness of the pharmacological interventions was less than the effectiveness of the full lifestyle interventions using the statistical analysis for comparing RRR. This finding is consistent with the NIH-DPP finding showing greater reductions in the risk for developing diabetes from diet and exercise interventions than from using the drug metformin.

Other modifications of the NIH-DPP, including reduced intervention sessions and virtual interventions, have promising but limited evidence. Lifestyle interventions with different numbers of intervention sessions have been reported in literature, ranging from 16 sessions in the NIH-DPP to 4 or 6 sessions.[20, 23–25,29–30] A few studies showed that lifestyle interventions with fewer sessions than the NIH-DPP were effective. For example, the Group Lifestyle Balance program, a 12-session group-based lifestyle intervention with the same goals for weight loss and physical activity as the NIH-DPP, helped participants achieve the weight-loss goal and improve fasting glucose levels in both RCT[20] and non-RCT studies.[37, 38,41] Another small-sized pilot study showed that a 6-week church-based prevention program resulted in participants decreasing fasting glucose levels and weight, similar to results from a 16-week intervention.[36]

Information technology-assisted approaches may be an alternative way to deliver diabetes prevention programs. Tate, Jackvony, and Wing's (2005) study suggested that an Internet behavioral program (e-counseling) may offer an alternative to more burdensome clinic-based programs and can be used for longer periods.[22] Ma et al. (2013) demonstrated that their diabetes prevention program delivered via DVDs was as effective as in-person programs.[20] However, the degree to which these virtual interventions can substitute for or complement standard diabetes prevention programs requires additional study.

TABLE 3: Studies with Interventions that Focused on Healthy Diet Only or Physical Activity Only but Not Combination of Both

Study	Quality Score	Group (G) or individual (I)	Personal (P) or virtual (V)	Main setting	Prediabetes (PD) or at risk (AR)	Sample size	Findings	Relative Risk Reduction (RRR)
RCTS								
Cole et al.[42]	6	G	P	Outpatient	PD	94	The nutrition-based shared medical appointment (SMA) and control participants lost a mean of 6.6 and 3.6 lbs., respectively; neither group met the 5% modest weight loss expected. The SMA and control group experienced a mean drop in fasting blood glucose of 6 mg/dL.	-29% (12% compared to control)
Morey et al.[43]	7	I	P/V	Home	PD	302	Both groups had small declines over time of approximately 6% in fasting blood glucose, but there were no significant differences between the physical activity counseling and control groups over time for any of the glycemic indicators.	N/A
Roberts et al.[44]	6	G	P	University	AR	36	12 weeks of resistance exercise training increased SHBG (p=0.01) and decreased FAI (p<0.05) and cortisol (p<0.05) compared to control group.	N/A
NON-RCT STUDY								
Swartz et al.[45]	N/A	I	V	Home	AR	18	During the intervention period, the participants increased their accumulated steps/day by 85% to 9,213, which resulted in beneficial changes in 2-hour post-load glucose levels (p<0.001), AUC glucose (p=0.025), systolic blood pressure (p<0.001), and diastolic blood pressure (p=0.002)	-6%

Note: Quality score is based on the criteria established by AHRQ for evaluating quality in RCTs (see Methodology Overview). A point is given based on each of the criteria for measuring quality and strength of evidence with 7 being the highest score.

WHAT ARE THE COSTS OF COMMUNITY-BASED DIABETES PREVENTION PROGRAMS?

The costs of the community-based prevention programs in this synthesis are largely unknown. When information on costs was reported, the studies did not follow any specific guidelines to gather and document complete and relevant cost information. One study of the YMCA model estimated that the costs for supplies, personnel, and administration during the first year of the program to be approximately $275–$375 per participant.[46] This cost is far less than the $1,400 participant cost of the NIH-DPP, yet funds to start up, evaluate,

market, spread, and sustain community-based programs are not readily available. Startup costs for the National Diabetes Prevention Program, for example, have typically to date been supported by public and private funders in replication efforts across the country. The large-scale YMCA implementation of the NIH-DPP has made some progress in securing health care reimbursements in various regions of the country. In New York, for example, a handful of commercial insurers, self-insured employers, and a Medicare Advantage plan have signed on to reimburse for National Diabetes Prevention Program participation, and efforts to establish further reimbursement are underway.

Although the costs of prevention efforts are not nominal and the complexity of raising consumer demand and participation in these programs should not to be understated, the costs are likely far less than the health care spending resulting from treatment of diabetes. In 2012, researchers from CDC estimated that a nationwide community-based lifestyle program like the National Diabetes Prevention Program could save $5.7 billion over 25 years.[47]

Similarly, information on the cost-effectiveness of community-based models for diabetes prevention programs has not been sufficiently studied. Another challenge to sustainable funding models is that the organization or insurer which invests up front in diabetes prevention often differs from the payer who stands to accrue savings in health care costs years later. Developing a more solid basis of evidence on program costs and the cost implications of programs should be an additional focus of future studies.

WHAT ARE THE LIMITATIONS AND GAPS OF THE EXISTING LITERATURE FOR DIABETES PREVENTION PROGRAMS?

Many studies have a small sample size and suffer from attrition. The existing diabetes prevention program studies tend to have small sample sizes (as small as eight) that decrease the statistical power of the studies to detect meaningful impact of their diabetes prevention programs. This issue is further complicated by the high attrition rate among participants over the study period. Many studies reported having participants complete the entire program, but finding that follow-up was challenging. As a result, studies with a small sample size usually indicated that they were underpowered to detect meaningful difference for their major outcome measures.

The majority of community-based diabetes prevention programs restricted enrollment to people with prediabetes, so little is known about the effect of the interventions with at-risk populations. Investigators may have made this choice because (1) people with prediabetes are proven to be at very high risk of developing diabetes and (2) the NIH-DPP already demonstrated convincing evidence that lifestyle interventions work for this population. This leaves us very limited evidence to understand whether lifestyle interventions will benefit at-risk persons to the same degree.

All studies use self-reported measures of diet and physical activity. Participants may underreport their food intake, record better food choices than were actually consumed, or overstate their level of physical activity. Research from both the psychology and health literature finds that study participants tend to underreport inappropriate behaviors and overreport appropriate behaviors.[48,49] Self-reporting bias may also occur because of recall errors (e.g., participants forgot what they ate the previous day or how much they exercised the previous week). Misstating diet choices and exercise levels can influence the outcome measures and make the interventions look less effective.

The studies in this review failed to provide detailed information on their communities' characteristics and how to implement the program in a community. Detailed descriptions are critical for replicating successful experiences in different community settings. The RE-AIM (Reach, Effectiveness, Adoption, Implementation, Maintenance) model provides a framework for what kind of details should be included in future evaluative studies of diabetes prevention programs.[50] According to the RE-AIM model, efficacy is required for programs to have public health impact. In addition, programs must also be able to reach a diverse sample representative of the population at risk. They must be made appealing to health care providers or community leaders and must be practical and realistic for adoption in specific practice or community settings. Programs must be able to be implemented as intended. Finally, programs must be sustainable, both by individual participants and in the clinical or community setting. These dimensions, involving both individual and organizational factors, interact to determine the overall population-based impact of a program. Detailed description of how these factors were addressed in a specific diabetes prevention program can help others learn how they might adapt and implement such programs in their own settings (See Appendix II for more details).

Conclusions

Keeping in mind the overall strength of the evidence and the limitations in current research, we are able to conclude with some degree of confidence:

Lifestyle interventions can work well outside of a research setting. Lifestyle interventions designed to reduce risk of developing diabetes can be successfully implemented in community settings. All lifestyle studies we identified implemented diabetes prevention programs in various community settings. Those community settings include primary care facilities, YMCAs, churches, homes, and neighborhoods. Although these studies had different degrees of success in improving related health outcomes, successful examples of translating the NIH-DPP into a community-based intervention exist.[20,21]

The NIH-DPP lifestyle intervention can be modified into a group-based intervention for community settings. Almost the entire body of literature on community-based diabetes prevention programs used group-based lifestyle interventions. The primary reason was to make the intervention less resource intensive so it becomes easier for communities with modest resource to adopt the intervention. Several RCTs and non-RCT studies with large sample sizes have demonstrated the effectiveness of group-based lifestyle interventions with varying degrees of success.[20,21,23]

Standardization of study designs and outcome measures would improve the ability to identify successful community-based programs. One of the challenges of comparing studies of diabetes prevention programs is that they vary in design, intervention, setting, eligibility criteria, duration, and health outcomes studied. This synthesis reveals the need for standards for describing eligibility, interventions, and outcome results to allow comparisons of different diabetes prevention programs. Without uniform outcome measures, making comparisons across studies is challenging. These studies also lack the most important and direct outcome measure for evaluating the effectiveness of diabetes prevention programs: reduction in risk of developing diabetes.

An effort must be made to include more minority participants in diabetes prevention programs to identify successful interventions for these at-risk populations. Minority populations are overrepresented in the population at risk for diabetes but underrepresented in studies of diabetes prevention programs. We need to identify best practices for how to identify, recruit, enroll, and retain minority populations in community-based prevention programs. Once minority populations are included in studies of prevention programs, researchers can study whether the same interventions that are successful in the majority population are similarly successful with minorities and how to effectively tailor programs for different populations.

IMPLICATIONS FOR POLICYMAKERS

We found that programs based on the NIH-DPP have been successfully implemented in groups and in community settings among individuals with prediabetes. In this synthesis, studies which adhered most closely to the NIH-DPP standards were generally the most effective, but this recommendation limits the reach of diabetes prevention. This synthesis identified specific elements of novel community-based diabetes prevention programs, such as alternative scheduling and virtual delivery of programming, that might reduce the costs of future programs and expand the reach of interventions while maintaining the success of the interventions. This synthesis also found very few programs that focus on people at risk for diabetes but without a formal laboratory-based diagnosis of prediabetes. Simplifying the screening process for program enrollment would vastly expand the pool of people who could benefit. However, current evidence for each of these elements is limited. In addition to further research on alternative approaches to diabetes prevention, there is a critical need for standardization of baseline and outcome definitions in future evaluations to compare different approaches to community-based prevention efforts. Future studies could include, at minimum, outcome measures such as changes in weight, HbA1c, blood pressure, and cholesterol.

An important next step for the public health research community is to build upon the elements of programs identified in this synthesis. Communities would benefit tremendously if a menu of prevention program options that are grounded in evidence and could be adapted to fit the community context were available. Communities can leverage the assets and resources they currently have to build culturally tailored programs that work for their residents.

Policymakers and other stakeholders can contribute to diabetes prevention efforts by improving the evidence base to identify effective community-based interventions in the following ways:

1. Support larger studies with sufficient power to determine whether weight loss and diabetes prevention are achievable in community settings, as they were in the original rigorously conducted RCTs.
2. Support studies to identify the most effective recruitment channels and methods to reach populations at high risk for developing diabetes and especially the most vulnerable. As our review reveals, more data are needed for males and minority populations.
3. Provide additional resources for post-intervention monitoring to assess whether there are long-term positive effects of diabetes prevention programs on population health.

Conclusions *(continued)*

4. Support more formal studies to gather accurate data on participants' dietary and exercise habits for unbiased evaluation of interventions.

5. Draw from the growing body of research on community-based diabetes prevention to determine what elements of prevention programs work best. Such information would be useful in developing models that communities can adapt to their own settings and available resources.

6. Support studies that thoroughly document details of operating a diabetes prevention program. The RE-AIM model provides a framework for what details should be specified in future evaluative studies of diabetes prevention programs (see Appendix II).

Appendix I: Methodology

SCOPE OF THE SYSTEMATIC REVIEW

To conduct this synthesis report, we defined a diabetes prevention program as an intervention for adult participants who are at risk for diabetes or diagnosed with prediabetes only. We defined at risk for diabetes to mean an individual who is overweight or obese and has at least one other modifiable risk factor for developing diabetes. These risk factors are listed in Table I-1. We defined prediabetes to mean individuals with glucose levels that are consistent with impaired fasting glucose (100–125 mg/dL) or impaired glucose intolerance (140–199 mg/dL, 2 hours after a 75-gram oral glucose tolerance test). This synthesis is limited to U.S. studies of adults at least 18 years of age.

TABLE I-1: Risk factors for diabetes

MODIFIABLE RISK FACTORS	NONMODIFIABLE RISK FACTORS
OVERWEIGHT/OBESITY BMI 18.5–24.9 Normal BMI 25–29.9 Overweight BMI 30+ Obese HIGH BLOOD GLUCOSE (FASTING) Healthy under 100 Prediabetes 100–125 Diabetes 125+ HYPERTENSION ABNORMAL LIPID METABOLISM IF LDL >100mg/dL HDL <40mg/dL (men), <50mg/dL (women) Triglycerides >150mg/dL INFLAMMATION AND HYPERCOAGULATION IF hs-CRP LEVELS ARE Low risk <1mg/L Average risk -3 mg/L High risk >3mg/L PHYSICAL INACTIVITY SMOKING	AGE 65+ at higher risk RACE/ETHNICITY Blacks, Mexican-Americans, American Indians, and Native Hawaiians at higher risk GENDER Men at higher risk Women post-menopause at higher risk FAMILY HISTORY

We conducted a comprehensive and systematic search using multiple electronic databases (MEDLINE, PubMed, ClinicalTrials.gov, Embase, PsycNet, Cochrane Library, ACP Journal Club, and CINAHL) for evaluation studies of interventions published between January 1, 2002, and July 31, 2013. The search was undertaken using medical subject headings and keywords

related to diabetes and its risk factors (see Table I-2). We supplemented the search with a manual search of the past two years of issues from selected journals with a high likelihood of publishing evaluations of diabetes prevention programs (e.g., *Diabetes Care, Diabetes Educator*). The manual search also included an examination of reference lists from initially identified studies and recent review articles on the topics of diabetes prevention and outcomes evaluation to identify qualified articles.

TABLE I-2: Search terms

pre-diabet* OR pre diabet* OR prediabet* OR glucose intoleran* OR impaired fasting glucose OR impaired fasting blood glucose OR impaired fasting glycemia OR impaired glucose toleran* OR impaired glucose metab* OR IGT OR insulin resistan* OR metabolic syndrome
obes* OR overweight OR over weight OR adipos* OR abdominal fat OR waist-hip ratio OR waist hip ratio
advanced age OR elderly OR senior citizen* OR old* OR male OR men OR African Americans OR Hispanic Americans OR Latino OR Asian Americans OR Indian OR Indian American OR Native American OR Pacific Islander OR African continental ancestry group OR American native continental ancestry group OR Asian continental ancestry group OR oceanic ancestry OR sedent* OR low physical activity OR low activity OR smok* OR tobacco OR nicotine OR alcohol OR alcohol drinking OR alcohol abuse OR alcohol* OR drink* OR drunk* OR intoxicat* OR hypertension OR high blood pressure OR elevated blood pressure OR dyslipid* OR hyperlipid* OR triglyceride* OR cholesterol OR LDL OR hypertriglycerid* OR high triglyceride* OR HDL OR low HDL OR inflamm* OR hypercoag* OR proinflamm* OR prothromb* OR pro inflamm* OR pro thromb* OR family OR family history OR PCOS OR PCOD OR poly cystic ovar* OR polycystic ovar* OR poly-cystic ovar* OR gestation* diabet* OR gestation* diabet* mellitus OR GDM OR diabet* in pregn* OR macrosom* OR large for gestational age OR excessive birth weight OR LGA
diabetes mellitus Type 2 OR Type 2 diabet* OR type II diabet OR non insulin depend* OR noninsulin depend* OR niddm OR adult onset diabet* OR matur$ onset diabet* OR slow onset diabet* OR MODY OR T2DM OR stable onset diabet*

In this synthesis, we primarily focused on lifestyle-related studies in the literature. We included both RCTs and non-RCT studies in our discussion for two reasons. First, although RCTs are considered the gold standard in study design and rank high in a hierarchical pyramid of evidence (that is, RCTs have high internal validity), they usually suffer from their low external validity, or the ability to replicate findings in real-world settings. Non-RCT studies, on the other hand, offer high external validity because they are conducted in real-world settings. Second, many translational diabetes prevention studies used pre-post study designs without control groups because the NIH-DPP trial had already established the evidence that lifestyle intervention participants benefited from the program.

To address the heterogeneity of study outcomes, we calculated the change in the risk of developing diabetes for each study. To do this, we used a prediction model for the risk of developing diabetes over the next 7.5 years.[19] The model includes multiple input variables, namely sex, Mexican-American ethnicity, fasting glucose, systolic blood pressure, high-density lipoprotein cholesterol level, body mass index (BMI), and family history. In cases in which

variables were missing from a study, data from the 2011–2012 National Health and Nutrition Examination Survey (NHANES) database were used to impute values from a population that was representative of the study population in terms of sex, age, and race and ethnicity.

We compared the studies by their estimated relative risk reduction. Bivariate analyses were conducted to examine associations between the estimated relative risk reduction and characteristics of the diabetes prevention intervention (e.g., group sessions vs. individual sessions, personal vs. virtual delivery of the intervention, community vs. noncommunity setting, prediabetes vs. at-risk participants). We identified a diabetes prevention program as community-based when it was implemented in settings such as community health centers, churches, YMCAs, schools, and homes. An intervention was considered virtual when personal, face-to-face interaction did not take place during the intervention phase. This category includes computer-based and telephonic interventions.

Two team members independently determined the relevance of identified studies and used a standardized form to extract data on study design, population characteristics, setting, intervention type, and reported outcomes from each study. When discrepancies existed, they were discussed and resolved by the research team until the data extraction was completed. To assess study quality and overall strength of evidence, we adopted the evaluation criteria from West et al. (2002).[18] The criteria include study design and domains in study question, study population, randomization, exposure or intervention, outcomes, statistical analysis, results, discussion, and funding and sponsorship.

ESTIMATION OF RISK OF DEVELOPING DIABETES

One of the larger challenges of this literature review is that studies either reported on different primary outcomes or reported on the same primary outcome with variability (e.g., reported percentage of body weight, BMI, percentage of participants who met weight loss-goal, kilograms for weight loss). In addition, many studies did not report standard deviations for their primary outcomes. The heterogeneity in reported outcomes of the studies makes the comparison of interventions challenging. Instead of using a meta-analysis, we adopted a multivariate prediction model of diabetes risk to address this problem.

Stern and his colleagues developed a multivariate prediction model to better identify high-risk individuals for diabetes.[19] They conducted a prospective cohort study and randomly selected 1,791 Mexican-Americans and 1,112 non-Hispanic whites without diabetes at baseline to participate in the study. Based on their data, they identified a risk prediction model for diabetes risk as follows:

$p = 1/(1 + e^{-x})$, where x = -13.415 + 0.028(age) + 0.661(sex) + 0.412(MA) + 0.079(FG) + 0.018(SBP) - 0.039(HDL) + 0.070(BMI) + 0.481(family history). In this equation, p = the probability of developing

diabetes over the 7.5-year follow-up period; age is in years; sex = 1 if female, 0 if male; MA = 1 if Mexican-American, 0 if non-Hispanic white; FG = fasting glucose in mg/dL; SBP = systolic blood pressure in mm Hg; HDL = high-density lipoprotein cholesterol level in mg/dL; BMI = body mass index in kg/m^2; and family history = 1 if at least one parent or sibling has diabetes or 0 if not.

METHODOLOGY OF IDENTIFYING ESTIMATED VALUES FOR MISSING INFORMATION

Of the studies evaluated, few reported mean values for every covariate in the Stern diabetes risk model. In these instances, nationally representative survey data from the 2011–2012 NHANES were used to impute the missing values. First, mean values for the covariates were calculated from NHANES data stratified by gender and race/ethnicity categories (non-Hispanic white, non-Hispanic black, Hispanic of any race, and other) within the age range of the study, where the age range was defined as the mean age, plus and minus one standard deviation. Then, we calculated a weighted average covariate value based on the study population's gender and race/ethnicity. Where distribution by gender and/or race/ethnicity was not reported by the study, the NHANES database was used to impute values from a population that was representative of the study population in terms of sex, age, and race and ethnicity. While most of the Stern covariates were equivalent to values reported in the NHANES dataset, two covariates used questions that were merely similar. The proportion of the study population that was Mexican-American was approximated by Hispanic ethnicity. Family history was approximated by the question, "Have you ever been told by a doctor or other health professional that you have health conditions or a medical or family history that increases your risk for diabetes?"

LIMITATIONS OF SYNTHETIC ANALYSIS

In this analysis, the results of multiple studies were synthesized using a peer-reviewed prediction model of diabetes incidence. Despite the beneficial characteristics of this model, it does have a number of limitations. The major limitations of using this predictive model in our risk estimation include: (1) race and ethnicity could be categorized as Mexican-American or non-Hispanic white only; therefore, the use of the model would be insensitive to other races/ethnicities (e.g., black, Asian, Native American, Puerto Rican, Cuban) and (2) the model does not include all outcome measures found in all studies. For example, if a study's diabetes prevention program only increased physical activity among its participants but not other variables included in the model, the pre- and post-risk estimates of this program based on the predictive model would not differ. Every predictive model has its own methodological assumptions and limitations. The estimated risk obtained from this model should be interpreted in perspective and in conjunction with the originally reported outcomes.

Appendix II: RE-AIM Model

The RE-AIM (Reach, Effectiveness, Adoption, Implementation, Maintenance) model provides a framework for what details should be specified in future evaluative studies of diabetes prevention programs.

1. REACH: Answers to how to reach a diverse sample representative of the population at risk will address the aforementioned issue of skewed study populations in existing literature. It is still unknown what the best strategies are to promote an efficacious prevention program to populations at risk and to recruit and retain participants.

2. EFFICACY: The NIH-DPP has provided solid proof that lifestyle intervention is efficacious in reducing incidence of diabetes through healthy diet, weight loss, and moderate physical activity in a highly controlled setting. For a translational diabetes prevention program modeled after the NIH-DPP lifestyle intervention, complete information on the contents of the program will not only help others to replicate the program, but also enable easy comparisons with other similar programs for evaluation.

3. ADOPTION: If a program is easy to implement and can demonstrate its benefits outweigh its costs, it will be appealing to health care providers and policymakers and realistic to adopt in specific practice settings. The existing literature provides very limited information on costs of intervention, not to mention the apparent lack of cost-effectiveness or cost-benefit analyses for insurers that will potentially reimburse the program. Complete evaluations of both short-term and long-term financial impact of implementing a program are also important for the program's initiation and sustainability. We also don't know the comparative effectiveness of implementing a diabetes prevention program in communities with limited access to healthy food or places for physical activity.

4. IMPLEMENTATION AND MAINTENANCE: Very few studies detailed how the infrastructure for the implementation of their interventions was established or what the procedure for the implementation was. Any individual- or community-level intervention is a collaborative effort. For example, a diabetes prevention program conducted in a church, YMCA, or a clinic setting (whether delivered 1:1 or via groups) requires successful collaboration of program leaders, host site leaders and stakeholders, and program participants. Establishing a strong partnership within a community is crucial to the future success and sustainability of any program implemented. Implementation science teaches us how to disseminate, implement, and assess sustainability of health interventions in real-world settings with diverse patient populations.[50–55] More research should be done using implementation science tools to evaluate the extent to which implementing diabetes prevention is effective in specific settings, prolongs sustainability, and promotes dissemination into other settings.

Appendix III:

Summary of Studies with Full Lifestyle Intervention

Authors	Study design	Type of intervention	Intervention/follow-up	Setting	Sample	Findings
Tate et al.[22]	RCT	E-counseling vs. control	1-hour introductory group weight-loss session, followed by Internet weight-loss program plus behavioral e-counseling for 1 year. Participants seen at baseline, 3, 6, and 12 months. Intervention recommendations: 1200–1500 kcal/d; fat intake of 20% or fewer calories; a minimum of 1000 kcal/wk of physical activity.	Home	92 prediabetes subjects (46 in intervention, 7 lost to follow-up; 46 in control, 8 lost to follow-up). 89–91% female; 89% white; mean age (SD) 48.5 (9.4).	Control: weight change 89.4kg to 87.1kg; treatment: 86.2kg to 80.9kg (p=0.04).
Ma et al.[20]	RCT	Coach-led group intervention vs. home-based DVD intervention vs. control	3-month intensive intervention phase (face-to-face in 12 weekly classes to diabetes prevention-led intervention participants or via a home-based DVD to self-directed intervention participants), and a 12-month maintenance phase via e-mails.	Primary care; home	241 prediabetes subjects (a diabetes prevention-led, group-delivered intervention (n=79), a self-directed DVD intervention (n=81), or usual care (n=81)). 6–7 participants lost to follow-up in each group. 47% female; 78% white; Mean age (SD) 52.9 (10.6).	BMI decrease from baseline in the diabetes prevention-led group vs. that in the usual care group (-2.2 vs. -0.9, P<0.001) and that in the self-directed group vs. usual care (-1.6 vs. -0.9, P=0.02). The percentages of participants who achieved the 7% DPP-based weight-loss goal were 37.0% (P=0.003) and 35.9% (P=0.004) in the diabetes prevention-led and self-directed groups, respectively, vs. 14.4% in the usual care group. Both interventions also achieved greater net improvements in waist circumference and fasting plasma glucose level.
Ockene et al.[27]	RCT	Community-based, literacy-sensitive, and culturally tailored lifestyle intervention ($661 per person) vs. control	3 individual and 13 group sessions over a 12-month period. The duration of the first group session was 1.5 hours and the remaining were 1 hour. The first individual visit was 1 hour and the last 2 were 30 minutes each. Follow-up for 1 year. Intervention aimed to promote positive attitudes toward dietary and physical activity changes.	Community	312 low-income, Latino, high-risk subjects; 162 in intervention, 150 control. 6.8% and 4.7% dropped out of intervention and control group. 74% female; 100% Latino; mean age 52.	Compared with the control group, the intervention group had significant weight reduction (-2.5 vs. 0.63 lb; P=.04), reduction in hemoglobin A1c (-0.10% vs. -0.04%; P=0.009), insulin resistance improvement, and greater reductions in percentage of calories from total and saturated fat. No significant difference in physical activity or fasting blood glucose between the two groups.

continued

Appendix III: Summary of Studies with Full Lifestyle Intervention *(continued)*

Authors	Study design	Type of intervention	Intervention/follow-up	Setting	Sample	Findings
Ackermann et al.[23]	RCT	DEPLOY pilot study. Group-based DPP intervention in YMCA vs. control	16 classroom-style meetings (intervention) or standard advice alone (controls). 6-month and 12-month follow-ups.	2 YMCAs	92 high-risk subjects (46 per group), 15% of intervention and 17% of control loss to follow-up after 6 months; 37% and 28% loss to follow-up after 12 months. 55% female; 81% white; mean age 58.3.	At 6 months, body weight decreased by 6.0% (95% CI 4.7, 7.3) in intervention participants and 2.0% (95% CI 0.6, 3.3) in controls (p<0.001; difference between groups). Intervention participants also had greater changes in total cholesterol (–22 mg/dL vs. 6 mg/dL controls; p<0.001). These differences were sustained after 12 months.
Ackermann et al.[24]	Based on the original RCT structure	An extension study to the DEPLOY pilot study	8-month lifestyle maintenance intervention.	2 YMCAs	66 high-risk subjects from original DEPLOY participants.	At 28 months, after both arms were offered the same 8-month lifestyle maintenance intervention, both arms had statistically significant weight losses compared to baseline (brief advice controls: 3.6%; 95% CI: 5.8 to 1.4; intensive lifestyle: 6.0%; 95% CI: 8.8 to 3.2). Participants initially assigned to the DPP also experienced significant improvements in blood pressure and total cholesterol.
Katula et al.[21]	RCT	Community-based, group-based translational DPP	Healthy Living Partnerships to Prevent Diabetes (HELP PD) Project: community-based translation of the DPP (weekly intensive sessions for 6 months), 12-month follow-up.	Community	301 prediabetes subjects (151 in intervention; 150 in usual care). 57.5% female; 74% white; mean age 57.9.	At the end of 12 months, compared with usual care participants, intervention participants experienced significantly greater decreases in blood glucose (-4.3 vs. -0.4 mg/dL; P<0.001), insulin (-6.5 vs. -2.7 µU/mL; P<0.001), homeostasis model assessment of insulin resistance (-1.9 vs. -0.8; P<0.001), weight (7.1 vs. 1.4 kg; P<0.001), BMI (2.1 vs. 0.3 kg/m2; P<0.001), and waist circumference (-5.9 vs. -0.8 cm; P<0.001).

continued

Appendix III: Summary of Studies with Full Lifestyle Intervention *(continued)*

Authors	Study design	Type of intervention	Intervention/follow-up	Setting	Sample	Findings
Liao et al.[26]	RCT	Lifestyle	6-month intervention; Treatment group: American Heart Association (AHA) step 2 diet (30% of total calories as fat, 7% saturated fat, 55% carbohydrate, and 200 mg cholesterol daily) plus endurance exercise for 1 hour three times a week; Control group: AHA step 1 diet (30% of total calories as fat, 10% saturated fat, 50% carbohydrate, and 300 mg cholesterol) plus stretching exercise three times a week; 6- and 24-month follow-up.	Primary care	64 prediabetes, Japanese-Americans (32 treatment; 32 control). 55% female; mean age 54.	The treatment group showed significantly greater reduction in percent of body fat (-1.4±0.4% vs. -0.3±0.3%); BMI (-1.1±0.2 vs. -0.4±0.1 kg/m^2); subcutaneous fat by computed tomography at the abdomen (-29.3±4.2 vs. -5.7±5.9 cm^2), thigh (-13.2±3.6 vs. -3.6±3.0 cm^2), and thorax (-19.6±3.6 vs. -8.9±2.6 cm^2); and skinfold thickness at the bicep (-2.0±0.6 vs. 1.1±0.6 mm) and triceps (-3.7±0.8 vs. -0.9±0.6 mm), which continued despite moving to home-based exercise for the last 18 months.
Parikh et al.[25]	RCT	A peer-led, community-based lifestyle intervention that focuses on enhancing participants' self-efficacy to make lifestyle changes.	Project HEED: a workshop consisting of eight 1.5-hour sessions over 10 weeks. 3-, 6-, and 12-month follow-up.	Community	99 prediabetes subjects (50 in intervention; 49 in control). 35 in intervention and 37 in control remained at 12 months. 85% female; 89% Hispanic; mean age 48.	The intervention group lost significantly more weight than the control group and maintained weight loss at 12 months (7.2 vs. 2.4 pounds; P<0.01). Limited behavioral changes from both groups. No changes in fat intake and physical activity.
Whittemore et al.[28]	Cluster RCT	Lifestyle change program vs. enhanced standard care program	Lifestyle change program modeled after NIH-DPP included 6 in-person sessions and 5 phone sessions over 6 months. Enhanced standard care program included 1 in-person session and 1 nutrition session. 6-month follow-up.	4 NP primary care practice sites	58 at-risk subjects (31 in intervention; 27 in control). 24 completed the intervention. 92% female; 45% white.	25% of lifestyle participants met treatment goals of 5% weight loss compared with 11% of standard care participants at 6 months. No significant difference was observed in other clinical outcomes from baseline between the two groups.
Almeida et al.[32]	Matched cohort longitudinal study	Single-session, theory-based, brief, small-group weight-loss intervention	A single 90-minute, small-group session in personal action planning for healthful eating, physical activity, and weight management. 12 month follow-up.	Health care organization	760 prediabetes subjects with 760 matched controls. 52.6% female; mean age (SD) 62.5 (10.4).	A significantly higher proportion of small-group participants lost at least 5% of their body weight compared with controls (22% vs. 15%, P=0.001).

continued

Appendix III: Summary of Studies with Full Lifestyle Intervention *(continued)*

Authors	Study design	Type of intervention	Intervention/follow-up	Setting	Sample	Findings
Vadheim et al.[40]	Pre-post, two groups	Adapted group-based DPP via telehealth video	16 weekly group-based core sessions followed by 6 monthly after-core sessions via on-site or participating via telehealth video conferencing (telehealth). Participants set targets to reduce fat intake and increase physical activity (at least 150 minutes per week) to achieve a weight-loss goal of 7%.	Health care facility vs. virtual	13 high-risk subjects on-site (100% completed); 16 telehealth (88% (n=14) completed). 69% female in on-site group; 93% female in telehealth group; mean age 53 for on-site group, 50 for telehealth group.	More than 45% of on-site and telehealth participants achieved the 7% weight-loss goal. No significant differences between groups.
Kramer et al.[38]	Pre-post	Community-based, Group Lifestyle Balance (GLB) program delivered by diabetes educators ($320 per person)	A 12-session group lifestyle intervention adapted from the DPP lifestyle intervention with the same goals for weight loss and physical activity as the DPP, including achievement of a weight loss of 7% from starting weight and an increase in physical activity to 150 minutes per week.	3 community health centers (rural, suburban, urban)	81 prediabetes subjects. 88% female; 96% white; mean age 53.	Significant decreases were noted in weight (-5.1%, p<0.001), fasting plasma glucose, low-density lipoprotein cholesterol (p=0.001), triglycerides (p<0.001), and blood pressure (p<0.001).
Kramer et al.[37]	Pre-post, two groups	Group Lifestyle Balance (GLB) program delivered via DVD	A 12-session group lifestyle intervention adapted from the DPP lifestyle intervention with the same goals for weight loss and physical activity as the DPP, including achievement of a weight loss of 7% from starting weight and an increase in physical activity to 150 minutes per week. Pre- and 3-month post-intervention measures were assessed.	Virtual	48 prediabetes subjects (22 GLB-DVD with 36% loss to follow-up; 26 GLB-group with 8.7% loss to follow-up). The intent was not to compare these two groups. 71% female; 83% white; mean age 59.7.	Significant physical activities increase and weight loss were observed in both groups. GLB-DVD with remote support may provide an effective alternative for GLB-group delivery.
Swanson et al.[30]	Pre-post	Diet-Exercise-Activity-Lifestyle (DEAL) program (In 2009, $2,566 per non-Medicare patient, $1,169 per Medicare patient)	Four 2-hour weekly group classes on nutrition and an individualized exercise counseling through a physical therapy assessment; 6- and 12-month follow-up, metformin after 6 month if necessary.	Primary care	221 prediabetes subjects 67% female; 88% white; mean age 62.	By 6 months after baseline, 59% had significantly lower fasting glucose concentrations, 59% had improvement in 2-hour glucose levels, and 61% had weight loss. Nearly 40% were nonresponders and had increased fasting glucose, 2-hour glucose, and weight. By the 12-month visit, significant declines in fasting glucose (P<0.001), 2-hour glucose (P<0.001), and weight (P =0.008) occurred in comparison with baseline values; however, no significant changes occurred in these measures between the 6- and 12-month visits (P>0.30 for all).

continued

Appendix III: Summary of Studies with Full Lifestyle Intervention *(continued)*

Authors	Study design	Type of intervention	Intervention/follow-up	Setting	Sample	Findings
Boltri et al.[35]	Pre-post	Church-based translational DPP	16-session translational DPP over 4 months; group interactive process and including prayer. 6- and 12-months post-intervention follow-up.	1 church	8 prediabetes subjects. 58% female; 100% black; mean age 52.	Following the intervention, weight, systolic and diastolic BP, and FG decreased by 7.5 lb (3.6%), 16 mm Hg (11.7%), 12 mm Hg (14.0%), and 5 mg/dL (4.8%), respectively ($P < 0.05$).
Boltri et al.[36]	Pre-post, two groups	Church-based translational DPP ($934/church for 6-week program; $1,075 per church for 16-week program)	6-session and 16-session church-based DPPs; 6- and 12-month follow-up.	5 churches (rural community)	37 prediabetes subjects (6-session (n=17); 16-session (n=20)). 70.3% female; 100% black; mean age (SD) 57.2 (9.0).	Overall, interventions were associated with decreased fasting glucose (108 to 101.7 mg/dL; p=0.037) and weight loss (-1.7 kg) after intervention; 16-session intervention had similar results with minimum improvement from 6-session. 12-month follow-up results remained similar without maintenance program.
Montana Cardiovascular Disease and Diabetes Prevention Program Workgroup (Amundson et al.)[31]	Pre-post	Adapted group-based DPP lifestyle intervention	16 weekly group-based core sessions followed by 6 monthly after-core sessions. Participants set targets to reduce fat intake and increase physical activity (at least 150 minutes per week) to achieve a weight-loss goal of 7%.	4 health care facilities	355 adults at high risk for cardiovascular disease and diabetes. 83% (n=295) completed the program. 80% female; mean age (SD) 53.6 (9.7).	There was a significant decrease among participants' weight from baseline (mean ± SD, 99.3 ± 19.7 kg) to week 16 (92.6 ± 18.8 kg; mean difference, 6.7 ± 4.0 kg, $P < 0.001$). 45% of the participants achieved the 7% weight-loss goal; 70% achieved the physical activity goal of 150 minutes or more per week.
Montana Cardiovascular Disease and Diabetes Prevention Program Workgroup (Vanderwood et al.)[29]	Pre-post	Adapted group-based DPP lifestyle intervention	16 weekly group-based core sessions followed by 6 monthly after-core sessions. Participants set targets to reduce fat intake and increase physical activity (at least 150 minutes per week) to achieve a weight-loss goal of 7%.	8 health care facilities	1,003 adults at high risk for cardiovascular disease and diabetes. 81% (n=816) completed the core; 58% (n=578) completed the after-core. 80% female; mean age (SD) 52.3 (11.6).	Of participants completing the core (n=816) and after-core (n=578), 45% and 49% achieved the 7% weight-loss goal, respectively. There were significant improvements in blood pressure, fasting glucose, and LDL cholesterol among participants completing the intervention.

continued

Appendix III: Summary of Studies with Full Lifestyle Intervention *(continued)*

Authors	Study design	Type of intervention	Intervention/follow-up	Setting	Sample	Findings
Seidel et al.[41]	Pre-post	Community-based, Group Lifestyle Balance (GLB) program	12-week community-based, DPP-modified GLB intervention, 3- and 6-month follow-ups. The goals of the intervention were to achieve a 7% weight loss and to progressively increase physical activity to 150 minutes per week.	An urban, medically underserved community	88 subjects individuals with metabolic syndrome; 69 completed 3-month follow-up; 50 (56.8%) completed 6-month follow-up. 84.1% female; 72.7% white; Mean age (SD) 54.0 (10.5).	Weight loss (46.4% lost ≥5% and 26.1% lost ≥7%) was observed after completion of the intervention. Of these subjects, 87.5% (n=28) and 66.7% (n=12) sustained the 5% and 7% reduction, respectively, at the 6-month reassessment. Additional improvements occurred in waist circumference (P<0.009) and blood pressure levels (P=0.04).
Davis-Smith et al.[34]	Pre-post	Modified version of NIH-DPP lifestyle intervention ($1,075: only cost for materials for this project)	6-session intervention modeled after NIH-DPP; 6- and 12-month follow-up.	1 church (rural community)	10 prediabetes subjects. 70% female; 100% black.	Mean weight loss of 7.9 lbs and 10.6 lbs right after the intervention and after 12 months.
Vadheim et al.[39]	Pre-post	Group-based, adapted DPP lifestyle intervention ($557 per participant)	16 weekly group-based core sessions followed by 6 monthly after-core sessions. Participants set targets to reduce fat intake and increase physical activity (at least 150 minutes per week) to achieve a weight-loss goal of 7%.	Health center (rural community)	84 at-risk subjects completed 16-week core program; 65 completed after-core program. 88% female; mean age (SD) 50.5 (11.1)	52% achieved the 7% weight-loss goal and 78% achieved at least a 5% weight loss during the core program.
Smith-Ray et al.[33]	Pre-post	Lifestyle change program focusing on physical activity and dietary habits changes	27 diabetes prevention classes for 1 month	Primary care	298 prediabetes subjects; 6 lost to follow-up. 62% female; mean age 62.	Participants significantly increased reported minutes of moderate ($p < 0.001$) and vigorous ($p = 0.028$) physical activity and their daily servings of fruits and vegetables ($p < 0.001$).

Appendix IV:

Summary of Studies with Diet-Only or Physical Activity-Only Intervention

Authors	Study design	Type of intervention	Intervention/follow-up	Setting	Sample	Findings
Cole et al.[42]	RCT	Nutrition-focused intervention	Nutrition-based shared medical appointment (SMA) intervention consisting of three 90-minute nutrition sessions over 3 months; 3-month and 1-year follow-ups.	Primary care	94 prediabetes subjects with 64% completion rate (34 in intervention, 31 in control). 46% female; 64% white; mean age (SD) 58.3 (9.6).	The SMA and control participants lost a mean of 6.6 and 3.6 lbs, respectively; neither group met the 5% modest weight loss expected. The SMA and control group experienced a mean drop in fasting blood glucose of 6 mg/dL.
Morey et al.[43]	RCT	Physical activities	12-month, home-based physical activity counseling (PAC) consisting of in-person baseline counseling session, telephone counseling, physician endorsement in clinic with monthly automated encouragement, and customized mailed materials.	Home	302 older adults with prediabetes (180 in PAC; 122 in usual care). 96.1% male; 71.7% white; mean age 67.1.	Both groups had small declines over time of approximately 6% in fasting blood glucose ($P < 0.001$), but there were no significant differences between the PAC and control groups over time for any of the glycemic indicators.
Roberts et al.[44]	RCT	Physical activities	Three 1-hour resistance exercise training (RT) sessions per week for 12 weeks	University	36 overweight/obese young men (28 RT, 8 control). Mean age 22.	12 weeks of RT increased SHBG ($P=0.01$) and decreased FAI ($P<0.05$) and cortisol ($P<0.05$) compared to control.
Swartz et al.[45]	Pre-post	Physical activities	8-week walking program (10,000 steps/day)	Home	18 inactive, at-risk females.	During the intervention period, the participants increased their accumulated steps/day by 85% to 9,213, which resulted in beneficial changes in 2-hour post-load glucose levels ($p<0.001$), AUC glucose ($p=0.025$), systolic blood pressure ($p<0.001$), and diastolic blood pressure ($p=0.002$).

Appendix V:

Summary of Studies with Pharmacological Intervention

Authors	Study design	Type of intervention	Intervention/follow-up	Setting	Sample	Findings
Osei et al.[56]	RCT	Drug	Each subject was instructed to ingest at least 250 g of carbohydrates in their regular meals for at least 3 days prior to the test. After a 10- to 12-hour overnight fast, blood samples were drawn for serum glucose, insulin, and C-peptide at t 0 minutes. The subjects then ingested 75 g of oral glucose load (Glucola, Baltimore, MD; 250 mL) over a 2-minute period. Blood samples were drawn at t 30, 60, 90, and 120 minutes for serum glucose, insulin, and C-peptide concentrations. Glucose tolerance status of the subjects was defined by the World Health Organization criteria.	Hospital	First-degree relatives of black patients with Type 2 diabetes and manifested IGT during an oral glucose tolerance test (OGTT) Treatment: 9; Control: 9.	The first-degree relatives of black patients with Type 2 diabetes who had newly diagnosed IGT tolerated glipizide GITS without any symptoms suggestive of hypoglycemia or hyperglycemia. GITS was not associated with significant weight gain when compared with the PLAC group. We found no biochemical or hematological abnormalities with the chronic use of GITS in our IGT patients when compared with the PLAC group.
Mitri et al.[57]	RCT	Drug	Patients received either cholecalciferol (2,000 IU once daily) or calcium carbonate (400 mg twice daily) for 16 weeks.	Hospital	Ambulatory adults who were 40 years of age or older. 23 (Vit D+Ca), 23 (Vit D+placebo), 22 (Ca+P), 24 (Both P).	In adults at risk for Type 2 diabetes, short-term supplementation with cholecalciferol improved beta cell function and had a marginal effect on attenuating the rise in HbA1c.
DeFronzo et al.[58]	RCT	Drug	Patients received either pioglitazone or placebo. Median follow-up: 2.4 years; fasting glucose was measured quarterly, and oral glucose tolerance tests were performed annually. Conversion to diabetes was confirmed on the basis of the results of repeat testing.	Health centers	Male and female patients 18 years of age or older with IGT; Treatment: 303; Control: 299.	As compared with placebo, pioglitazone reduced the risk of conversion of impaired glucose tolerance to Type 2 diabetes mellitus by 72% but was associated with significant weight gain and edema.
The Navigator Study Group[59]	RCT	Drug & lifestyle	Patients received valsartan (up to 160 mg daily) or placebo (and nateglinide or placebo) in addition to lifestyle modification. We then followed the patients for a median of 5.0 years for the development of diabetes (6.5 years for vital status).	Outpatient (clinics)	9,306 patients with impaired glucose tolerance and established cardiovascular disease or risk factors; Treatment: 4,631; Control: 4,675.	Among patients with impaired glucose tolerance and cardiovascular disease or risk factors, the use of valsartan for 5 years, along with lifestyle modification, led to a relative reduction of 14% in the incidence of diabetes but did not reduce the rate of cardiovascular events.

continued

Appendix V: Summary of Studies with Pharmacological Intervention *(continued)*

Authors	Study design	Type of intervention	Intervention/follow-up	Setting	Sample	Findings
The Navigator Study Group[60]	RCT	Drug & lifestyle	Participants received nateglinide (up to 60 mg three times daily) or placebo, in a 2-by-2 factorial design with valsartan or placebo, in addition to participation in a lifestyle modification program. We followed the participants for a median of 5.0 years for incident diabetes (and a median of 6.5 years for vital status).	Outpatient (clinics)	9,306 patients with impaired glucose tolerance and established cardiovascular disease or risk factors; Treatment: 4,645, Control: 4,661.	Among persons with impaired glucose tolerance and established cardiovascular disease or cardiovascular risk factors, assignment to nateglinide for 5 years did not reduce the incidence of diabetes or the coprimary composite cardiovascular outcomes.
Maki et al.[61]	RCT	Drug	Subjects (n=39) consumed breakfast meals containing 75 g of carbohydrates, each of which contained 1, 2, 4, or 8 g of HV-HPMC or a cellulose control. Each subject completed tests with control and two HV-HPMC doses (1 meal with control, 2 with HV-HPMC dose).	Research center/clinic	39 patients required to have adequate venous access and be in apparent good health; Subjects were a subset of participants in two trials with elevated peak postprandial glucose [7.8 mmol/L (140 mg/dL)] and body mass index (BMI) 27 kg/m^2.	Among subjects at risk for Type 2 diabetes mellitus, 1.0–8.0 g of HV-HPMC blunted postprandial glucose and insulin responses in a dose-dependent manner. Additional research is warranted to assess whether chronic consumption might retard the development or progression of glucose intolerance.
Song et al.[62]	RCT	Drug	Randomly assigned to receive vitamin C (ascorbic acid, 500 mg every day), vitamin E (RRR-a-tocopherol acetate, 600 IU every other day), beta-carotene (50 mg every other day), or their respective placebos. Median follow-up of 9.2 years.	Not specified	8,171 female health professionals aged 40 years old or older with either a history of cardiovascular disease (CVD) or 3 CVD risk factors (randomly vitamin C or placebo, vitamin E or placebo, then beta or placebo).	Our randomized trial data showed no significant overall effects of vitamin C, vitamin E, and beta-carotene on risk of developing Type 2 diabetes in women at high risk of CVD.
The DREAM (Diabetes Reduction Assessment with ramipril and rosiglitazone Medication) Trial Investigators[63]	RCT	Drug	Participants received rosiglitazone (8 mg daily; n=2,365) or placebo (n=2,634) and followed for a median of 3 years; 17-day placebo run-in period.	Not specified	5,269 adults aged 30 years or older with impaired fasting glucose or impaired glucose tolerance, or both, and no previous cardiovascular disease from 191 sites in 21 countries; Treatment: 2,635, Control: 2,634.	Rosiglitazone at 8 mg daily for 3 years substantially reduces incident Type 2 diabetes and increases the likelihood of regression to normoglycaemia in adults with impaired fasting glucose or impaired glucose tolerance, or both.

continued

Appendix V: Summary of Studies with Pharmacological Intervention *(continued)*

Authors	Study design	Type of intervention	Intervention/follow-up	Setting	Sample	Findings
Saremi et al.[64]	RCT	Drug	Pioglitazone treatment (4.76×10–3 mm/year; 95% CI: 2.39×10–3–7.14×10–3 mm/year); placebo (9.69×10–3 mm/year; 95% CI: 7.24×10–3–12.15×10–3 mm/year); Average follow-up of 2.3 years.	Hospital	Participants included adults (≥18 years) with impaired glucose tolerance (IGT). In addition, all IGT subjects had fasting plasma glucose (FPG) of 92 to 125 mg/dL, were overweight, and had at least 1 other risk factor for T2DM; Treatment: 303, Control: 299.	Pioglitazone slowed progression of CIMT, independent of improvement in hyperglycemia, insulin resistance, dyslipidemia, and systemic inflammation in prediabetes. These results suggest a possible direct vascular benefit of pioglitazone.
Buchanan et al.[65]	RCT	Drug	Participants received placebo (n=133) or the insulin-sensitizing drug troglitazone (400 mg/day; n=133) administered in double-blind fashion. Fasting plasma glucose was measured every 3 months, and oral glucose tolerance tests (OGTTs) were performed annually to detect diabetes. Intravenous glucose tolerance tests (IVGTTs) were performed at baseline and 3 months later to identify early metabolic changes associated with any protection from diabetes. Women who did not develop diabetes during the trial returned for OGTTs and IVGTTs 8 months after study medications were stopped.	Outpatient/ community	Hispanic women with high risk of developing Type 2 diabetes; Treatment: 114, Control: 122.	A 50% reduction in the incidence of Type 2 diabetes in young Hispanic women with recent GDM who were treated with an insulin-sensitizing drug. Protection from diabetes persisted 8 months after the drug was stopped, and it was associated with preservation of beta-cell compensation for stable insulin resistance. Perhaps most importantly, protection required an improvement in SI soon after initiation of treatment, but was most closely linked to a reduction in the amount of insulin required from beta-cells.

continued

Appendix V: Summary of Studies with Pharmacological Intervention *(continued)*

Authors	Study design	Type of intervention	Intervention/follow-up	Setting	Sample	Findings
Zappe et al.[66]	RCT	Drug	16 week (+2-week washout and 2-week placebo at beginning) [16-week therapy with valsartan 320 mg⁄d (n=189), hydrochlorothiazide (HCTZ)25 mg⁄d (n=190), or valsartan⁄HCTZ 320⁄25 mg⁄d (n=187)]	Not Specified	Patients were 18–75 years old, obese, and hypertensive. V: 189; V/H: 187; H: 190.	There were no statistically significant differences in HOMA-IR among the 3 groups. HCTZ significantly increased hemoglobin A1c and triglyceride concentrations and lowered serum potassium levels vs. valsartan. HCTZ also increased plasma aldosterone and C-reactive protein levels. Blood pressure reduction and blood pressure control rates were highest with valsartan⁄HCTZ. There were no differences between combination valsartan⁄HCTZ or monotherapies on a measure of insulin sensitivity; however, the negative metabolic effects of HCTZ (increase in triglyceride and hemoglobin A1c values) were absent with valsartan⁄HCTZ, indicating an ameliorating effect of valsartan on these measures.
The DREAM Trial Investigators[67]	RCT	Drug	Participants received ramipril (titrated to a maximum of 15 mg) or matching placebo and, simultaneously, rosiglitazone (titrated to a maximum of 8 mg) or matching placebo, in a two-by-two balanced factorial design. Participants had OGTTs done after 2 years and at final visit, and at other yearly visits if FPG or HbA values were elevated (2), and were followed for a median of 3 years.	Outpatient	3,269 participants aged 30 years or older with impaired fasting plasma glucose and/or IGT.	In people allocated to ramipril compared with those not allocated ramipril during the trial, the post-washout normoglycemia incidence was higher. In people allocated to rosiglitazone compared with those not allocated rosiglitazone during the trial, the post-washout incidence of diabetes was significantly lower and the incidence of normoglycemia was higher. During the washout period, diabetes incidence was the same for ramipril versus placebo and for rosiglitazone versus placebo. Rosiglitazone delays disease progression during treatment, but the process resumes at the placebo rate when the drug is stopped.

continued

Appendix V: Summary of Studies with Pharmacological Intervention *(continued)*

Authors	Study design	Type of intervention	Intervention/follow-up	Setting	Sample	Findings
The DREAM Trial Investigators[68]	RCT	Drug	Participants received ramipril (up to 15 mg per day) or placebo (and rosiglitazone or placebo) and were followed for a median of 3 years.	Outpatient	5,269 participants with cardiovascular disease but with impaired fasting glucose levels or impaired glucose tolerance [Ram-2623; C- 2646].	Among persons with impaired fasting glucose levels or impaired glucose tolerance, the use of ramipril for 3 years does not significantly reduce the incidence of diabetes or death but does significantly increase regression to normoglycemia.
Hanley et al.[69]	RCT	Drug	OGTTs at baseline, after 2 years, and at the end of the study, with blood samples drawn fasting as well as 30 and 120 minutes after the glucose challenge.	Outpatient	982 patients from DREAM On trial centers in Canada who had oral glucose tolerance tests at baseline, after 2 years, and at the end of the study.	Treatment with rosiglitazone, but not ramipril, resulted in significant improvements in measures of ßcell function over time in subjects with prediabetes. Although the long-term sustainability of these improvements cannot be determined from the present study, these findings demonstrate that the diabetes preventive effect of rosiglitazone was in part a consequence of improved ßcell function.
DREAM On (Diabetes Reduction Assessment with remipril and rosiglitazone Medication Ongoing follow-up) Investigators[70]	RCT	Drug	3 years of therapy with rosiglitazone	Outpatient, follow-up study was conducted at 49 of the 191 DREAM On sites	2,464 (eligible participants at DREAM On sites); 1,653 (outcome free on therapy); 1,361 (final primary outcome status available); 416 (source of participants analyzed for sensitivity analysis, which was restricted to participants from 15 sites that provided final outcome assessment for at least 90% of participants).	Time-limited exposure to rosiglitazone reduces the longer-term incidence of diabetes by delaying but not reversing the underlying disease process.
Ali et al.[71]	RCT/ crossover	Drug	6 month, crossover for 6 months; Participants received 6-month sequences of chromium picolinate or placebo at 1 of 2 dosages (500 or 1,000 mcg daily).	Hospital (hospital where outcomes measured)	Patients enrolled were 18 years old or older and were identified as having IGT, IFG, or metabolic syndrome; patients were excluded if they had diabetes; 500 mcg- 30; 1,000 mcg- 29.	59 participants were enrolled. No changes were seen in glucose level, insulin level, or HOMA-IR (all, P>.05) after 6 months of chromium at either dosage level (500 mcg or 1,000 mcg daily) when compared with placebo. None of the secondary outcomes improved with either chromium dosage compared with placebo (P>0.05).

continued

Appendix V: Summary of Studies with Pharmacological Intervention *(continued)*

Authors	Study design	Type of intervention	Intervention/follow-up	Setting	Sample	Findings
Hutchins et al.[72]	Crossover (each participant serves as their own control)	Drug	Participants consumed 0, 13, or 26 g ground flaxseed for 12 weeks. Glucose, insulin, homeostatic model assessment (HOMA-IR), and normalized percent of α-linolenic fatty acid (ALA) were significantly different by treatment (multiple analysis of variance, P = .036, P = .013, P = .008, P = .024 respectively).12 weeks.	Community/ home	Overweight men and postmenopausal women with prediabetes (n=25).	The current study found that a low dose of daily flaxseed supplementation decreased insulin resistance in overweight and obese, glucose-intolerant people.
Durbin [73]	Observational (treatment depends on initial meeting/ physician seen)	Drug	Patients in the active treatment group (n=101) had received troglitazone for an average of 10 months before being randomly switched to rosiglitazone (4 mg/day) or pioglitazone (30 mg/day). Patients were switched when troglitazone was withdrawn from the U.S. market because of liver toxicity concerns. Patients with IGT and IR who received no anti-diabetic medication served as a control group (n=71). HbA1c and C-peptide levels were measured at baseline (2 years) and study end point (3 years). Kaplan–Meier testing, using time to outcome as the main outcome variable, determined risk reduction in the TZD group relative to the control group.	Outpatient	Multiethnic patients with IGT and IR; Treatment: 101 (r-39, p-62); Control: 71.	Mean HbA1c and C-peptide levels decreased for patients receiving either TZD at the 2-year assessment, and reductions were maintained at study end point. After 2 years, none of the patients receiving TZD therapy progressed to T2DM; three patients progressed to T2DM by study end point. In the control group, 11 patients developed diabetes after 2 years and 19 patients developed diabetes by the end of the study. The incidence (risk reduction) of diabetes after 3 years was 88.9% lower in the TZD group compared with the control group (p< 0.001).
Xiang et al. [74]	Observational	Drug	Participants were offered participation in the Pioglitazone In Prevention Of Diabetes (PIPOD) study for a planned 3 years of drug treatment and 6 months of post-drug washout.	Outpatient/ community	86 Hispanic women with prior gestational diabetes who had completed participation in the Troglitazone In Prevention Of Diabetes (TRIPOD) study.	The risk of diabetes, which occurred at an average rate of 4.6% per year, was lowest in women with the largest reduction in total IVGTT insulin area after 1 year of treatment. The similarity of findings between the PIPOD and TRIPOD studies supports a class effect of thiazolidinedione drugs to enhance insulin sensitivity, reduce insulin secretory demands, and preserve pancreatic beta-cell function, all in association with a relatively low rate of Type 2 diabetes, in Hispanic women with prior gestational diabetes.

Appendix VI: REFERENCES

1 American Diabetes Association, "Diabetes Basics: Type 2," http://www.diabetes.org/diabetes-basics/type-2/, accessed January 2015.

2 Centers for Disease Control and Prevention, "National Diabetes Statistical Report, 2014: Estimates of Diabetes and Its Burden in the United States," http://www.cdc.gov/diabetes/pubs/statsreport14/national-diabetes-report-web.pdf, accessed January 2015.

3 Boyle, J.P.; Thompson, T.J.; Gregg, E.W.; Barker, L.E.; and Williamson, D.F. (2010). Projection of the year 2050 burden of diabetes in the US adult population: dynamic modeling of incidence, mortality, and prediabetes prevalence. *Population Health Metrics*, 8:29.

4 New York State Health Foundation and Healthcare Association of New York State, "Diabetes: A Hidden Health Care Cost Driver in New York," http://nyshealthfoundation.org/uploads/resources/hidden-health-care-cost-driver-analysis-october-2010.pdf, accessed January 2015.

5 Gerstein, H.C.; Santaguida, P.; Raina, P.; Morrison, K.M.; Balion, C.; Hunt, D.; Yazdi, H.; and Booker, L. (2007). Annual incidence and relative risk of diabetes in people with various categories of dysglycemia: a systematic overview and meta-analysis of prospective studies. *Diabetes Research and Clinical Practice*, 78(3), 305–12.

6 Meneilly, G.S. and Elahi, D. (2005). Metabolic alterations in middle-aged and elderly lean patients with Type 2 diabetes. *Diabetes Care*, 28(6), 1498–99.

7 Brown, A.F.; Gregg, E.W.; Stevens, .MR.; Karter, A.J.; Weinberger, M.; Safford, M.M.; Gary, T.L.; Caputo, D.A.; Waitzfelder, B.; Kim, C.; and Beckles, G.L. (2005). Race, ethnicity, socioeconomic position, and quality of care for adults with diabetes enrolled in managed care: the Translating Research Into Action for Diabetes (TRIAD) study. *Diabetes Care*, 28(12), 2864–70.

8 Wexler, D.J.; Grant, R.W.; Meigs, J.B.; Nathan, D.M.; and Cagliero, E. (2005). Sex disparities in treatment of cardiac risk factors in patients with Type 2 diabetes. *Diabetes care*, 28(3), 514–20.

9 Arslanian, S.A.; Bacha, F.; Saad, R.; and Gungor, N. (2005). Family history of Type 2 diabetes is associated with decreased insulin sensitivity and an impaired balance between insulin sensitivity and insulin secretion in white youth. *Diabetes Care*, 28(1), 115–19.

10 Wannamethee, S.G., and Shaper, A.G. (1999). Weight change and duration of overweight and obesity in the incidence of Type 2 diabetes. *Diabetes Care*, 22(8), 1266–72.

11 Morrato, E.H.; Hill, J.O.; Wyatt, H.R.; Ghushchyan, V.; and Sullivan, P.W. (2007). Physical activity in U.S. adults with diabetes and at-risk for developing diabetes, 2003. *Diabetes Care*, 30(2), 203–09.

12 U.S. Department of Health and Human Services, "The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General," http://www.surgeongeneral.gov/library/reports/50-years-of-progress/full-report.pdf, accessed January 2015.

13 Huang, E.S.; Basu, A.; O'Grady, M.; and Capretta, J.C. (2009). Projecting the future diabetes population size and related costs for the U.S. *Diabetes Care*, 32(12), 2225–29.

14 American Diabetes Association (2013). Economic costs of diabetes in the U.S. in 2012. *Diabetes Care*, 36(4), 1033–46.

15 Pan, X.R.; Li, G.W.; Hu, Y.H.; Wang, W.Y.; An, Z.X.; Lin, J.; Xiao, J.Z.; Cao, H.B.; Liu, P.A.; Jiang, X.G.; Jiang, Y.Y.; Wang, J.P.; Zheng, H.; Zhang, H.; Bennett, P.H.; and Howard, B.V. (1997). Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. *Diabetes Care*, 20(4), 537–44.

16 Tuomilehto, J.; Lindström J.; Eriksson, J.; Hämäläinen, H.; Ilanne-Parikka, P.; Keinänen-Kiukaanniem, S.; Laakso, M.; Louheranta, A; Rastas, M.; Salminen, V.; and Uusitupa, M. (2001). Prevention of Type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *New England Journal of Medicine*, 344(18), 1343–50.

17 Knowler, W. C.; Barrett-Connor E.; Fowler, S.E.; Hamman, R.F.; Lachin, J.M.; Walker, E.A.; Nathan, D.M.; and Diabetes Prevention Research Group (2002). Reduction in the incidence of Type 2 diabetes with lifestyle intervention or metformin. *New England Journal of Medicine*, 346(6), 393–403.

18 West, S; King, V.; Carey, T.S.; Lohr, K.N.; McKoy, N; Sutton, S.F., and Lux, L. (2002). Systems to Rate the Strength of Scientific Evidence. Evidence Report, Technology Assessment No. 47. AHRQ Publication No. 02-E016. Rockville, MD: Agency for Healthcare Research and Quality, http://www.ncbi.nlm.nih.gov/books/NBK11930/, accessed January 2015.

Appendix VI *(continued)*

[19] Stern, M.; Williams, K.; and Haffner, S. (2002). Identification of persons at high risk for Type 2 diabetes mellitus: do we need the oral glucose tolerance test? *Annals of Internal Medicine*, 136(8), 575–81.

[20] Ma, J.; Yank, V.; Xiao, L.; Lavori, P.W.; Wilson, S.R.; Rosas, L.G.; and Stafford, R.S. (2013). Translating the Diabetes Prevention Program lifestyle intervention for weight loss into primary care: a randomized trial. *JAMA Internal Medicine*, 173(2), 113–21.

[21] Katula, J.; Vitolins, M.Z.; Rosenberger, E.L.; Blackwell, C.S.; Morgan, T.M.; Lawlor, M.S.; and Goff, D.C. (2011). One-year results of a community-based translation of the Diabetes Prevention Program: Healthy-Living Partnerships to Prevent Diabetes (HELP PD) Project. *Diabetes Care*, 34(7), 1451–57.

[22] Tate, D.; Jackvony, E.; and Wing, R. (2003). Effects of Internet behavioral counseling on weight loss in adults at-risk for Type 2 diabetes: a randomized trial. *Journal of the American Medical Association*, 289(14), 1833–36.

[23] Ackermann, R.T.; Finch, E.A.; Brizendine, E.; Zhou, H.; and Marrero, D.G. (2008). Translating the Diabetes Prevention Program into the community. The DEPLOY Pilot Study. *American Journal of Preventive Medicine*, 35(4), 357–63.

[24] Ackermann, R.T.; Finch, E.A.; Caffrey, H.M.; Lipscomb, E.R.; Hays, L.M.; and Saha, C. (2011). Long-term effects of a community-based lifestyle intervention to prevent Type 2 diabetes: the DEPLOY extension pilot study. *Chronic Illness*, 7(4), 279–90.

[25] Parikh, P.; Simon, E.P.; Fei, K.; Looker, H.; Goytia, C.; and Horowitz, C.R. (2010). Results of a pilot diabetes prevention intervention in East Harlem, New York City: Project HEED. *American Journal of Public Health*, 100 Suppl. 1, S232–39.

[26] Liao, D.; Asberry, P.; Shofer, J.; Callahan, H.; Matthys, C.; Boyko, E.J.; Leonetti, D.; Kahn, S.E.; Austin, M.; Newell, L.; Schwartz, R.S.; and Fujimoto, W.Y. (2002). Improvement of BMI, body composition, and body fat distribution with lifestyle modification in Japanese Americans with impaired glucose tolerance. *Diabetes Care*, 25(9), 1504–10.

[27] Ockene, I.S.; Tellez, T.L.; Rosal, M.C.; Reed, G.W.; Mordes, J.; Merriam, P.A., Olendzki, B.C.; Handelman, G.; Nicolosi, R.; and Ma, Y. (2012). Outcomes of a Latino community-based intervention for the prevention of diabetes: the Lawrence Latino Diabetes Prevention Project. *American Journal of Public Health*, 102(2), 336–42.

[28] Whittemore, R.; Melkus, G.; Wagner, J.; Dziura, J.; Northrup, V.; and Grey, M. (2009). Translating the diabetes prevention program to primary care: a pilot study. *Nursing Research*, 58(1), 2-12.

[29] Vanderwood, K.K.; Hall, T.O.; Harwell, T.S.; Butcher, M.K.; Helgerson, S.D.; and Montana Cardiovascular Disease and Diabetes Prevention Workgroup, (2010). Implementing a state-based cardiovascular disease and diabetes prevention program. *Diabetes Care*, 33(12), 2543–45.

[30] Swanson, C.M.; Bersoux, S.; Larson, M.H.; Aponte-Furlow, R.T.; Flatten, S.S.; Olsen, C.L.; LaRosa, C.; Verona, P.M.; Jameson, K.A.; and Cook, C.B. (2012). An outpatient-based clinical program for diabetes prevention: an update. *Endocrine Practice*, 18(2), 200–08.

[31] Amundson, H.A.; Butcher, M.K.; Gohdes, D.; Hall, T.O.; Harwell, T.S.; Helgerson, S.D.; Vanderwood, K.K.; and Montana Cardiovascular Disease and Diabetes Prevention Program Workgroup (2009). Translating the diabetes prevention program into practice in the general community: findings from the Montana Cardiovascular Disease and Diabetes Prevention Program. *The Diabetes Educator*, 35(2), 209–10, 213–14, 216–20 passim.

[32] Almeida, F.; Shetterly, S.; Smith-Ray, R.; and Estabrooks, P. (2010). Reach and effectiveness of a weight loss intervention in patients with prediabetes in Colorado. *Preventing Chronic Disease*, 7(5), 1–5.

[33] Smith-Ray, R.L.; Almeida, F.A.; Bajaj, J.; Foland, S.; Gilson, M.; Heikkinen, S.; Seagle, H.; and Estabrooks, P.A. (2006). Translating Efficacious Behavioral Principles for Diabetes Prevention Into Practice. *Health Promotion Practice*, 10(1), 58–66.

[34] Davis-Smith, Y.; Boltri, J.; Seale, J.; Shellenberger, S. Blalock, T.; and Tobin, B. (2007). Implementing a diabetes prevention program in a rural African-American church. *Journal of the National Medical Association*, 99(4), 440–46.

[35] Boltri, J.; Davis-Smith, Y.; Seale, J.; Shellenberger, S.; Okosun, I.; and Cornelius M. (2008). Diabetes prevention in a faith-based setting: results of translational research. *Journal of Public Health Management and Practice*, (14):1, 29–32.

Appendix VI *(continued)*

[36] Boltri, J.; Davis-Smith, M.; Okosun, I.; Seale, J.; and Foster, B. (2011). Translation of the National Institutes of Health Diabetes Prevention Program in African American Churches. *Journal of the National Medical Association*, 103(3),194–202.

[37] Kramer, M.K.; Kriska, A.M.; Venditti, E.M.; Semler, L.N.; Miller, R.G.; McDonald, T.; Siminerio, L.M.; and Orchard, T.J. (2010). A novel approach to diabetes prevention: evaluation of the Group Lifestyle Balance program delivered via DVD. *Diabetes Research and Clinical Practice*, 90(3), e60–63.

[38] Kramer, M.K.; McWilliams, J.R.; Chen, H.Y.; and Siminerio, L.M. (2011). A community-based diabetes prevention program: evaluation of the group lifestyle balance program delivered by diabetes educators. *The Diabetes Educator*, 37(5), 659–68.

[39] Vadheim, L.M.; Brewer, K.A.; Kassner, D.R.; Vanderwood, K.K.; Hall, T.O.; Butcher, M.K.; Helgerson, S.D.; and Harwell, T.S. (2010). Effectiveness of a lifestyle intervention program among persons at high risk for cardiovascular disease and diabetes in a rural community. *The Journal of Rural Health*, 26(3), 266–72.

[40] Vadheim, L.M.; McPherson, C.; Kassner, D.R.; Vanderwood, K.K.; Hall, T.O.; Butcher, M.K.; Helgerson, S.D.; and Harwell, T.S. (2010). Adapted diabetes prevention program lifestyle intervention can be effectively delivered through telehealth. *The Diabetes Educator*, 36(4), 651–56.

[41] Seidel, M.; Powell, R.; Zgibor, J.; Siminerio, L.; and Piatt, G. (2008). Translating the Diabetes Prevention Program into an urban medically underserved community: a nonrandomized prospective intervention study. *Diabetes Care*, 31(4), 684–89.

[42] Cole, R.E.; Boyer, K.M.; Spanbauer, S.M.; Sprague, D.; and Bingham, M. (2013). Effectiveness of prediabetes nutrition shared medical appointments: prevention of diabetes. *The Diabetes Educator*, 39(3), 344–53.

[43] Morey, M.C.; Pieper, C.F.; Edelman, D.E.; Yancy, W.S.; Green, J.B.; Lum, H.; Peterson, M.J.; Sloane, R.; Cowper, P.A.; Bosworth, H.B.; Huffman, K.M.; Cavanaugh, J.T.; Hall, K.S.; Pearson, M.P.; and Taylor, G.A. (2012). Enhanced fitness: a randomized controlled trial of the effects of home-based physical activity counseling on glycemic control in older adults with prediabetes mellitus. *Journal of the American Geriatrics Society*, 60(9), 1655–62.

[44] Roberts, C.K.; Croymans, D.M.; Aziz, N.; Butch, A.W.; and Lee, C.C. (2013). Resistance training increases SHBG in overweight/obese, young men. *Metabolism - Clinical and Experimental*, 62(5), 725–33.

[45] Swartz, A.M.; Strath, S.J.; Bassett, D.R.; Moore, J.B.; Redwine, B.A.; Groër, M.; and Thompson, D.L. (2003). Increasing daily walking improves glucose tolerance in overweight women. *Preventive Medicine*, 37(4), 356–62.

[46] Ackermann, R.T. and Marrero, D.G. (2007). Adapting the Diabetes Prevention Program lifestyle intervention for delivery in the community: the YMCA model. *The Diabetes Educator*, 33(1):69, 74–75, 77–78.

[47] Zhuo, X.; Zhang, P.; Gregg, E.W.; Barker, L.; Hoerger, T.J.; Pearson-Clarke, T.; and Albright, A. (2012). A nationwide community-based lifestyle program could delay or prevent Type 2 diabetes cases and save $5.7 billion in 25 years. *Health Affairs*, 31(1), 50–60.

[48] Donaldson, S.I. and Grant-Vallone, E.J. (2002). Understanding self-report bias in organizational behavior research. *Journal of Business and Psychology*, 17(2), 245–60.

[49] Brener, N.D.; Billy, J.O.G.; and Grady, W.R. (2003). Assessment of factors affecting the validity of self-reported health-risk behavior among adolescents: Evidence from the scientific literature. *Journal of Adolescent Health*, 33(6), 436–57.

[50] Glasgow, R.E.; Vogt, T.M.; and Boles, S.M. (1999). Evaluating the public health impact of health promotion interventions: the RE-AIM framework. *American Journal of Public Health*, 89(9), 1322–27.

[51] Damschroder, L.J.; Aron, D.C.; Keith, R.E.; Kirsh, S.R.; Alexander, J.A.; and Lowery, J.C. (2009). Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. *Implementation Science*, 4:50.

[52] Damschroder, L.J. and Lowery, J.C. (2013). Evaluation of a large-scale weight management program using the consolidated framework for implementation research (CFIR). *Implementation Science*, 8:51.

[53] Glasgow, R.E. (2013). What does it mean to be pragmatic? Pragmatic methods, measures, and models to facilitate research translation. *Health Education & Behavior*, 40(3), 257–65.

[54] Glasgow, R.E. and Chambers, D. (2012). Developing robust, sustainable, implementation systems using rigorous, rapid and relevant science. *Clinical and Translational Science*, 5(1), 48–55.

[55] Greenhalgh, T.; Robert, G.; Macfarlane, F.; Bate, P.; and Kyriakidou, O. (2004). Diffusion of innovations in service organizations: systematic review and recommendations. *The Milbank Quarterly*, 82(4), 581–629.

[56] Osei, K.I; Rhinesmith, S.; Gaillard, T.; and Schuster, D. (2004). Beneficial metabolic effects of chronic glipizide in obese african americans with impaired glucose tolerance: implications for primary prevention of Type 2 diabetes. *Metabolism- Clinical and Experimental*, 53(4), 414–22.

[57] Mitri, J.; Dawson-Hughes, B.; Hu, F.B.; and Pittas, A.G. (2011). Effects of vitamin D and calcium supplementation on pancreatic beta cell function, insulin sensitivity, and glycemia in adults at high risk of diabetes: the Calcium and Vitamin D for Diabetes Mellitus (CaDDM) randomized controlled trial. *American Journal of Clinical Nutrition*, 94(2), 486–94.

[58] DeFronzo, R.A.; Tripathy, D.; Schwenke, D.; Banerji, M.; Bray, G.A.; Buchanan, T.A.; Clement, S.C.; Henry, R.R.; Hodis, H.N.; Kitabchi, A.E.; Mack, W.J.; Mudaliar, S.; Ratner, R.E.; Williams, K.; Stentz, F.B.; Musi, N.; Reaven, P.D.; and ACT NOW Study (2011). Pioglitazone For Diabetes Prevention in Impaired Glucose Tolerance. *New England Journal of Medicine*, 364(12):1104–15.

[59] McMurray J.; Holman, R.; Haffner, S.; Bethel, M.A.; Holzhauer, B.; Hua, T.A.; Belenkov, Y.; Boolell, M.; Buse, J.B.; Buckley, B.M.; Chacra, A.R.; Chiang, F.T.; Charbonnel, B.; Chow, C.C.; Davies, M.J.; Deedwania, P.; Diem, P.; Einhorn, D.; Fonseca, V.; Fulcher, G.R.; Gaciong, Z.; Gaztambide, S.; Giles, T.; Horton, E.; Ilkova, H.; Jenssen, T.; Kahn, S.E.; Krum, H.; Laakso, M.; Leiter, L.A.; Levitt, N.S.; Mareev, V.; Martinez, F.; Masson, C.; Mazzone, T.; Meaney, E.; Nesto, R.; Pan, C.; Prager, R.; Raptis, S.A.; Rutten, G.E.; Sandstroem, H.; Schaper, F.; Scheen, A.; Schmitz, O.; Sinay, I.; Soska, V.; Stender, S.; Tamás, G.; Tognoni, G.; Tuomilehto, J.; Villamil, A.S.; Vozár, J.; and Califf, R.M. (2010). Effect of valsartan on the incidence of diabetes and cardiovascular events. *New England Journal of Medicine*, 362(16), 1477–90.

[60] Holman, R.; Haffner, S.; McMurray, J.; Bethel, M.A.; Holzhauer, B.; Hua, T.A.; Belenkov, Y.; Boolell, M.; Buse, J.B.; Buckley, B.M.; Chacra, A.R.; Chiang, F.T.; Charbonnel, B.; Chow, C.C.; Davies, M.J.; Deedwania, P.; Diem, P.; Einhorn, D.; Fonseca, V.; Fulcher, G.R.; Gaciong, Z.; Gaztambide, S.; Giles, T.; Horton, E.; Ilkova, H.; Jenssen, T.; Kahn, S.E.; Krum, H.; Laakso, M.; Leiter, L.A.; Levitt, N.S.; Mareev, V.; Martinez, F.; Masson, C.; Mazzone, T.; Meaney, E.; Nesto, R.; Pan, C.; Prager, R.; Raptis, S.A.; Rutten, G.E.; Sandstroem, H.; Schaper, F.; Scheen, A.; Schmitz, O.; Sinay, I.; Soska, V.; Stender, S.; Tamás, G.; Tognoni, G.; Tuomilehto, J.; Villamil, A.S.; Vozár, J.; and Califf, R.M. (2010). Effect of nateglinide on the incidence of diabetes and cardiovascular events. *New England Journal of Medicine*, 362(16), 1463–76.

[61] Maki, K.C.; Reeves, M.S.; Carson, M.L.; Miller, M.P.; Turowski, M.; Rains, T.M.; Anderson, K.; Papanikolaou, Y.; and Wilder, D.M. (2009). Dose-response characteristics of high-viscosity hydroxypropylmethylcellulose in subjects at-risk for the development of Type 2 diabetes mellitus. *Diabetes Technology & Therapeutics*, 11(2), 119–25.

[62] Song, Y.; Cook, N.R.; Albert, C.M.; Van Denburgh, M.; and Manson, J.E. (2009). Effects of vitamins C and E and beta-carotene on the risk of Type 2 diabetes in women at high risk of cardiovascular disease: a randomized controlled trial. *American Journal of Clinical Nutrition*, 90(2), 429–37.

[63] Gerstein, H.C.; Yusuf, S.; Bosch, J.; Poque, J.; Sheridan, P.; Dinccaq, N.; Hanefeld, M.; Hoogwerf, B.; Laakso, M.; Mohan, V.; Shaw, J.; Zinman, B.; and Holman, R.R. (2006). Effect of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomised controlled trial. *Lancet*, 368(9541), 1096-1105.

[64] Saremi, A.; Schwenke, D.C.; Buchanan, T.A.; Hodis, H.N.; Mack, W.J.; Banerji, M.; Bray, G.A.; Clement, S.C.; Henry, R.R.; Kitabchi, A. E.; Mudalier, S.; Ratner, R.A.; Stentz, F.B.; Musi, N.; Tripathy, D.; DeFronzo, R.A.; and Reaven, P.D. (2002). Pioglitazone Slows Progression of Atherosclerosis in Prediabetes Independent of Changes in Cardiovascular Risk Factors. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 33(2), 393–99.

[65] Buchanan, T.; Xiang, A.; Peters, R.; Kjos, S.L.; Marroquin, A.; Goico, J.; Ochoa, C.; Tan, S.; Berkowitz, K.; Hodis, H.N.; and Azen, S.A. (2002). Preservation of pancreatic beta-cell function and prevention of Type 2 diabetes by pharmacological treatment of insulin resistance in high-risk hispanic women. *Diabetes*, 51(9), 2796–2803.

[66] Zappe, D.H.; Sowers, J.R.; Hsueh, W.A.; Haffner, S.M.; Deedwania, P.C.; Fonseca, V.A.; Keeling, L.; and Sica, D.A. (2008). Metabolic and antihypertensive effects of combined angiotensin receptor blocker and diuretic therapy in prediabetic hypertensive patients with the cardiometabolic syndrome. *Journal of Clinical Hypertension*, 10(12), 894-903.

[67] DREAM Trial Investigators, (2011). Incidence of Diabetes Following Ramipril or Rosiglitazone Withdrawal. *Diabetes Care*, 34(6):1265–69.

[68] DREAM Trial Investigators, Bosch, J.; Yusuf, S.; Gerstein, H.C.; Poque, J.; Sheridan, P.; Dagenais, G.; Diaz, R.; Avezum, A.; Lanas, F.; Probstfield, J.; Fodor, G.; and Holman, R.R. (2006). Effect of Ramipril on the Incidence of Diabetes. *New England Journal of Medicine*, 355(15), 1551–62.

[69] Hanley, A.J.; Zinman, B.; Sheridan, P.; Yusuf, S.; Gerstein, H.C.; Diabetes Reduction Assessment with Ramipril and Rosiglitazone Medication (DREAM) Investigators (2013). Effect of Rosiglitazone and Ramipril on beta-cell function in people with impaired glucose tolerance or impaired fasting glucose: the DREAM trial. *Diabetes Care*, 33(3), 608–13.

[70] DREAM On Investigators; Gerstein, H.C.; Mohan,V.; Avezum, A.; Bergenstal, R.M.; Chiasson, J.L.; Garrido, M.; MacKinnon, I.; Rao, P.V.; Zinman, B.; Jung, H.; Joldersma, L.; Bosch, J.; and Yusuf, S. (2011). Long-term effect of rosiglitazone and/or ramipril on the incidence of diabetes. *Diabetologia*, 54(3), 487–95.

[71] Ali, A.; Ma, Y.; Reynolds, J.; Wise, J.P. Sr.; Inzucchi, S.E.; and Katz, D.L. (2011). Chromium effects on glucose tolerance and insulin sensitivity in persons at-risk for diabetes mellitus. *Endocrine Practice*, 17(1), 16–25.

[72] Hutchins, A.M.; Brown, B.D.; Cunnane, S.C.; Domitrovich, S.G.; Adams, E.R.; and Bobowiec, C.E. (2013). Daily flaxseed consumption improves glycemic control in obese men and women with prediabetes: a randomized study. *Nutrition Research*, 33(5), 367–75.

[73] Durbin, R.J. (2004). Thiazolidinedione therapy in the prevention/delay of Type 2 diabetes in patients with impaired glucose tolerance and insulin resistance. *Diabetes, Obesity and Metabolism*, 6, 280–85.

[74] Xiang, A.; Peters, R.; Kjos, S.; Marroquin, A.; Goico, J.; Ochoa, C.; Kawakubo, M.; and Buchanan, T.A. (2006). Effect of pioglitazone on pancreatic beta-cell function and diabetes risk in Hispanic women with prior gestational diabetes. *Diabetes*, 55(2), 517–22.

NYS HEALTH FOUNDATION

Improving the state of
New York's health

VOICE: 212-664-7656
FAX: 646-421-6029
MAIL: 1385 Broadway,
23rd Floor
New York, NY 10018
WEB: www.nyshealth.org