Diabetes Prevention Programs: Effectiveness and Value

Evidence Report

June 6, 2016

Institute for Clinical and Economic Review

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DATE OF PUBLICATION: June 6, 2016

We would also like to thank Erin Lawler and Anne Loos for their contributions to this report.

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Table of Contents

Executive Summary ES1

1. Background 1

1.1 Introduction 1

2. The Topic in Context 5

2.1 National and California Landscape 5

2.2 Barriers and Opportunities 10

3. Public and Private Coverage for DPPs 16

3.1 Health Insurance Coverage for DPPs 16

3.2 Employer and Purchaser Coverage of DPPs 18

4. Comparative Clinical Effectiveness 19

4.1 Overview 19

4.2 Methods 20

4.3 Results 23

5. Other Benefits or Disadvantages 35

6. Comparative Value 36

6.1 Overview 36

6.2 Prior Published Evidence on Costs and Cost-Effectiveness of Diabetes Prevention Programs 36

6.3 Potential Budget Impact 42

6.4 Summary and Comment 47

References 49

Appendix A. Search Strategies and Results 58

Appendix B. Key Informant Interviews 63

Appendix C: Topic in Context Supplemental Information 65

Appendix D. Clinical Guidelines 67

Appendix E. Public and Representative Private Insurer Coverage Policies 72

Appendix F. Previous Systematic Reviews and Technology Assessments 75

Appendix G. Ongoing US Studies 79

Appendix H. Comparative Clinical Effectiveness Supplemental Information 83

Appendix I. Comparative Value Supplemental Information 98

List of Acronyms Used in this Report

ACA	Affordable Care Act
ACO	Accountable care organization
ADA	American Diabetes Association
AE	Adverse event
AHIP	America's Health Insurance Plans
AHRQ	Agency for Healthcare Research and Quality
AMA	American Medical Association
BI	Budget impact
BMI	Body mass index
CDC	Centers for Disease Control and Prevention
CDPH	California Department of Public Health
CEA	Cost-effectiveness analysis
CI	Confidence interval
CMMI	Center for Medicare and Medicaid Innovation
CMS	Centers for Medicare & Medicaid Services
CVD	Cardiovascular disease
DHCS	Department of Health Care Services
DM	Diabetes mellitus
DPP	Diabetes prevention program
DPPOS	Diabetes Prevention Program Outcomes Study
DPRP	Diabetes Prevention Recognition Program
EHR	Electronic health record
FPG	Fasting plasma glucose
GDM	Gestational diabetes mellitus
HbA1c	Hemoglobin A1c
HRQOL	Health-related quality of life
HHS	Health & Human Services
ICSI	Institute for Clinical Systems Improvement
IFG	Impaired fasting glucose
IGT	Impaired glucose tolerance
NDEP	National Diabetes Education Program
NDPP	National Diabetes Prevention Program
NHANES	National Health and Nutrition Examination Survey
NIH	National Institutes of Health
OGTT	Oral glucose tolerance test
P4P	Pay for performance
PICOTS	Population, Intervention, Comparators, Outcomes, Timing, and Settings
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PSA	Public service advertisement
QALY	Quality-adjusted life-year
RCT	Randomized controlled trial
ROI	Return on investment
RR	Risk ratio
RRR	Relative risk reduction
SF-36	36-Item Short-Form Health Survey
STAT	Screen, Test, Act Today
UCLA	University of California, Los Angeles
USPSTF	United States Preventive Services Task Force
VLM	Virtual Lifestyle Management
WHO	World Health Organization

Executive Summary

Background

According to the Centers for Disease Control and Prevention (CDC), approximately 86 million Americans age 20 and older (37%) have prediabetes (i.e., blood glucose levels higher[a] than normal but not high enough to be diagnosed with diabetes) and 90% of those with prediabetes do not know they have it.[1] Obesity is strongly associated with both diabetes and prediabetes. In California, a recent study found that 13 million adults in the state (approximately 46% of the state adult population) have prediabetes or undiagnosed diabetes.[2]

Interventions to prevent or delay the development of diabetes have the potential both to improve individual health and quality of life through disease avoidance (e.g., eye, kidney, and nerve damage; strokes; heart attacks) and to save the health care system substantial medical costs by reducing the incidence of diabetes and its associated complications. Without such interventions, it is estimated that 15-30% of individuals with prediabetes will develop type 2 diabetes mellitus (DM) within five years.[1] The Diabetes Prevention Program Trial (DPP Trial) demonstrated that the incidence of diabetes could be reduced using intensive diet and lifestyle counseling for individuals at high risk for developing diabetes.[3] Since publication of the trial results in 2002, many commercial programs have been developed to implement a less expensive, scalable version of the DPP Trial intervention.

Topic in Context

This report addresses several key issues related to diabetes prevention programs (DPPs) for patients, provider organizations, payers, and other policymakers and includes: 1) a landscape analysis of available DPP approaches and relevant policy considerations; 2) a comparative effectiveness evaluation of DPPs participating in the CDC Diabetes Prevention Recognition Program (DPRP); and 3) an assessment of the costs, cost-effectiveness, and potential budget impact of DPPs.

Studies have shown that 5-7% weight loss can prevent or delay the development of diabetes in individuals with elevated levels of blood sugar consistent with prediabetes, and many clinicians and researchers use weight loss as a surrogate measure for effective prevention of diabetes.[4,5] Participants in the DPP Trial lowered their body weight by approximately 7% after one year (decreasing to weight loss of about 4% after four years), which led to a 58% reduction in the risk of

[a] Hemoglobin A1c (HbA1c) between 5.7 and 6.5%, fasting plasma glucose (FPG) between 100-125, and oral glucose tolerance test (OGTT) between 140 and 199. As explained in section 6.3 of the full report, use of a FPG threshold for prediabetes of 110 mg/dL rather than 100 mg/dL decreases the number of people estimated to have prediabetes by about two-thirds.

progressing to diabetes over three years compared with standard lifestyle recommendations plus a placebo.[3,6] The lifestyle intervention was also more effective than drug therapy with metformin, an antidiabetic agent that has also been shown to promote weight loss.[3]

Because the initial DPP Trial involved individual counseling and the one-year program cost was about $1,400 per participant, subsequent research and practice have focused on replicating the results with programs that could be distributed more widely at a lower cost. Several published studies have examined the effectiveness of DPPs delivered in community settings, and more recently, in digital/online formats, both of which have reported significant weight loss.[7-9]

The CDC developed the National Diabetes Prevention Program (NDPP), a public/private partnership working to offer evidence-based, cost-effective interventions across the US with the goals of reducing the growing problem of prediabetes and type 2 DM as well as to build on the DPP Trial results with a focus on scalability. Organizations delivering a DPP with three key components – a CDC-approved curriculum[b] that promotes 5-7% weight loss and increased physical activity, a lifestyle coach, and a peer support group of program participants – can apply for CDC recognition through the Diabetes Prevention Recognition Program (DPRP). To achieve recognition, programs must submit data annually on participant weight and duration of physical activity in minutes, which are used by CDC to assess program impact on preventing or delaying the onset of type 2 DM.

Barriers and Opportunities

Scalability

To attain the NDPP goal of scalability, the format of DPPs has evolved from individual in-person counseling in the DPP Trial to in-person group sessions, and more recently to digital programs delivered via computer, tablet, or phone (see Table ES1). In addition to the considerable heterogeneity among in-person DPP delivery models, some of the currently available digital programs are delivered to virtual groups that are assigned a human coach while another delivers coaching messages through a fully-automated system based on algorithms.

[b] In addition to the DPP curriculum publicly available from the CDC, organizations offering DPPs can submit their curricula to the CDC for review. If approved, organizations can then seek recognition.

Table ES1. Key Features of DPPs

Format	Scalability	Cost*	Typical Group Size	Key Resources	Examples
In-person, individual coaching	Lowest	Highest	1	Humans, facilities	DPP Trial
In-person, group coaching	Medium	Medium	8-15	Humans, facilities	Weight Watchers for Prediabetes Y
Digital, human coaching (virtual interaction)	High	Medium	1-24	Humans, technology	Virtual Lifestyle Management (VLM™, Canary Health, Inc.) Omada® (Omada Health, Inc.)
Digital, fully-automated coaching (based on algorithms)	Highest	Lowest	1+†	Technology	Alive-PD™ (Turnaround Health)

*Average costs and cost-offsets by program type are available in Appendix Table I2

† No group counseling, but participants can join optional virtual teams. The team size was 10 in the published trial.[10]

Coverage of DPPs by Health Plans and Purchasers

One of the major goals of the CDC and its NDPP partners is to increase access to DPPs by promoting health insurance coverage in both public and private settings. Medicare does not currently cover DPPs, and only one state Medicaid program (Montana) does. There is wide variation among private health plans in their coverage of DPPs, but at least 30 private plans currently cover DPPs for some of their lines of business.[11] Some private and public purchasers are incorporating DPPs into their health plans or wellness programs, or offering them as standalone benefits, but it is challenging to assess how extensive these practices are. Increased payer coverage of DPPs may be forthcoming based on 1) a proposal by Medicare to expand coverage of DPPs to all Medicare beneficiaries (using a 110 mg/dL FPG threshold to define prediabetes), 2) a CDC initiative to partner with two to three states to expand Medicaid coverage for DPPs, and 3) two US Preventive Services Task Force (USPSTF) recommendations related to DPPs with a grade of B (i.e., services that must be covered by private plans without patient cost sharing to be compliant with the Affordable Care Act [ACA]).

Additional DPP Implementation Considerations

Despite several national and state efforts to increase awareness of prediabetes and the use of DPPs, the expansion of DPPs is challenged by several factors that are discussed in greater detail in the full report and include:

1) A steep learning curve in terms of data collection and analysis requirements for DPPs seeking CDC recognition, as well as limitations on data sharing among providers, patients, DPP vendors, and plans;

2) A need for better, culturally-appropriate methods to reach underserved communities with populations at high risk of diabetes based on race/ethnicity, literacy, and income; and a need for innovative approaches to retain such participants in the year-long program;
3) A need for greater provider awareness of prediabetes and increased referral by providers of patients to DPPs, as well as more linkages between clinicians and DPPs;
4) The extensive efforts required to screen, identify, train, and retain skilled lifestyle program coaches who can connect to the community targeted by the DPP; and
5) A lack of awareness of prediabetes by many individuals who are at risk of developing diabetes and who must be willing to make a commitment to a year-long program of behavior change.

Comparative Clinical Effectiveness of DPPs

Since publication of the initial results of the DPP Trial, there have been more than 50 studies translating the lifestyle intervention to real world settings. Several systematic reviews found that these programs decrease body weight, decrease fasting plasma glucose, improve blood pressure and cholesterol levels, and prevent or delay the onset of type 2 DM.[12-17] The CDC and the Community Preventive Services Task Force recently commissioned a review of programs that promote dietary changes and physical activity to prevent or delay the onset of diabetes.[15] This high-quality systematic review and meta-analysis summarized 53 studies describing 66 diet and activity programs published through February 2015. They found that diet and exercise programs reduced diabetes incidence by 41% (95% confidence interval [CI]: 34% to 48%) compared with usual care. The programs also reduced body weight by 2.2% (95% CI: 1.4% to 2.9%) and FPG by 2.2 mg/dL (95% CI: 0.9 to 3.6 mg/dL). The more intensive programs, like the DPP Trial intervention, were more effective.[15]

This evidence review summarizes the published literature for lifestyle interventions in the US that have full or pending recognition through the DPRP. The literature search identified 10 studies that met our inclusion criteria (five randomized controlled trials [RCTs] and five case-series using a pre-post design).[7-9,18-32] The studies are grouped by degree of human contact ranging from in-person individual counseling performed on a weekly, one-on-one basis with a trained health care professional (DPP Trial) to digital with fully-automated counseling (Alive-PD). Studies using in-person group counseling were the most common, and included four studies in the Y system (formerly referred to as the YMCA), one supported by the Montana Department of Public Health and Human Services, one at Weight Watchers, and one at Wake Forest University.

Quality of the Studies

The original DPP Trial was a large, good-quality trial with long enough follow-up (15 years) to assess the impact of the intervention on diabetes incidence.[3] Three of the implementation trials were randomized trials of good quality (RAPID, Alive-PD, HELP-PD), though the Alive-PD trial has only

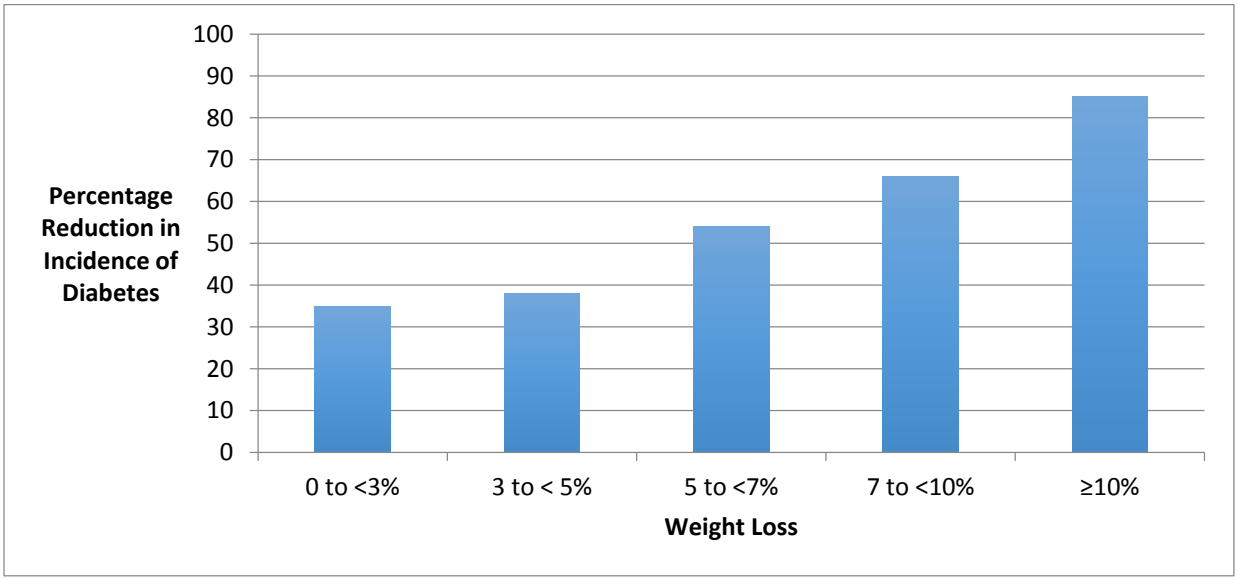
published six-month outcomes.[19,22,28] The lifestyle changes necessary to prevent or delay the development of diabetes need to be sustained for decades, so outcomes beyond the initial intensive intervention period are preferred. The two other randomized trials (DEPLOY, Weight Watchers) were judged to be of fair quality because of baseline differences between the groups and significant loss to follow-up.[7,8]

Among the pre-post case series, one (Omada, formerly called Prevent) was judged to be of fair quality; although case series provide weaker evidence than RCTs, the study included a careful description of the participants, and featured adequate length and completeness of follow-up, objective outcome measures, and appropriate analysis methods.[9,31] The other four were judged to be of poor quality because of the small number of participants with prediabetes, the use of self-reported outcomes, and significant loss to follow-up.[24,25,30,32]

Weight Loss

In the DPP Trial, weight loss was the primary predictor of the reduction in diabetes incidence,[4,5] ranging from a 35% reduction in diabetes incidence among participants with 0-3% weight loss to an 85% reduction in diabetes incidence for participants with >10% weight loss (see Figure ES1).[5] Participants in the lifestyle intervention also had reductions in blood pressure and improvements in cholesterol measurements that may translate into additional benefits in the long term prevention of cardiovascular disease.[33]

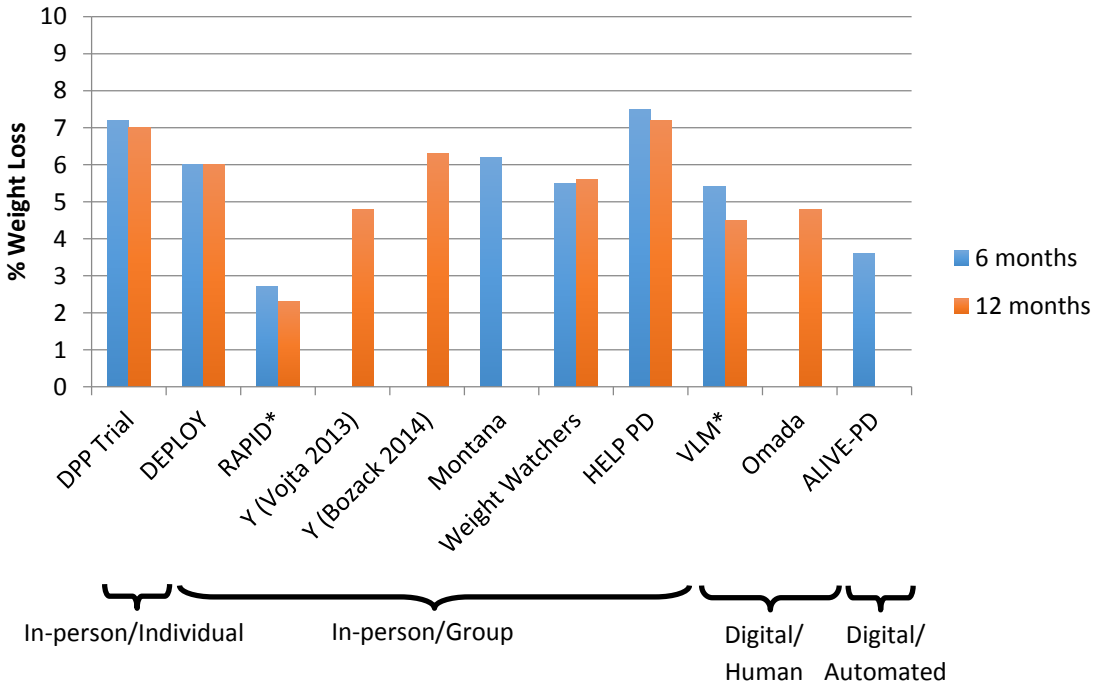
Figure ES1. Correlation of Percentage Weight Loss with Reduction in the Risk of Diabetes for Patients in the Intensive Lifestyle Intervention Arm of the DPP Trial



With one exception, weight loss at one year was consistently in the 5-7% range across the studies of in-person counseling (individual or group), with the DPP Trial and the HELP-PD studies at the upper

end of the range (see Figure ES2). The weight loss results for the two programs using a digital with a human coach design were somewhat lower (4-5%). The VLM study did not report percentage weight loss overall but was estimated to be about 4.5% (from data and figures in the published results). In the Omada trial, the average weight loss at 12 months was 4.8%. The study results of a digital DPP with fully-automated counseling design (Alive-PD) showed a 3.6% weight loss at six months, which is only about half the weight loss reported in the DPP Trial at six months; this may reflect the lack of a mandatory weight loss goal-setting component in their program.

Figure ES2. Percentage Weight Loss at Six and 12 Months for Translational DPPs compared with the DPP Trial



* Estimated from results in publication

Glycemic Control

Half of the available studies reported some measure of change in glycemic control during follow-up. In the original DPP Trial, there was only a small reduction in HbA1c (-0.1%) and in FPG (-5 mg/dL) at one year in the lifestyle group. Among the in-person group counseling programs, the DEPLOY study had a similar reduction in HbA1c at six and 12 months (-0.1%); the Weight Watchers study reported a greater reduction in HbA1c at 12 months (-0.26%) but a smaller reduction in FPG (-2.8 mg/dL); and the HELP-PD study only reported changes in FPG (-4.5 mg/dL) at 12 months.

Among the digital with human coach programs, only the Omada study reported results, but the change in HbA1c (-0.4% at 12 months) was the largest reported of any program including the

original DPP Trial. Interestingly, even though the Alive-PD program (digital with fully automated counseling) reported a relatively low percentage weight loss at 6 months (3.6%), the reductions in HbA1c (-0.3%) and FPG (-7.4 mg/dL) were greater than those observed in most other studies. This may reflect the greater focus on diabetes prevention and control as the primary goal of their dietary intervention rather than weight loss.

Diabetes Incidence

Most of the studies of DPP implementations were of too short a duration to assess incident diabetes. The HELP-PD study (in-person group counseling) reported that the diabetes incidence at two years was non-significantly lower in the lifestyle group than in the usual care group (3.0% versus 8.7%, p=0.10). In the DPP Trial, the cumulative incidence of diabetes was approximately 4% in the lifestyle intervention group and 13% in the usual care group.[34]

Other Cardiovascular Risk Factors

The DPP Trial reported reductions in blood pressure and improvements in total and HDL-cholesterol levels (Appendix Table H10). These improvements, though small, could contribute to an overall reduction in cardiovascular disease independent of the reduction in diabetes incidence. Among the in-person group counseling programs, the DEPLOY study reported greater improvements in cholesterol than those reported in the DPP Trial. The Weight Watchers study reported similar reductions in blood pressure compared with the DPP Trial and a greater increase in HDL-cholesterol, but also a small increase in total cholesterol. Finally, the VLM study (digital with a human coach) reported twice the reduction in systolic blood pressure compared with the DPP Trial, but a slight increase in diastolic blood pressure. None of the other digital programs reported changes in blood pressure or cholesterol levels.

Harms

There was no excess rate of adverse events or serious adverse events in patients randomized to the lifestyle intervention in any of the randomized trials. The DPP Trial and other RCTs specifically assessed myalgias, arthralgias, fractures and other musculoskeletal complaints potentially arising from lifestyle interventions and no significant increases were observed for participants in the lifestyle group.

Controversies and Uncertainties

The degree of weight loss observed in translational DPP studies is somewhat less than that attained by participants in the DPP Trial, and the long-term sustainability of this weight loss has not yet been demonstrated. The primary uncertainty is whether the one-year weight loss observed in these studies will lead to a significant reduction in the incidence of diabetes in these patients and whether

the reduction (or delay) in the diagnosis of diabetes will result in meaningful reductions in the complications of diabetes for patients with prediabetes. At 15 years of follow-up, there was no reduction in either microvascular disease or cardiovascular disease in the DPP Trial.

Additional controversy arises from the definition of prediabetes. In clinical practice, patients with prediabetes are usually diagnosed by measurement of FPG. In the US, the American Diabetes Association (ADA) defines an FPG of 100-125 mg/dL as prediabetes, but the World Health Organization (WHO) definition requires an FPG of 110-125. Patients with an FPG of 100-109 mg/dL are at lower risk for progression to diabetes and may receive less benefit from intensive lifestyle interventions. Furthermore, critics of the term "prediabetes" have raised concerns about the adverse effects of labeling patients given that those with prediabetes are at high risk for diabetes but do not yet have a diagnosed disease.[35]

Comparative Clinical Effectiveness: *Summary and Comment*

We judge the evidence for the CDC-recognized intensive lifestyle programs using an in-person group coaching design to provide an incremental or better (B+) net health benefit when compared to usual care for patients with prediabetes. There is no question that these programs yield modest weight loss in the short term compared with usual care. However, there is moderate certainty of a net benefit because of the uncertainties about the long-term durability of weight loss and the long-term improvements in health from the modest weight reductions demonstrated after one to two years of follow-up in the published studies.

We also judge the evidence for the CDC-recognized intensive lifestyle programs using a digital with human coach design to provide an incremental or better (B+) net health benefit when compared to usual care for patients with prediabetes. There is more uncertainty in this judgment than that for in-person group coaching because the number of studies is smaller (two) and because there are no good-quality trials. However, there is clearly modest weight loss with these programs through two years compared with usual care that is similar in magnitude to that observed with the in-person group coaching programs. There is uncertainty about the long-term durability of weight loss and subsequent long-term health improvements similar to that described for the in-person group counseling programs.

We judge the evidence for the CDC-recognized intensive lifestyle programs using a digital with fully-automated coaching design to provide comparable or better (C+) net health benefit when compared to usual care for patients with prediabetes. There is greater uncertainty of a net benefit for the fully-automated approach because there is only one trial, it only reported six-month outcomes, and the weight loss was qualitatively less than that observed in the original DPP Trial and the majority of the other translational programs. However, it was a high-quality randomized trial that showed statistically significant improvements in body weight and glycemic control compared with usual care.

We judge that there is Insufficient Evidence (I) to distinguish the efficacy of any one approach (in-person group counseling; digital with a human coach; digital with fully-automated counseling) from the others. There are no randomized trials or cohort studies that directly compare any two of the approaches, and the evidence base is currently too sparse to perform a network meta-analysis.

Other Benefits or Disadvantages

The primary additional benefit would be the public health benefits that may result from decreasing weight and increasing physical activity of a large segment of the population. In addition to the likely reductions in diabetes and cardiovascular disease described above, there may be reductions in some of the many complications of obesity, including arthritis, sleep apnea, and esophageal reflux disease. Further, exercise has been proposed to improve mental health and quality of life, and to decrease long-term disability.

Comparative Value of DPPs

We reviewed the published literature for analyses that have examined the economic impact of DPPs in the US with full or pending recognition from the CDC DPRP. We also explored the potential health system budget impact of DPPs over a shorter-term time horizon, utilizing published or otherwise publicly-available information on program planning, implementation, and ongoing treatment costs; any cost offsets; and the potential population eligible for such services.

Cost-Effectiveness Analyses

Li et al. conducted a systematic review of economic analyses of "diet and physical activity promotion programs with at least two sessions over at least three months delivered to persons at increased risk for type 2 DM."[36] Overall, the median cost per quality-adjusted life-year (QALY) gained for the eight US-based analyses was $9,824, with an interquartile range of $1,930 to $41,982 per QALY gained. However, the authors noted that few studies included information on recruitment costs, or on the cost to implement and scale up these programs.

In-person, Individual Coaching

DPP Trial

The DPP Research Group has conducted multiple analyses based on the DPP Trial. From a health system perspective, the cost per QALY for the intensive lifestyle intervention decreased as the time horizon increased, from $32,000/QALY at three years,[37] to $13,000/QALY at 10 years,[38,39] and $1,100/QALY using a lifetime time horizon.[40]

In contrast to the above analyses, Eddy et al. conducted a cost-effectiveness analysis (CEA) of the DPP lifestyle intervention using the Archimedes model, which simulates detailed anatomic and physiologic components of several diseases.[41] Over a 30-year time horizon, they found that the DPP Trial intervention would cost approximately $143,000 per QALY gained from a health system perspective. The primary differences from the DPP Research Group models were that Eddy et al. assumed that the clinical benefits of the DPP would diminish over time, that there would be a lower rate of glycemic progression (i.e., slower progression from prediabetes to diabetes, and from diabetes diagnosis to complications). Their health system perspective analysis also assumed a rate of participant turnover, which would lead to higher estimated cost-effectiveness ratios than in the DPP Trial evaluations.

In-person, Group Coaching

DPP Trial

As part of the DPP Research Group's within-trial CEA of the DPP Trial,[37] they evaluated the DPP as a group intervention rather than an individual one, assuming lower costs but equal effectiveness. The group DPP was estimated to cost $4,500 per diabetes case prevented and $9,000 per QALY gained from a health system perspective at three years. In their evaluation of the lifetime cost-effectiveness of the DPP Trial intervention, Herman and colleagues[40] also estimated the impact if costs could be reduced by implementing the lifestyle intervention in groups of 10 participants rather than one-to-one coaching, assuming equal clinical effectiveness. They estimated that the program would be cost-saving over a lifetime, even if effectiveness were reduced by 50%. Finally, Eddy et al.[41] evaluated a scenario where the DPP was provided as a group intervention costing $217 per year, and they estimated a cost per QALY of $27,000 from a health system perspective.

Y DPP

RTI International[42] conducted an evaluation of the Y DPP using claims analysis based on the Center for Medicare & Medicaid Services' (CMS) Chronic Conditions Data Warehouse through 2014. The authors compared 1,679 participants to propensity score-matched Medicare beneficiaries diagnosed with prediabetes, and found statistically significant reductions in spending for the treatment group in the first five calendar quarters of the program with no significant differences in subsequent quarters. The overall weighted average quarterly spending differential was calculated as $455 per member per quarter.

The CMS Office of the Actuary developed a model to project net costs per beneficiary over a lifetime horizon, as detailed in a Certification of Medicare DPP memorandum.[43] The model estimated net costs or savings per year from lowering the probability of progression to diabetes and thus delaying diabetes-related costs, and it assumed that the Medicare DPP expansion would be somewhat less effective than the DPP Trial because it was less intensive. Their analysis estimated

that near-term savings would be offset by higher Medicare spending due to lower mortality, making it unclear whether the DPP expansion would break even over a lifetime horizon. If the mortality reduction is ignored (as required in the certification process), the model suggested that the DPP would reduce Medicare expenditures.

Digital, Human Coaching

Omada (Omada Health)

A recent analysis examined the return on investment (ROI) of the Omada digital DPP.[44] A Markov-based model with a 10-year time horizon was used to compare Omada DPP participants with propensity score-matched community controls with prediabetes. Their simulation found a break-even point at three years, with a positive ROI of $1,565 at five years. One limitation of this study is that it relied on only 26 weeks of weight loss data from Omada participants, which required assumptions about longer-term weight loss.

VLM (Canary Health)

Smith et al. assessed the cost-effectiveness of the VLM DPP using a Markov model with a 10-year time horizon.[45] Costs and changes in weight came from a pre-post study of the VLM intervention, which estimated an incremental cost of $458 and incremental gain of approximately 0.06 QALYs compared to usual care in a hypothetical cohort without diabetes. They estimated that the intervention would cost approximately $7,800 per QALY gained from a health system perspective. Using a $100,000 per QALY threshold, the intervention was found to be cost-effective in over 95% of model iterations in a probabilistic sensitivity analysis. However, it should be noted that these results are based on data from one study using a one-year before/after design in only 50 patients, 14 of whom already had diabetes.

Digital, Fully-automated Coaching

We were unable to locate any publicly-available CEAs of digital DPPs with fully-automated coaching.

Potential Budget Impact

We also estimated the potential budget impact of different types of DPPs among candidate populations for such treatment in the US. Our estimates are based on those found in the published and grey literature for in-person and digital human coached programs; no published data were available for digital fully automated DPPs. We combined estimates of the mean cost per participant with estimates of the prediabetes population potentially eligible for DPPs, as well as different assumed levels of uptake of such programs.

Potential budget impact was defined as the total incremental cost of DPPs for the enrolled population, calculated as the incremental health care costs of DPPs minus any health care costs that were offset in enrolled participants. All costs were undiscounted and estimated over one- and five-year time horizons. The five-year timeframe was of primary interest, given the potential for cost offsets to accrue over time. The candidate population size is approximately 93.7 million individuals in the US using FPG of 100-125 mg/dL as the definition of prediabetes, and approximately 31.2 million individuals using 110-125 mg/dL.[46] We assumed that 2% of the eligible population would enroll in each year.

Over the entire five-year time horizon, 10% uptake for individuals meeting the ADA definition (i.e., including individuals with FPG of 100-109 mg/dL) would lead to approximately 9.4 million individuals enrolled in a DPP for one or more years. Across this timeframe, the weighted potential budget impact (i.e., adjusted for differing periods of utilization and associated cost-offsets) for in-person individual programs is approximately $2,800 per participant, leading to an average annual potential budget impact of approximately $5.2 billion. Estimated savings from enrollment in in-person group programs, which are cost-saving after one year, continue to accrue over five years, resulting in estimated potential savings of $2.2 billion per year. Digital programs with human coaches increase costs by $220 million over a one-year time horizon, but generate potential cost savings of approximately $1.2 billion over a five-year time horizon. Preliminary analyses suggest that digital automated DPPs appear to be cost-saving at one and five years, although no published data are available (see section 6.3 for analyses based on unpublished data). Results of the potential budget impact analysis using the broader definition of prediabetes are presented in Table ES2, while results using the narrower definition can be found in section 6.3 of the full report.

Table ES2. Total Potential Budget Impact (BI) of DPPs Based on 10% Uptake at One and Five Years Using FPG of 100-125 mg/dL (n=9,366,203)*

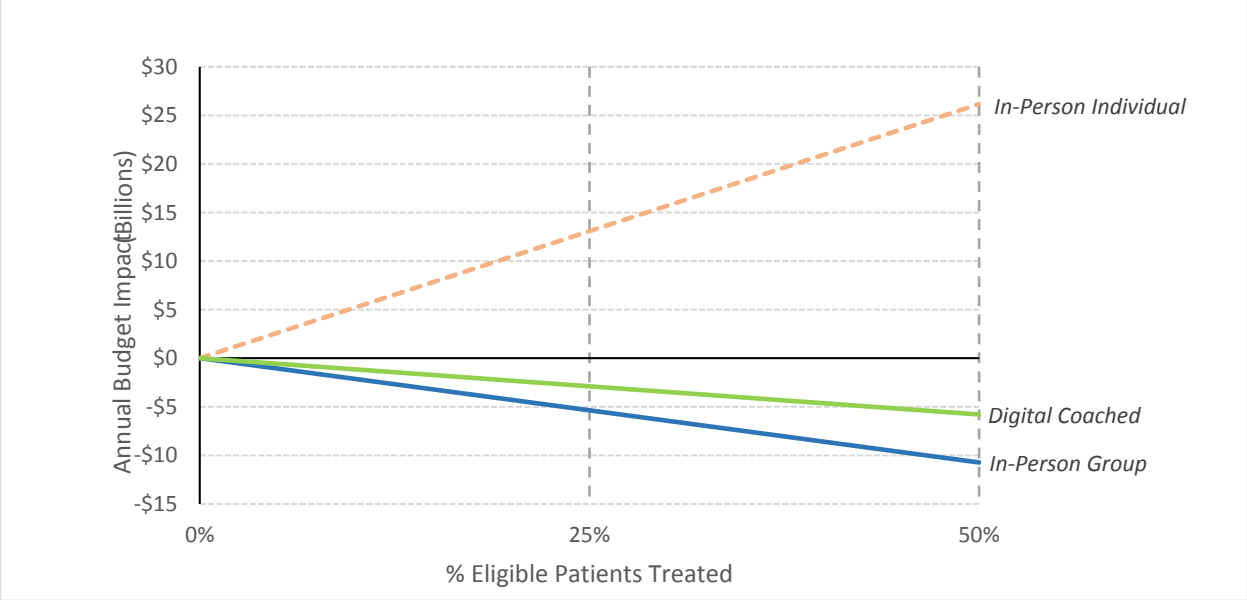
DPP Type	Analytic Horizon = 1 Year			Analytic Horizon = 5 Years		
	Number Enrolled (millions)	Annual BI per Participant ($)†	Total BI (billions)	Number Enrolled (millions)	Weighted BI per Participant ($)*	Average BI per year (billions)
In-person, Individual Coaching	1.87	$1,902	$3.56	9.37	$2,793	$5.23
In-person, Group Coaching	1.87	-$455	-$0.85	9.37	-$1,146	-$2.15
Digital, Human Coaching	1.87	$117	$0.22	9.37	-$618	-$1.16

* Preliminary estimates for digital fully-automated programs are reported in separately (see section 6.3), as no published or publicly-presented data were available.

†Weighted budget impact calculated by subtracting cost offsets from DPP costs for one-year horizon. For five-year horizon, DPP costs and cost offsets apportioned assuming 20% of patients in uptake target initiate therapy each year

Figure ES3 demonstrates the variation in potential budget impact levels associated with different uptake assumptions when using the 100-125 mg/dL definition. Varying rates of uptake using the 110-125 mg/dL definition would result in a similar pattern (see Appendix Figure I1), but with smaller annualized costs for individual in-person programs and smaller annualized savings for in-person group and digital human-coached programs.

Figure ES3. Potential Budget Impact Graph for DPPs Provided to Varying Proportions of the US Population with FPG 100-125 mg/dL



Note: Colored lines represent the annualized potential budget impact of different uptake patterns (percent of eligible population enrolled) for each type of DPP.

Comparative Value: *Summary and Comment*

With one exception,[41] the consensus in the literature is that the cost-effectiveness of an in-person DPP at the individual level is well below commonly-accepted thresholds. Providing the program in a group setting appears to be cost-saving over time, with little or no apparent loss in effectiveness relative to individual coaching. Delivering the DPP via digital adaptations with human coaches also appears to be cost-effective or cost-saving, although these findings are based on fewer studies with only short-term effectiveness data available to date. We were unable to find any published evaluations of the cost-effectiveness of digital fully-automated programs for delivery of a DPP. While online adaptations are less costly than in-person DPPs, longer-term studies are needed to determine whether online versions of the DPP will provide comparable effectiveness over time. In addition, it should be noted that analyses sometimes differed in how they defined program participation (e.g., enrollment vs. completion) and in how that relates to program costs; more standardized definitions would make comparisons across program types more comparable.

Our estimates of the short-term potential budget impact of these programs were more variable and depended on using averages across relatively sparse data, especially for the digital programs. Using averages of the available data within program type and the assumptions in our analysis, in-person individual DPPs had positive annual budget impacts over five years, while in-person group and digital coached programs appear to be cost-saving in the short-term. We estimated that a digital fully-automated program was relatively budget neutral or slightly cost-saving, but available data was most limited for this category of programs.

A limitation of this analysis is that there was wide variation in the 1) sources of data and 2) the number and types of analyses performed, which may influence the comparability of results across program types. It should also be noted that this analysis was based on annual program costs that did not include development or start-up costs for these programs, which may be substantial. One area where further research would be helpful is the tabulation of such costs, as well as detailed cost and cost offset data from implementations of DPPs in different settings.

Furthermore, our estimates of levels of DPP uptake in the health care system by five years were based on arbitrary assumptions, so actual uptake may not reach these levels this quickly. In addition, the costs used in our analysis came from a specific set of programs, and so may not be representative of the costs for such programs in other settings in the US.

Finally, further data on the long-term effectiveness of these programs in maintaining weight loss and diabetes risk reductions would confirm whether these programs will actually be cost-effective or cost-saving over time. This would be especially useful for the newer, digital adaptations of the DPP. There is also a need for data on the costs and effectiveness of these programs in different populations and settings, evaluation of the efficacy of maintenance modules of the digital programs, and a need to measure the efficiency of extending these programs to lower-risk groups.

1. Background

1.1 Introduction

The Centers for Disease Control and Prevention (CDC) estimates that 29.1 million Americans, or 9.3% of the population, have diabetes and 1.7 million adults are newly diagnosed with diabetes each year.[47] According to the CDC National Center for Chronic Disease Prevention and Health Promotion, approximately 86 million Americans age 20 and older (37%) have prediabetes (i.e., blood glucose levels higher[c] than normal but not high enough to be diagnosed with diabetes) and 90% of those with prediabetes do not know they have it.[1] Obesity is strongly associated with both prediabetes and diabetes. Nationally representative data for the United States (US) show that the prevalence of diabetes increases from 8% of individuals with normal weight to 15% of those who are overweight, and 23% to 43% of those who are obese.[48] Similarly, the prevalence of prediabetes increases from 28% of individuals with normal weight to 36% of those who are overweight, and 40% of those who are obese.[49] Interventions to prevent or delay the development of diabetes have the potential both to improve individual health and quality of life through disease avoidance (e.g., eye, kidney, and nerve damage; strokes; heart attacks) and to save the health care system substantial medical costs by reducing the incidence of diabetes and its associated complications. Without such interventions, it is estimated that 15-30% of individuals with prediabetes will develop diabetes within five years.[1] Clinical guidelines developed by professional societies and the US Preventive Services Task Force (USPSTF) recommend behavioral counseling for a healthy lifestyle, a core component of such interventions, for those with prediabetes (see Appendix D).

The costs of diabetes were estimated to total $245 billion in 2012 ($176 billion for direct medical costs and $69 billion in indirect cost due to disability, lost productivity, and premature death).[47] The additional medical costs associated with elevated blood glucose levels for people with prediabetes were $44 billion in 2012.[50]

In California, a recent study by the University of California, Los Angeles (UCLA) found that 13 million adults (age 18 or above) in the state (approximately 46% of the state adult population) have prediabetes or undiagnosed diabetes and about 2.5 million have diabetes (9%).[2] Of the 46% with prediabetes or undiagnosed diabetes, the numbers in the two groups are not estimated separately, although it is noted that nationally about 3.9% of adults have undiagnosed diabetes.[2,51, d] This study also estimated that the economic burden for adult Californians with diabetes totals more than $27

[c] Hemoglobin A1c (HbA1c) between 5.7 and 6.5%, fasting plasma glucose (FPG) between 100-125, and oral glucose tolerance test (OGTT) between 140 and 199.

[d] Methodological differences are believed to account for most of the difference between the national and California prevalence rates.

billion ($19 billion for direct medical expenses and $8 billion for indirect costs associated with diabetes), with another $8.1 billion in direct medical care costs estimated for individuals with prediabetes ($5.3 billion) and undiagnosed diabetes ($2.8 billion).

The Diabetes Prevention Program Trial (DPP Trial) demonstrated that the incidence of diabetes could be reduced using intensive diet and lifestyle counseling for individuals at high risk for developing diabetes.[3] In addition, the lifestyle intervention improved the quality of life for participants.[52] Since publication of the trial results in 2002, many commercial programs have been developed to implement a scalable version of the DPP Trial intervention using fewer resources.

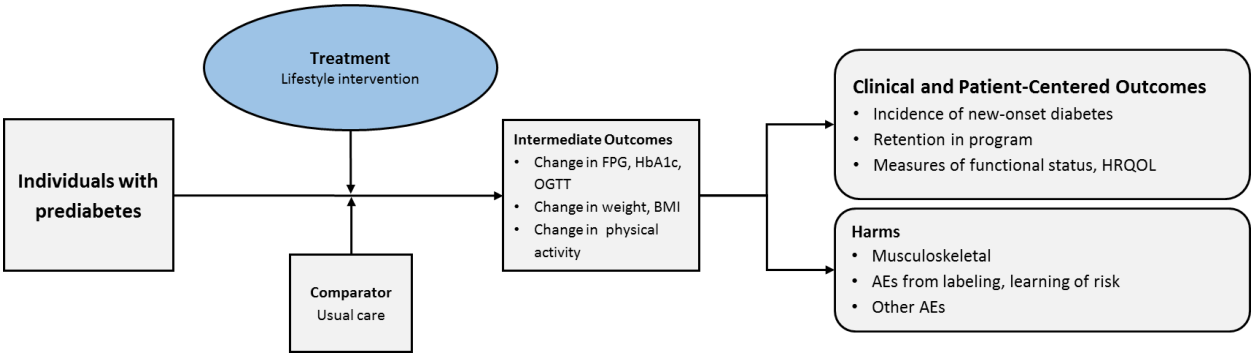
Scope of the Assessment

The scope for this assessment is described below using the PICOTS (Population, Intervention, Comparators, Outcomes, Timing, and Settings) framework. Evidence was culled from randomized controlled trials (RCTs) and comparative cohort studies as well as high-quality systematic reviews where available. We also included case series that met certain quality criteria (e.g., sample retention, consecutive patients, clearly-defined entry criteria, sample size thresholds, length of follow-up thresholds), and described data from these studies separately. We supplemented our review of published studies with data from regulatory documents, information submitted by vendors, and other grey literature when the evidence met ICER standards (for more information, see http://icer-review.org/methodology/icers-methods/icer-value-assessment-framework/grey-literature-policy/).

Analytic Framework

The analytic framework for this assessment is depicted in Figure 1.

Figure 1. Analytic Framework



AE: adverse event, BMI: body mass index, FPG: fasting plasma glucose, HbA1c: hemoglobin A1c, HRQOL: health-related quality of life, OGTT: oral glucose tolerance test

Populations

The population of focus for the review was adults ages 18 and older with prediabetes. We attempted to examine the impact of different definitions of prediabetes on the outcomes of interest, but there was insufficient data to perform this analysis.

Interventions

The interventions of interest included lifestyle interventions to prevent or delay the development of type 2 diabetes mellitus (DM) that have full or pending recognition from the CDC Diabetes Prevention Recognition Program (DPRP), including programs incorporating smartphone and web-assisted delivery methods. Medical and surgical therapies were not considered.

Comparators

Wherever possible, we sought head-to-head studies of these interventions. In the absence of head-to-head studies, the primary comparator was usual care, which in clinical practice is a discussion between a provider and patient and/or provision of educational materials regarding the risk for diabetes and recommendations to lose weight and increase exercise.

Outcomes

This review examined clinical and health care utilization outcomes related to lifestyle interventions to prevent or delay the development of diabetes that have full or pending recognition from the CDC DPRP. Listed below are the outcomes of interest:

- Incidence of type 2 DM
- Hemoglobin A1c as a measure of glycemic control
- Fasting plasma glucose as a measure of glycemic control
- Glucose tolerance test at 2 hours as a measure of glycemic control
- Change in body weight and body mass index (BMI)
- Change in physical activity
- Retention in program
- Measures of functional status, and/or health-related quality of life
- Harms (musculoskeletal, adverse events (AEs) from labeling, learning of risk, other AEs)
- Costs and cost-effectiveness of diabetes prevention programs

Timing

Evidence on intervention effectiveness and harms was derived from studies of at least one year's duration in order to capture the maintenance phase of the intervention, as many people quickly regain weight that has been lost following dieting. Information from studies greater than one year

in duration also allowed for a more complete examination of important program effects on long-term clinical outcomes.

Settings

All relevant settings were considered, including telephonic, online, clinic, employer-based, community-based, and hybrid settings in the US.

In addition to conducting a review of available literature and analyzing the comparative value of diabetes prevention programs (DPPs), ICER conducted 34 semi-structured telephone interviews with key stakeholders involved in the design and delivery of interventions seeking to prevent or delay the onset of diabetes. We sought perspectives from federal and state government, public and private payers, public and private purchasers, patient advocacy organizations, and vendors. A full methodology and a list of organizations represented in interviews are available in Appendices A and B.

This report addresses several key issues related to DPPs for patients, provider organizations, payers, and other policymakers and includes: 1) a landscape analysis of available DPP approaches; 2) a comparative effectiveness evaluation of DPPs; and 3) an assessment of the costs, cost-effectiveness, and potential budget impact of DPPs.

2. The Topic in Context

2.1 National and California Landscape

As noted in section 1, prediabetes refers to blood glucose levels higher than normal but not high enough to be diagnosed with diabetes. There is some controversy about how prediabetes is defined clinically, but in practice, diagnosis involves the establishment of impaired fasting glucose (IFG) through measurement of FPG, or impaired glucose tolerance (IGT), through the administration of a two-hour oral glucose tolerance test (OGTT) (see Table 1). In the US, the American Diabetes Association (ADA) defines a FPG of 100-125 mg/dL as prediabetes, and this is the definition that the CDC uses in its estimates.[53,54] In contrast, the World Health Organization (WHO) definition requires a FPG of 110-125.[55] Patients with a FPG of 100-109 mg/dL are at lower risk for progression to diabetes and may receive less benefit from intensive lifestyle interventions. As explained in section 6.3, use of a FPG threshold for prediabetes of 110 mg/dL rather than 100 mg/dL decreases the number of people estimated to have prediabetes by about two-thirds. HbA1c may also be used to diagnose prediabetes, though there is some disagreement regarding the appropriateness of its use. The ADA defines HbA1c values from 5.7%-6.4% as prediabetes, while the WHO does not recommend the use of HbA1c to diagnose prediabetes.[53,54]

Table 1. ADA and WHO Definitions of Prediabetes

Organization	HbA1c	FPG	OGTT
ADA	5.7 – 6.4%	100 – 125 mg/dL	140 – 199 mg/dL
WHO	N/A	110 – 125 mg/dL	140 – 199 mg/dL

HbA1c: hemoglobin A1c, FPG: fasting plasma glucose, OGTT: oral glucose tolerance test

Studies have shown that 5-7% weight loss can prevent or delay the development of diabetes in people with elevated levels of blood sugar consistent with prediabetes, and many clinicians and researchers use weight loss as a surrogate measure for effective prevention of diabetes.[4,5] The Diabetes Prevention Program Trial (DPP Trial) demonstrated that the incidence of diabetes could be reduced using intensive diet and lifestyle counseling for individuals with prediabetes who were at high risk for developing diabetes.[3] This study randomized over 3,200 individuals with elevated glucose levels to one of three interventions: metformin plus standard lifestyle recommendations, placebo plus standard lifestyle recommendations, and an intensive lifestyle modification program. Results showed that a structured intensive behavioral counseling intervention involving a low-fat diet and increased physical activity lowered body weight by approximately 7% after one year, decreasing to a reduction of about 4% after four years; this weight loss led to a 58% reduction in the risk of progressing to diabetes over three years compared with standard lifestyle recommendations plus a placebo.[3,6] The lifestyle intervention was also more effective than drug therapy with metformin, an antidiabetic agent that has also been shown to promote weight loss.[3]

Because the initial DPP Trial involved individual coaching and the one-year program cost was about $1,400 per participant, subsequent research and practice have focused on replicating the results with programs that could be distributed more widely at a lower cost. Several published studies have examined the effectiveness of DPPs delivered in community settings. Studies of lifestyle programs at the YMCA (now referred to as the Y) and Weight Watchers, for example, have reported significant weight loss at 12 months of 6% and 5.6%, respectively, compared to control groups who had 1.8% and 0.2% weight loss, respectively.[7,8] An important cost-saving feature of these programs is the delivery of the lifestyle intervention in a group setting; the Y also uses trained lay staff rather than health care personnel. Other recent efforts have involved the use of technology (i.e., applications accessible on computers, tablets, and smartphones) to deliver lifestyle programs to even wider audiences online, again showing significant weight loss results compared to control groups.[9] Omada Health reported that individuals completing four or more lessons of the curriculum using their digital DPP, Omada® (formerly called Prevent), lost 5% of their body weight after six months, 4.7% after 12 months, and 4.2% after 24 months;[9] Turnaround Health, which offers a fully-automated (i.e., without human coaches) digital DPP, Alive-PD™, reported weight loss of about 3.5% over a six-month period.[22]

National Landscape

CDC Initiatives

The CDC developed the National Diabetes Prevention Program (NDPP), a public/private partnership working to offer evidence-based, cost-effective interventions across the US with the goals of reducing the growing problem of prediabetes and type 2 DM as well as to build on the DPP Trial results with a focus on scalability. Organizations delivering a DPP with three key components – a CDC-approved curriculum[e] that promotes a 5-7% weight loss and increased physical activity, use of trained lifestyle coaches as facilitators, and a peer support group of program participants – can apply for CDC recognition through the DPRP. To achieve recognition, programs must submit data annually on participant weight and duration of physical activity in minutes, which are used by CDC to assess program impact on preventing or delaying the onset of type 2 DM; both in-person and digital programs are eligible for recognition. CDC-recognized lifestyle change programs must be science-based and include the following:[56]

- Emphasize the overarching goal of preventing type 2 DM
- Focus on making lasting lifestyle changes rather than simply completing the curriculum
- Build up to moderate changes in diet and physical activity that lead to 5% to 7% weight loss in the first six months

[e] In addition to the DPP curriculum publicly available from the CDC, organizations offering DPPs can submit their curricula to the CDC for review. If approved, organizations can then seek CDC recognition.

- Discuss strategies for self-monitoring of diet and physical activity, building participant self-efficacy and social support to maintain lifestyle changes, and problem-solving to overcome common weight loss, physical activity, and healthy eating challenges
- Provide participant materials to support program goals

DPPS are required to submit data on weight loss, physical activity, and participant retention/class attendance. Only year-long programs are eligible for CDC recognition and under the 2015 DPRP standards, organizations must have an average session attendance of nine during months one through six and an average session attendance of three monthly sessions during months seven through 12. At least one session per month must be held in each of months seven through 12.[57] In CDC-recognized DPPs, participants must be aged 18 years or older and have a BMI ≥24 (≥22 if Asian). Also, at least 50% of a program's participants must be determined to be eligible by biometric markers such as blood test results while a maximum of 50% of participants may be determined as eligible based on the results of a seven-question prediabetes screening test (see Appendix Table C1). As shown in Table 2, the number of programs with pending or full recognition status has greatly increased since 2012, and as of March 31, 2016, there were 54 organizations with full recognition and over 780 with pending recognition.

Table 2. Number of DPPs Recognized by the CDC DPRP by Year[58]

Year	Number of Organizations with Pending Recognition Status†	Number of Organizations with Full Recognition Status†	Total Organizations with Pending/Full Recognition Status†
2012	218	N/A*	218
2013	447	N/A*	447
2014	510	9	519
2015	706	25	731
As of 03/31/16	787	54	841

*Not applicable, as the evaluation for full DPRP recognition takes at least two years

†All numbers reflect end-of-year DPRP recognition status (except for 2016) and do not account for the specific time an organization applied for recognition

In March 2016, CDC released a revised curriculum, "Prevent T2," that reflects new literature on self-efficacy, physical activity, diet, and sleep; the curriculum was developed in English at a 6th grade reading level and in Spanish at a 5th grade reading level (i.e., it was not simply translated from English to Spanish) and is available for free to anyone. The one-year program has a 26-module core curriculum that emphasizes self-monitoring, self-efficacy, and problem solving; 16 modules must be delivered in the first six months of the program and at least six of the remaining 10 modules in the next six months (see Appendix Table C3 for an overview of curriculum content). Program goals include 1) increased physical activity to at least 150 minutes per week, 2) 5% or greater weight loss within six months, and 3) maintenance of weight loss throughout the program and beyond.

With a goal of expanding access by increasing the number of DPPs, the CDC is using several grant opportunities to increase awareness of prediabetes among providers and the overall population, increase provider referrals to DPPs, and encourage coverage for DPPs through public or private insurance or through employer wellness programs. In addition to its grant-based efforts, the CDC is partnering with several other national organizations on initiatives to address prediabetes. These efforts focus on increased access to and coverage for DPPs and health care provider referral to these programs, as well as outreach to populations at high-risk of prediabetes based on race/ethnicity or income, and are discussed in further detail below.

Prevent Diabetes STAT[59]

The American Medical Association (AMA) and the CDC are partnering on the Prevent Diabetes STAT (Screen, Test, Act Today) program, which targets information to three audiences – patients, health care professionals, and employers/insurers. It encourages 1) patients to be screened for prediabetes and those with prediabetes to participate in a DPP, 2) providers to screen and refer patients with prediabetes to DPPs, and 3) employers/insurers to provide health insurance coverage for DPPs.

AHIP[60]

Four members of American's Health Insurance Plans (AHIP) – Denver Health, EmblemHealth, Florida Blue, and Molina Healthcare – have implemented DPPs for a diverse group of populations at risk for prediabetes as part of a CDC grant. These plans have focused on expanding access to DPPs through a variety of mechanisms including engaging diverse populations through use of culturally and linguistically appropriate resources (e.g., through the use of bilingual outreach workers and coaches), and addressing the needs of low income and low literacy populations (e.g., by offering materials at 4th or 6th grade reading levels). Other areas of focus include offering DPPs in workplace settings, leveraging partnerships with physician practices to increase referrals, and using health plan retail centers (walk-in customer service locations) to increase access.

PSA Campaign[61]

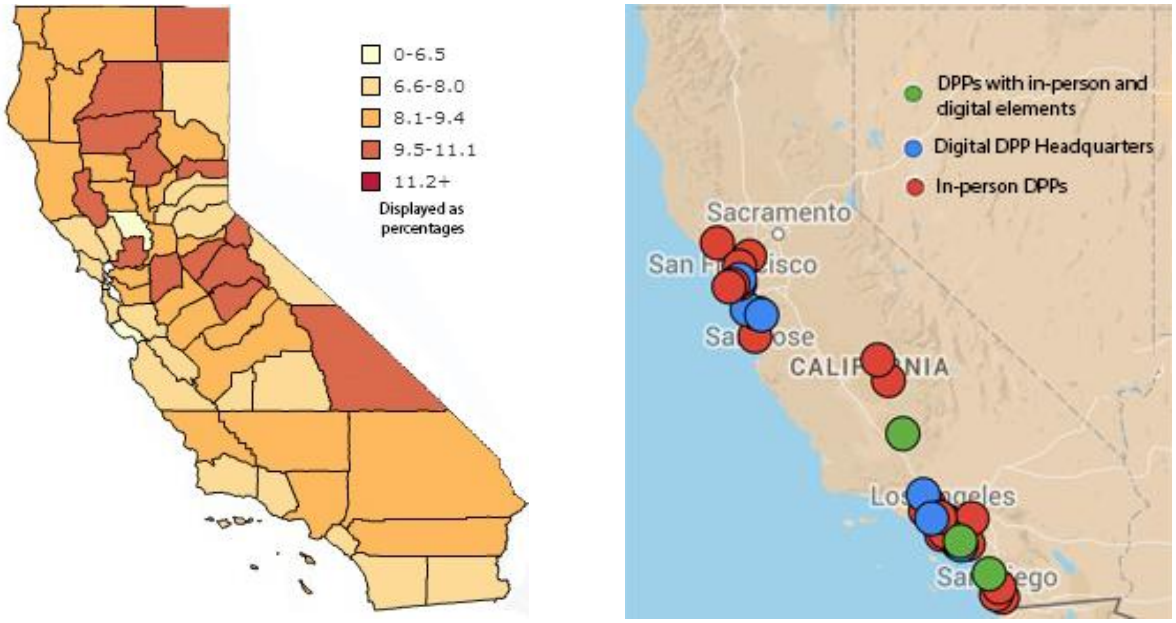
The first national public service advertising (PSA) campaign about prediabetes was launched in January 2016 as a partnership among the CDC, the ADA, the AMA, and the Ad Council. The campaign encourages individuals to take a short online survey at DoIHavePrediabetes.org to assess their risk for prediabetes, to confirm their results with a doctor, and to participate in a CDC-recognized lifestyle change program; this website provides lifestyle tips and links to the CDC and DPPs recognized through the DPRP.

California Landscape

A number of diabetes prevention initiatives in California are being led by the California Department of Public Health (CDPH) and other entities including local health departments. CDPH has received two CDC grants to raise awareness of prediabetes and to increase the number and use of DPPs in the state; the department shares these funds with county health departments who are most knowledgeable about needs in their counties and can best implement programs to meet those needs. In addition to the grants to support statewide efforts, two California cities – Los Angeles and San Diego – received CDC grants. CDPH has also partnered with the CDC and AMA on the Prevent Diabetes STAT program and is leading the development of a statewide action plan to address prediabetes. This plan will be developed in the summer of 2016 with a planned implementation in the fall.

Prediabetes disproportionately affects some races and ethnicities in California.[2] The highest proportions of the population with prediabetes or undiagnosed diabetes are Pacific Islanders (55%), American Indians (51%), and African Americans (50%); by contrast, prediabetes or undiagnosed diabetes affects 42% of Asians. While the burdens of diabetes are greatest in low-income, ethnically diverse populations, interviewees noted that there have historically been few DPPs or diabetes self-management programs available in geographic areas where the needs are greatest (see Figure 2). For example, interviewees noted that rates of prediabetes are higher in the Central Valley, but that relatively few DPPs have been located there. In contrast, more DPPs are available along the California coast, where rates of prediabetes are lower. As of May 6, 2016, the CDC has granted full or pending recognition to 32 in-person DPPs and three DPPs with in-person and digital elements in California; seven vendors of digital DPPs have their headquarters in the state and are included in Figure 2, though access to these programs is not constrained by geographic location.[62] It should be noted that the location of in-person Weight Watchers programs are not included in Figure 2, since the CDC registry lists only the New York headquarters of the company. Similarly, other organizations with multiple sites whose recognition is tied to a single location would also not be fully represented in this figure.

Figure 2. Prevalence of Diagnosed Diabetes in California by County, 2012; Location of DPPs



Sources: http://www.cdc.gov/diabetes/atlas/countydata/atlas.html (left map), https://nccd.cdc.gov/DDT_DPRP/Programs.aspx (right map data, downloaded May 6, 2016) https://www.google.com/maps/d/ (right map)

Although this review is restricted to the adult population, several interviewees highlighted the importance of prevention efforts targeted at children and adolescents to lower the risk of developing type 2 DM later in life, with a focus on low-income communities and early exposure to the importance of choosing healthier foods and engaging in physical activity.

2.2 Barriers and Opportunities

Scalability

As noted above, to attain the NDPP goal of scalability, the format of DPPs has evolved from individual in-person coaching in the DPP Trial to in-person group sessions, and more recently to digital programs delivered via computer, tablet, or phone; Table 3 summarizes the key features of DPPs. In addition to the considerable heterogeneity among in-person DPP delivery models, some digital programs are delivered to virtual groups that are assigned a human coach while another delivers coaching messages through a fully-automated system.

Table 3. Key Features of DPPs

Format	Scalability	Cost*	Typical Group Size	Key Resources	Examples
In-person, individual coaching	Lowest	Highest	1	Humans, facilities	DPP Trial
In-person, group coaching	Medium	Medium	8-15	Humans, facilities	Weight Watchers for Prediabetes Y
Digital, human coaching (virtual interaction)	High	Medium	1-24	Humans, technology	Virtual Lifestyle Management (VLM™, Canary Health, Inc.) Omada® (Omada Health, Inc.)
Digital, fully-automated coaching (based on algorithms)	Highest	Lowest	1+†	Technology	Alive-PD™ (Turnaround Health)

*Average costs and cost-offsets by program type are available in Appendix Table I2

† No group counseling, but participants can join optional virtual teams. The team size was 10 in the published trial.[10]

For in-person and digital programs that use them, and regardless of whether they are health care professionals or lay personnel, human coaches must be effective facilitators and support the group processes that relate to behavior change.[63] Coaches help participants develop and maintain healthy eating and physical activity habits, and further support participants through education, encouragement, and problem-solving support to address challenges or barriers that arise.[63] Due to the time it takes to recruit and train lifestyle coaches, there will be limits on the ability of any platform involving human coaches to be able to reach a broad population with prediabetes in the US. While completely automated digital solutions would primarily require technology to be scaled, it is unclear if this approach will best serve all audiences.

While individual coaching has the lowest scalability and the highest cost, it was the model used in the DPP Trial and has served as the foundation for subsequent DPP implementation. Several of the initial efforts to increase scalability through in-person group coaching involving trained laypersons were led by the Y. As of January 2016, the Y had over 1,450 class locations for its DPP in 44 states.[64] Weight Watchers also offers a DPP that includes an online activation video as well as in-person meetings and online tools. Some interviewees noted that social support provided by members of the group and the coach is a benefit of in-person programs, but they also mentioned that the need to attend a weekly class on a set schedule is a constraint for some participants, particularly those with inadequate access to transportation. As noted above, there is substantial variation in the in-person group programs, particularly in terms of the staff coaches. For example, the Y uses trained laypersons, while some other programs use health care professionals such as diabetes educators (i.e., DPPs delivered by organizations accredited by the American Association of Diabetes Educators [AADE]) or registered dietitian nutritionists. National organizations with many programs sites could potentially add scale to in-person DPPs relatively quickly.

All of the digital programs, which have the greatest potential for scalability, offer the flexibility of completing lessons on one's own schedule. Digital programs also are more likely to be available any time a participant wants to enroll and begin the program, whereas there may be a wait for some in-person programs until enough participants enroll to form a group or until staff are available. Many digital programs integrate with other technology (e.g., devices or apps for tracking physical activity, electronic scales). The availability of digital programs and the larger numbers of participants they are able to reach may allow research on what approach works best for specific subpopulations to be conducted more quickly. Nearly all interviewees said that a "one size fits all" solution would not address the needs of all potential participants (i.e., some individuals would prefer a digital DPP while others would prefer an in-person DPP), while acknowledging that more needed to be learned about how to engage and activate specific populations in lifestyle change.

Sustainability

Grant funding has been the predominant means of paying for DPPs in many community-based programs. Several interviewees noted that this is not a sustainable model and that reliance on grant funding is an impediment to scaling. While insurer and purchaser coverage has not yet been extensive, there is interest and movement in this direction by some employers and plans. Coverage by health plans in particular may be accelerated if a Medicare proposal to cover DPPs is implemented and if more health plans interpret two relevant USPSTF recommendations as requiring coverage of DPPs (additional information is located in section 3.1). In California, some interviewees noted that a lack of steady payment sources has contributed to a lack of program availability statewide. Many interviewees thought that coverage of DPPs by all payers, public and private, is necessary to achieve large-scale impact. There was widespread enthusiasm for the March 2016 Medicare announcement that a proposal would be forthcoming to cover DPPs and a perception that this might be an impetus for private plans to accelerate coverage of DPPs and for more Medicaid programs to cover DPPs.

While many DPPs have relied on grant funding and/or one-on-one contracting relationships with payers, there is at least one company (Solera) that acts as an intermediary by connecting patients, payers, and clinicians with DPPs. Potential benefits of such an intermediary include: health plans can offer both in-person and digital DPPs through one vendor, eligible patients can be matched to a DPP with the format that best suits them, more enrollees can be directed to DPPs leading to a steadier revenue stream, providers can easily refer patients to a DPP, and payments can be tied to key milestones (e.g., enrollment, engagement at 4 weeks and 9 weeks, ≥ 5% weight loss).

Among the vendors offering digital programs, several indicated that they are engaged in pay-for-performance (P4P) contracts in which they are paid based on the number of people who enroll and achieve certain attendance and weight loss goals, rather than receiving a fee per health plan enrollee or employee offered the DPP. Although details of such P4P arrangements vary and are

proprietary, representatives of both private health plans and purchasers indicated that they are seeking these types of arrangements. With such risk-sharing, DPP vendors therefore have a greater financial incentive to identify participants who are ready to engage in the program; if such participants are higher-risk, it is expected that they will benefit more from the program, thereby making the return on investment (ROI) more favorable.

There has been little study of individuals who pay privately for DPPs, but it appears that this has not been a major source of revenue or a significant focus for most vendors. Individuals who are interested in purchasing a DPP on their own can do so through the Y, Weight Watchers, and various digital providers.

Additional DPP Implementation Considerations

In addition to issues related to scalability and sustainability, interviewees were asked about other factors that may limit the use of DPPs. Several of these issues and potential solutions are described below.

Data

Many interviewees noted the steep learning curve for programs seeking CDC recognition, particularly in terms of data collection and analysis. Some described the importance of having coaches who are committed to and understand the importance of analyzing data to assess program effectiveness, as the time requirements for reviewing and submitting data from food and activity logs, participant weight measurement, and attendance were substantial. Several interviewees thought there may be a role for electronic health records (EHRs) in diabetes prevention, particularly in helping providers to identify patients with HbA1c levels that meet the prediabetes criteria (5.7-6.5%) and in communicating patient results back to their health care providers. Employers were interested in data sharing that meets high security standards and that can be used to enhance communication among providers, patients, DPP vendors, and plans.

Culturally Appropriate Curricula/Strategies to Reach High-risk Populations

A recent review of the effectiveness of DPPs in community-based settings noted that, unlike in the DPP Trial, the majority of those enrolled were white, non-Hispanic, and female.[65] These findings demonstrate that efforts to reach other populations, including racial/ethnic groups at higher risk of developing diabetes are necessary, and many interviewees articulated a need for better methods to reach these underserved communities. While noting the development of the new Prevent T2 curriculum in Spanish as a positive, interviewees highlighted the importance of the curriculum being available in a language that participants can understand and that is also culturally appropriate (e.g., dietary recommendations should reflect the foods most commonly consumed in ethnic subpopulations). Several interviewees noted the need for materials in a variety of Asian languages.

While agreeing that curriculum availability in other languages is an important goal, it was noted that to ensure fidelity to the DPP model, efforts to reach these populations should not deviate too far from the DPP curriculum.

In addition to language and cultural appropriateness, interviewees identified low literacy and illiteracy as another factor affecting accessibility of DPPs. It was noted that the emphasis on collecting data may be challenging for these populations because individuals who cannot track their food and physical activity may feel as though they cannot participate fully in the program, which may impact attendance and program attrition. One example was given of a pictorial version of a DPP that had not been submitted to CDC for review but could potentially meet the needs of this population.

For lower-income populations, participation and attrition were significant concerns for in-person DPP vendors. Factors that interviewees identified as potentially helpful in encouraging consistent participation were availability of child care; locations in communities that are easily accessible to participants so transportation was not a deterrent; incentives for participants such as measuring cups, food and weight scales, or raffles; and reminders to attend class via email, text, or a phone call. In terms of ability to access digital DPPs, some interviewees perceived that lower-income populations may not have as much access to computers or the internet as higher-income populations, but the extent to which this affects participation is unclear. A 2015 study by the Pew Research Center reported that 50% of American adults with annual incomes less than $30,000 and 71% of those with incomes between $30,000 and $50,000 now own a smartphone.[66]

Efforts to Engage Providers and Community Organizations

Several interviewees highlighted the importance of partnerships with clinicians and the role of provider referrals, as well as the need for feedback loops between DPPs and clinicians. Some interviewees felt that the best opportunity for patient engagement occurs if providers immediately refer individuals to a DPP when their blood test results indicate they have prediabetes. Even if individuals with prediabetes are made aware of their condition, providers may be hesitant to refer patients to DPPs if the programs are not covered by insurance. Some others felt that individuals referred by clinicians were more likely to participate in a DPP than those who self-referred.

Provider engagement was noted as a challenge, with a call for education about USPSTF screening recommendations, prediabetes, and the availability of DPPs, as well as increased provider referrals to DPPs overall. The need for more education in medical schools regarding diabetes prevention and prediabetes was also noted.

As noted earlier, to be eligible for CDC recognition, DPPs must enroll ≥ 50% of participants based on biometric markers such as blood glucose test results rather than on the results of a prediabetes risk-factor survey, so DPPs closely affiliated with provider groups and some health plans may have

access to blood test results for program participants and thus may be able to meet this requirement more easily. However, some interviewees from community-based programs noted that it is challenging to meet this threshold and articulated a need for better linkages and relationships between clinicians and community-based DPPs, both to increase referrals and to provide a place for participants to have biometric tests.

Representatives of in-person DPPs also identified the need to work with organizations such as faith-based organizations and others that are already enmeshed in their communities to serve as ambassadors for diabetes prevention efforts including screening and referral to DPPs. These organizations can also be the source of coaches and outreach workers.

Coach Workforce Identification, Training, and Retention

Almost all DPPs use human coaches to some extent and, as noted earlier, their availability is a rate-limiting factor to program scalability. Many interviewees articulated that extensive efforts are required to screen, identify, train, and retain skilled lifestyle program coaches who can connect to the community targeted by the DPP. For in-person programs, interviewees said that coaches who are sensitive to the culture of those enrolled in the program and involved in the community have opportunities to engage with participants outside of class (e.g., at grocery stores, schools, faith-based organizations). Digital DPPs may facilitate more efficient use of human coaches when compared to in-person DPPs since participant data can be automatically analyzed as it is entered into the system, allowing coaches to more efficiently provide customized feedback.

Importance of Prediabetes Awareness and Readiness to Change

Amongst the areas cited most often by interviewees as a challenge to more widespread access to and use of DPPs was the lack of awareness of prediabetes. Several national and statewide efforts are underway to increase awareness of prediabetes for individuals and health care providers. Some interviewees said that to encourage retention in and completion of a DPP, the role of participant readiness to change may be an important factor. Retention would be expected to be higher for individuals who understand and are prepared to make the year-long commitment for the DPP; are interested in learning about healthy eating, exercise, and stress management; and are willing to make lifestyle changes to realize the benefits of such changes.

3. Public and Private Coverage for DPPs

To understand the insurance landscape for DPPs, we reviewed the publicly available coverage policies of the Centers for Medicare & Medicaid Services (CMS), California Department of Health Care Services (DHCS), Aetna, Anthem, CIGNA, Humana, UnitedHealthcare, Health Net, and Blue Shield of California. At the time of this report's publication, none of these plans had publicly available coverage policies, though many are engaged in pilot efforts to roll out DPP benefits for their covered populations; details on these programs are available in Appendix E. In the absence of specific details on coverage policy, this section will explore the current payer and purchaser landscape as it relates to DPPs.

3.1 Health Insurance Coverage for DPPs

One of the major goals of the CDC and its NDPP partners is to increase access to DPPs by promoting health insurance coverage in both public and private settings. Information on current coverage and potential future coverage is discussed below.

Medicare and Medicaid

Medicare does not currently cover DPPs, and only one state Medicaid program (Montana) does. However, the Secretary of Health & Human Services (HHS) announced in March 2016 that the DPPs tested as part of a Center for Medicare and Medicaid Innovation (CMMI) grant produced favorable health outcomes while saving money over a 15-month period, and that CMS plans to release a proposal to expand coverage to all Medicare beneficiaries at high risk for developing diabetes (using a 110 mg/dL FPG threshold to define prediabetes). For successful service delivery models such as this, the Secretary is allowed, through rulemaking, to expand the duration and scope of the model being tested if it meets certain quality of care, spending, and coverage/benefit criteria; the proposal to expand coverage to all Medicare beneficiaries will be open to a public comment process.[43]

In addition to the Montana Medicaid program, which covers DPPs and uses diabetes educators, the CDC is in the process of identifying two to three states whose Medicaid programs would provide DPP coverage for beneficiaries in value-based plans (e.g., managed care plans, accountable care organizations [ACOs]) through pilot projects focused on participant engagement and retention strategies. Several interviewees noted that the Medicaid population is at higher risk for prediabetes and diabetes, and is more ethnically and racially diverse than the privately insured population. While many interviewees expressed a desire for all Medicaid beneficiaries to have access to DPPs, there was an acknowledgement that the reality of limited resources in Medicaid funding and in Medicaid managed care plan contracts would likely mean that efforts would need to be targeted to

reach individuals at the highest levels of diabetes risk within this population first rather than making DPPs available to all beneficiaries who meet the criteria for prediabetes.

Private Health Plans

Among the plans we interviewed, one plan has developed its own DPP in conjunction with the CDC and the Y (though it has not yet applied for recognition through the DPRP), another pays for DPPs when claims are submitted for reimbursement, while another does not yet offer a specific DPP but is exploring options to offer its enrollees. Nationally, at least 30 private plans currently cover DPPs,[11] but interviewees noted that such coverage was often in response to requests from purchasers and would likely not apply to all lines of business. Private plans we interviewed indicated that they are interested in the effectiveness of DPPs both in terms of member-centric clinical outcomes and costs; they also expressed a desire for information on populations most likely to benefit from DPPs (e.g., by age, ethnicity, clinical status, psychological readiness).

The Affordable Care Act (ACA) requires most commercial plans to cover a range of preventive services without any patient cost-sharing; by contrast, Medicare and Medicaid are not required to cover these services.[67,68] There are two recent USPSTF screening recommendations with a grade of B that must be covered by private plans and are relevant to DPPs (see Table 4). Among the private plans we interviewed, there was variation in the interpretation and implementation of these recommendations, with some interpreting these recommendations to mean that DPPs should be a covered preventive benefit with no cost-sharing. It is unknown whether this is the interpretation of all plans; it is also unknown to what extent plans will provide coverage for one or more specific DPPs vs. for any DPP that a member chooses.

Table 4. USPSTF Recommendations Pertaining to DPPs

Topic	Population	Recommendation*	Grade
Behavioral Counseling to Promote a Healthful Diet and Physical Activity for Cardiovascular Disease Prevention in Adults with Cardiovascular Risk Factors (2014)[69]	Adults who are overweight or obese and have additional cardiovascular disease (CVD) risk factors	The USPSTF recommends offering or referring adults who are overweight or obese and have additional CVD risk factors to intensive behavioral counseling interventions to promote a healthful diet and physical activity for CVD prevention.	B
Screening for Abnormal Blood Glucose and Type 2 Diabetes Mellitus (2015)[70]	Adults aged 40 to 70 years who are overweight or obese	The USPSTF recommends screening for abnormal blood glucose as part of cardiovascular risk assessment in adults aged 40 to 70 years who are overweight or obese. Clinicians should offer or refer patients with abnormal blood glucose to intensive behavioral counseling interventions to promote a healthful diet and physical activity.	B

*The USPSTF summary recommendations have been reproduced verbatim

In the absence of clear guidance that DPPs represent a preventive benefit that must be covered by ACA-compliant private plans, there are several reasons these plans may be reluctant to cover DPPs. These include program costs; administrative burdens associated with evaluating the effectiveness of individual programs, establishing relationships with DPP vendors, and validating claims; the use by some programs of lay providers with whom plans do not have a billing relationship; and the year-to-year turnover of enrollees in health plans that make a longer-term ROI difficult to justify. One barrier to reimbursement was alleviated on January 1, 2016, when the AMA released a new CPT code (0403T) specifically for DPPs.[71]

3.2 Employer and Purchaser Coverage of DPPs

Some private and public purchasers have incorporated DPPs into their health plans or wellness programs, or as standalone benefits, but it is challenging to assess how extensive these practices are. At the state purchaser level, eight states (Colorado, Kentucky, Louisiana, Maine, Minnesota, New Hampshire, Ohio, and Washington) provided DPPs for their employees as of August 2015, and several others are considering adding DPPs as a covered health benefit.[72] The local and state government purchasers in California that we interviewed expressed an interest in having DPPs as a covered benefit but indicated that current coverage of DPPs is left to the discretion of the health plans with whom they contract.

Among the private employers and business coalitions we interviewed, there was an interest in making DPPs available either through wellness programs or health plan coverage, with particular interest in digital solutions. Employers acknowledged that DPPs are a medium- to long-term investment, and were therefore not as focused on short-term ROI as insurers. Key factors identified by purchasers in making DPPs available include program effectiveness and effective participant engagement; risk sharing and paying for results rather than paying for enrollees; capacity for data sharing with high security standards among health plans, providers, and DPPs; communication support to inform employees about the program; and CDC recognition.

Purchaser interviewees emphasized that individuals with prediabetes will differ in the type of program that best fits their need and that programs should be available to reach people in a manner (in-person or digital) that works best for the individual. One purchaser noted the importance of immediate referral to a DPP when a blood test shows prediabetes, since this is when the person is most keenly interested; in addition, it is important to pair the referral with direct human contact to make sure the person knows what steps to take next to address their condition.

Some employers that offer DPPs through their health plans are also engaging in broader efforts to improve work environments by increasing access to healthy foods (e.g., in cafeterias or vending machines, at staff meetings) and making physical activity easier (e.g., by carpeting stairs, adding walking trails).

4. Comparative Clinical Effectiveness

4.1 Overview

Three large, high-quality randomized trials begun more than 20 years ago have demonstrated that lifestyle interventions focusing on diet and exercise can decrease the progression to diabetes among individuals with prediabetes.[3,73,74] Appendix Table H1 summarizes the inclusion and exclusion criteria for the three trials and details of their lifestyle interventions. The Diabetes Prevention Program Trial (DPP Trial) is the largest of the three trials and the one most relevant for the US population (Appendix Table H2).

The DPP Trial investigators randomized 3,234 individuals to the lifestyle intervention, metformin, or placebo. After approximately three years of follow-up, there was a 58% reduction in the incidence of diabetes in the lifestyle group compared with the placebo group (95% confidence interval [CI] 48% to 66%) and a 31% reduction in the metformin group compared to the placebo group. The lifestyle intervention was also significantly more effective than the metformin intervention (relative risk reduction [RRR] 39%, 95% CI: 24% to 51%). The reduction in the incidence of diabetes declined over time to 27% at 15 years, but members of the metformin and placebo groups were offered the lifestyle intervention at the end of the initial follow-up period, which may have decreased the difference in diabetes incidence between the two groups (Appendix Table H3). More than half of patients in the lifestyle intervention arms of the three trials developed diabetes after 15 years of follow-up, so it may be more appropriate to speak of a delay in diagnosis rather than prevention. In the DPP Trial, the delay in diagnosis estimated from cumulative incidence curves is approximately three years.[34] Long term follow-up continues for all three trials in order to examine the impact of the interventions on diabetic microvascular disease (eye, kidney, and nerve damage) and cardiovascular disease (strokes and heart attacks). At 15 years of follow-up, there was no significant reduction in microvascular disease in the DPP Trial (risk ratio [RR] 0.91, 95% CI: 0.78 to 1.07). However, at 23 years of follow-up, there was a significant reduction in death from cardiovascular disease in the Chinese Da Qing Diabetes Prevention Study (RR 0.59, 95% CI: 0.36 to 0.96).

Since publication of the initial results of the DPP Trial, there have been more than 50 studies translating the lifestyle intervention to real-world settings. Many systematic reviews and health technology assessments have demonstrated that these programs decrease body weight, decrease FPG, improve blood pressure and cholesterol levels, and prevent or delay the onset of type 2 DM (see Appendix F).[12-17,75-98] For example, Ali and colleagues[12] evaluated 28 real-world implementation studies and found that the average weight loss at one year was 4-5% and that the more sessions participants attended, the more weight they lost. Neamah and colleagues[17] found that participants in programs with fewer deviations from the original DPP Trial approach had significantly greater

weight loss at 12 months. Additional detail on these two systematic reviews can be found in Appendix F.

The CDC and the Community Preventive Services Task Force commissioned a systematic review of programs that promote dietary changes and physical activity to prevent or delay the development of diabetes.[15] Eight reviewers evaluated more than 11,300 publications and extracted data from 53 studies describing 66 diet and activity programs for adults with prediabetes published through February 2015. They found that diet and exercise programs reduced diabetes incidence by 41% (95% CI: 34% to 48%) compared with usual care. The programs also reduced body weight by 2.2% (95% CI: 1.4% to 2.9%) and FPG by 2.2 mg/dL (95% CI: 0.9 to 3.6 mg/dL). Six studies (five randomized) compared less intensive to more intensive lifestyle interventions. The more intensive programs, such as the DPP Trial intervention, were more effective (44% to 72% greater reduction in incident diabetes).[15]

The CDC established the DPRP to identify programs with proven effectiveness at delivering a lifestyle intervention to prevent or delay the development of type 2 DM. The goals of the DPRP are to ensure the quality of programs designed to deliver such lifestyle interventions, to maintain a registry of such organizations, and to provide technical assistance to local DPPs.

Accordingly, our intent for this evidence review is to summarize the published literature for lifestyle interventions in the US that have full or pending recognition by the DPRP. We extended the search that was commissioned by the CDC through April 2016 but limited our review to those programs recognized by the DPRP.

4.2 Methods

Data Sources and Searches

The systematic literature search assessing the evidence on lifestyle interventions to prevent or delay the development of type 2 DM followed established best practices used for systematic review research.[99] We conducted the review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[100] The PRISMA guidelines include a checklist of 27 items, further detail of which is available in Appendix Table A1.

We used the systematic review commissioned by the CDC as the foundation for our search.[15] We repeated their search, limiting it to the two years prior to April 7, 2016 in order to identify studies indexed or published since the end of their search timeline (February 27, 2015). We searched MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials. We limited each search to studies of human subjects and excluded articles indexed as guidelines, letters, editorials, narrative review s, case reports, conference abstracts, or news items. To supplement the above searches and ensure optimal and complete literature retrieval, we performed a manual check of the

references of recent relevant reviews and meta-analyses. We also contacted the CDC and known organizations that support CDC-recognized lifestyle interventions. Further details on the search algorithm are available in Appendix Table A2.

Study Selection

We performed screening at both the abstract and full-text level. A single investigator screened all abstracts identified through electronic searches for lifestyle programs with full or pending recognition from the CDC DPRP. We did not exclude any study at abstract-level screening due to insufficient information. For example, an abstract that did not report an outcome of interest would be accepted for further review in full text.

We retrieved the citations that were accepted during abstract-level screening for full text appraisal. One investigator reviewed full papers and provided justification for exclusion of each excluded study.

Data Extraction and Quality Assessment

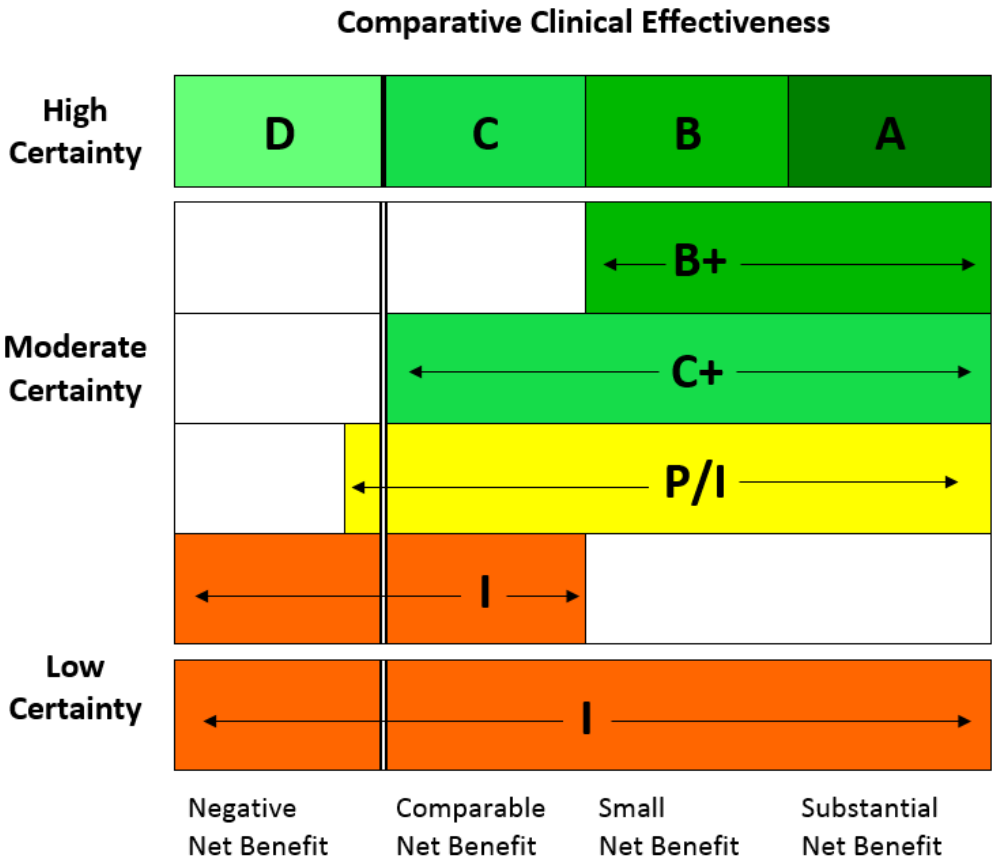
Our data extraction and review process is detailed in Appendix H. Summary tables are available in Appendix Tables H4 through H11. We used criteria published by the USPSTF to assess the quality of RCTs and comparative cohort studies, using the categories "good," "fair," or "poor."[101]

Assessment of Level of Certainty in Evidence

We used the ICER Evidence Rating Matrix (see Figure 3) to evaluate the evidence for a variety of outcomes. The evidence rating reflects a joint judgment of two critical components:

a) The **magnitude** of the difference between a therapeutic agent and its comparator in "net health benefit" – the balance between clinical benefits and risks and/or adverse effects AND
b) The level of **certainty** in the best point estimate of net health benefit.[102]

Figure 3. ICER Evidence Rating Matrix



A = "Superior" **-** High certainty of a substantial (moderate-large) net health benefit
B = "Incremental" **-** High certainty of a small net health benefit
C = "Comparable"**-** High certainty of a comparable net health benefit
D="Negative"**-** High certainty of an inferior net health benefit
B+="Incremental or Better" **–** Moderate certainty of a small net health benefit, with high certainty of at least incremental net health benefit
C+="Comparable or Better" **-** Moderate certainty of a comparable net health benefit, with high certainty of at least comparable net health benefit
P/I = "Promising but Inconclusive" - Moderate certainty of a small or substantial net health benefit, small (but nonzero) likelihood of a negative net health benefit
I = "Insufficient" **–** Either moderate certainty that the best point estimate of comparative net health benefit is comparable or inferior; or any situation in which the level of certainty in the evidence is low

Data Synthesis and Statistical Analyses

Given the small numbers of studies for programs recognized by the CDC DPRP, the inclusion of case series without control groups, and the meta-analyses performed as part of prior systematic reviews that included a wider range of studies, we judged that it would not be helpful or appropriate to perform formal meta-analysis to generate pooled estimates of treatment effect. We cannot directly compare in-person to digital programs because there are no head-to-head trials or cohorts comparing programs, and there were insufficient trials with control groups to allow conduct of a network meta-analysis.

4.3 Results

Study Selection

The updated literature search for lifestyle interventions to prevent or delay the development of type 2 DM identified 1,489 potentially relevant references (see Appendix Figure A1), of which 18 publications describing 10 studies met our inclusion criteria (five RCTs and five case-series using a pre-post design).[7-9,18-32] Details of the included studies are summarized in Appendix Tables H4 through H11. The original DPP Trial data are also summarized in Appendix Tables H4 through H11 to serve as a standard for comparison with the implementation trials. The studies are grouped in the tables by degree of human contact from the DPP, ranging from in-person individual coaching performed on a weekly, one-on-one basis with a trained health care professional to the Alive-PD system which is digital with fully automated coaching. Studies using in-person group coaching were the most common, and included four studies in the Y system, one supported by the Department of Public Health and Human Services in Montana, one at Weight Watchers, and one at Wake Forest University. Two of the programs (Virtual Lifestyle Management [VLM], Omada) were digital with a human coach. Finally, as noted above, one digital system was completely automated and provided no human counselor. (Alive-PD).

The study populations were remarkably similar (Appendix Table H6). The average weight of the participants was approximately 100 kg across the studies with an average BMI of approximately 34 kg/m^2, and the average age in the trials ranged from 51 to 57 years. The Omada trial, which recruited participants from the Internet, was an outlier with respect to age; the average age of participants in the Omada trial was 44 years. Across the studies, two-thirds of the participants were women, with the exception of the Alive-PD study (32% female). The mean HbA1c was approximately 5.9% when reported. As in the DPP Trial, the race/ethnicity composition of the studies was diverse with the notable exception of the DEPLOY study (93% white) and the VLM study (86% white). The Alive-PD study was 25% Asian, reflecting the composition of the Bay Area population where the study was performed.

Quality of Individual Studies

The quality of the individual studies is summarized in Appendix Table H11. The original DPP Trial was a large, good-quality trial with long enough follow-up to assess the impact of the intervention on diabetes incidence.[3] Three of the implementation trials were randomized trials of good quality (RAPID, Alive-PD, HELP-PD), though the Alive-PD trial has only published 6-month outcomes.[19,23,28] The lifestyle changes necessary to prevent or delay the development of diabetes need to be sustained for decades, so outcomes beyond the initial intensive intervention period are preferred. The two other randomized trials (DEPLOY, Weight Watchers) were judged to be of fair quality because of baseline differences between the groups and significant loss to follow-up.[7,8]

Among the pre-post case series, one (Omada, formerly called Prevent) was judged to be of fair quality; although case series provide weaker evidence than RCTs, the study included a careful description of the participants, and featured adequate length and completeness of follow-up, objective outcome measures, and appropriate analysis methods.[9,31] The other four were judged to be of poor quality because of the small number of participants with prediabetes, the use of self-reported outcomes, and significant loss to follow-up.[24,25,30,32]

Key Studies

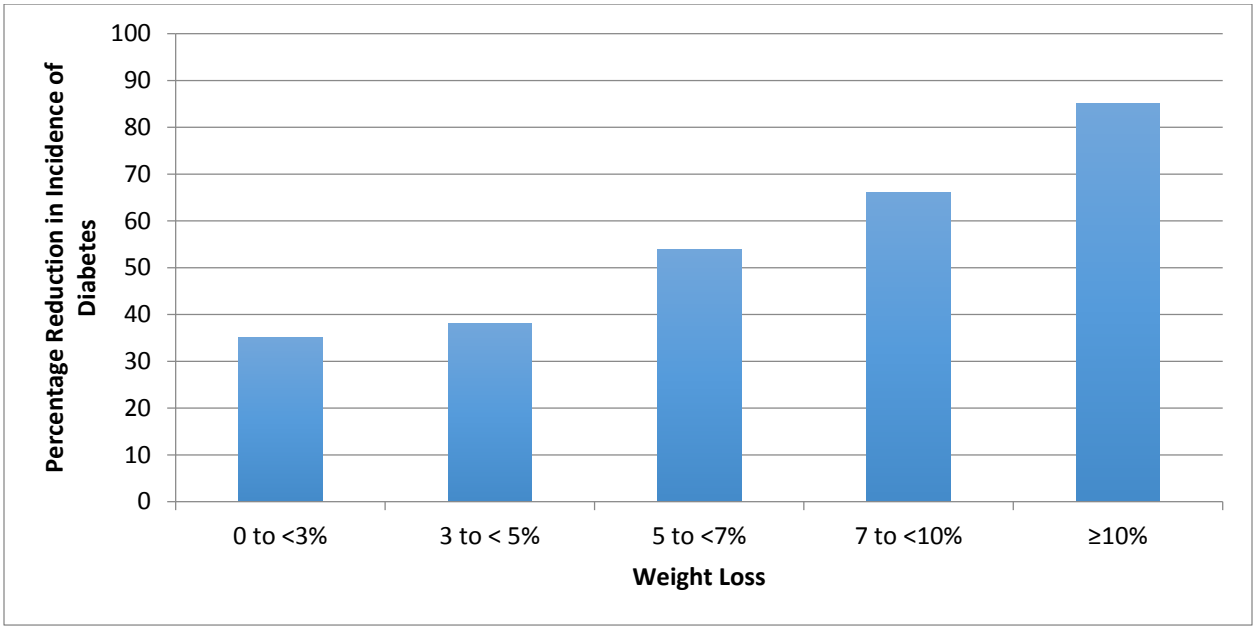
In-person, Individual Coaching

The Diabetes Prevention Program Trial

All of the CDC-recognized DPPs attempt to implement the DPP Trial intervention in a cost-efficient and scalable approach. We describe the DPP Trial methods and results here and include the DPP Trial in all of the report and appendix tables to serve as a reference to guide the evaluation of the implementation studies. The original DPP Trial randomized 1,079 individuals to the intensive lifestyle intervention.[3] All participants were required to have prediabetes defined by an OGTT at two hours between 140 and 199 mg/dL. The intervention consisted of 16 core lessons delivered weekly one-on-one with a lifestyle coach (primarily dieticians). This was followed by eight monthly individual post-core sessions to problem solve, support adherence, and to reinforce the original material. The three goals of the intervention included a 7% reduction in body weight, 150 minutes of moderate intensity exercise (brisk walking) every week, and a reduction of fat intake to less than 25% of total calories. The trial also offered group exercise classes, gym memberships, and other support to help participants in the lifestyle intervention group to reach their goals.

More than 95% of the participants attended nine or more of the 16 core sessions, and follow-up for outcomes was 98% complete at three years. At one year, participants had lost an average of 7 kg or 7% of their initial body weight. Half of the participants met the weight loss goal of 7% or more of their body weight. Over the first three years of follow-up, this translated into a 58% reduction in the incidence of diabetes (14.4% versus 28.9%). Weight loss was the primary predictor of the reduction in diabetes incidence,[4,5] ranging from a 35% reduction in diabetes incidence among participants with 0-3% weight loss to an 85% reduction in diabetes incidence for participants with >10% weight loss (see Figure 4).[5] Participants in the lifestyle intervention also had reductions in blood pressure and improvements in cholesterol measurements that should translate into additional benefits in the long term prevention of cardiovascular disease.[33] In addition, there were significant improvements in quality of life with the lifestyle intervention compared with the placebo group using the 36-Item Short-Form Health Survey (SF-36).[52] There were improvements in general health (+3.2 versus placebo, $p<0.001$), physical function (+3.6 versus placebo, $p<0.001$), bodily pain (+1.9 versus placebo, $p=0.01$), and vitality (+2.1 versus placebo, $p=0.01$).

Figure 4. Correlation of Percentage Weight Loss with Reduction in the Risk for Diabetes for Participants in the Intensive Lifestyle Intervention Arm of the DPP Trial



In-person, Group Coaching

Diabetes Education & Prevention with a Lifestyle Intervention Offered at the Y (DEPLOY)

The DEPLOY study was an early and widely-cited example of translating the DPP Trial intervention to a real-world setting and evaluating the results.[7,18,20,29] In order to improve the efficiency and scalability of the program, the lifestyle curriculum was delivered in groups of 8-12 participants rather than individually. The groups met for the 16 core lessons of the DPP in weekly classroom meetings that focused on knowledge building, goal setting, self-monitoring, and problem-solving. These were followed by monthly large group meetings for additional educational sessions.

DEPLOY was a pilot cluster randomized trial at two Y facilities in Indiana, though with only two clusters, it was more akin to a cohort study. A total of 92 participants (46 at each site) were recruited on the basis of BMI ≥24 kg/m^2, elevated risk for diabetes using a diabetes risk assessment tool, and a non-fasting finger stick glucose level of 110-199. The DPP curriculum was delivered by trained Y staff in 16 group meetings of 8-12 people, with goals of a 5-7% weight loss and 150 minutes per week of moderate exercise. The control group received personalized advice about their risk for diabetes and was advised that modest weight loss (5-10%) and moderate exercise 30 minutes a day were safe and effective at preventing diabetes. The control group intervention was supplemented with the Small Steps, Big Rewards educational materials from the National Diabetes Education Program (NDEP). There were important baseline differences between the lifestyle and control groups (age, 56.5 versus 60.1 years; female, 50% versus 61%; and race, 4% versus 20%

African American). There was substantial loss to follow-up in the study. In the lifestyle intervention group, 35/46 (76%) of the participants attended at least one session. Among participants who attended at least one session, the average attendance was 12/16 core sessions (75%). At one year, individuals in the lifestyle intervention group who were evaluated (29/46, 63%) lost an average of 6% of their baseline weight compared with 1.8% in the control group (p=0.008). Adjustment for baseline differences in the two groups did not change the magnitude or statistical significance of the difference in weight loss. At a median follow-up of 28 months, 72% of the lifestyle group returned for assessment, and the lifestyle group continued to weigh an average of 6.0% less than their baseline weight. At one year, there was a significant decrease in total cholesterol in the DPP group (-13.5 versus +11.8 mg/dL, p=0.002). There were no significant differences in change in HbA1c or systolic blood pressure.

Weight Watchers

Weight Watchers studied the impact of their standard weight management program augmented with a 45-minute activation session focused on educating participants about the meaning of prediabetes and the role of lifestyle modification in decreasing their risk for diabetes.[8] The Weight Watchers core curriculum covers the same behavioral topics used in the DPP, though the materials differ. There are weekly in-person meetings at multiple sites throughout the country. The Weight Watchers intervention also comes with optional digital tools to track weight, diet, and physical activity and offers periodic tips on adherence.

Academic investigators randomized 225 participants with prediabetes to Weight Watchers or to brief coaching that consisted of personalized advice about their risk for diabetes, a goal of 5-10% weight loss via caloric restriction with moderate physical activity, and educational materials from the NDEP Small Steps, Big Rewards program. The participants in the two groups were well balanced at randomization, but there was substantial loss to follow-up that differed by group (16% in Weight Watchers group; 28% in control group). Participants in the Weight Watchers group attended an average of 21.6 group sessions over the year, and 63% used the online app at least once. At one year, the Weight Watchers group lost an average of 5.5 kg or 5.6% of their initial weight (0.2 kg and 0.25%, respectively for the control group, p<0.001 for both). The difference in mean weight loss at 12 months was 5.3% without imputation for missing values and 5.5% when multiple imputation was performed for missing weight measurements at six and 12 months. Participants also had improvements in glycemic control and other cardiovascular risk factors, but none of these changes were significantly different from the control group.

Digital, Human Coaching

Omada (Omada Health)

Omada is a DPP-based lifestyle intervention that includes an online social network of 10-15 people for group support, weekly core DPP lessons available for access at the participants' convenience, health coaching, a wireless scale, and a pedometer. There are no in-person meetings, but there are virtual groups and an assigned health coach for each group.

The company sponsored a longitudinal pre-post study in 220 participants recruited online that followed the CDC DPRP guidelines for inclusion criteria and for data analysis.[9,31] Overall, 85% of the participants competed at least four of the core lessons, and they completed an average of 13.8/16 core lessons and 3.2/9 post-core monthly lessons. A total of 70% (155/220) completed at least nine of the core lessons. The core participants lost an average of 4.9 kg or 4.8% of their baseline weight at one year and 4.2% at two years. Their HbA1c declined by an average of 0.4% at one and two years of follow-up.

Virtual Lifestyle Management (VLM, Canary Health)

VLM is a DPP-based lifestyle intervention delivered online via audio-narrated lessons.[30] There are 16 weekly core lessons followed by eight monthly lessons all adapted from the CDC curriculum. Each participant receives a pedometer and a book detailing the fat and calorie content of common foods. Participants receive email prompts for pending lessons as well as prompts to weigh themselves and enter the results on the website. Each participant is assigned a nurse educator lifestyle coach who monitors the participant's progress and writes coaching notes with support and suggestions. These notes are sent weekly for the first 16 weeks and every two weeks thereafter.

The company sponsored a single site pre-post pilot study in 50 patients from a single academic primary care practice at the University of Pittsburgh. The patients were between the ages of 18 and 80, had a BMI ≥25 kg/m^2, and had at least one weight-related cardiovascular risk factor (hypertension, dyslipidemia, diabetes, or impaired fasting glucose). Only 8/50 (16%) had impaired fasting glucose or prediabetes, and their results were not reported separately. The participants completed an average of 12.8 lessons. Among participants completing the visit at month 12 (n=45, 90%), the average weight loss was 4.8 kg, and 31% lost at least 5% of their initial weight. These participants' systolic blood pressure declined an average of 7.3 mm Hg and their diastolic blood pressure increased an average of 0.3 mm Hg. The study did not assess any measure of glycemic control.

Digital, Fully Automated Coaching

Alive-PD (Turnaround Health)

Alive-PD is an automated program that uses email, individualized web-based resources, smartphones, and interactive voice response technology to support weekly goal-setting, reminders, and tracking. Participants may join an optional virtual team of any size with other participants, and earn points through engagement and progress. Individuals and teams can compete to receive monetary rewards, with higher scores improving the likelihood of winning. There are no group sessions or personal contact from human coaches either in-person or remotely.[10] The system is designed to reduce the risk for diabetes though long-term changes in physical activity and diet. A detailed history is taken at the beginning on the program and a series of goals are set based on that personal profile. Both resistance training and aerobic activity are encouraged. Weight loss is encouraged, but it is not a primary goal of the intervention. Dietary changes focus on reducing added sugars, refined carbohydrates, saturated and trans fats and increasing fruit and vegetable intake.

The company sponsored a randomized trial of 339 patients with prediabetes. All participants were given brief advice about their risk for diabetes and the value of physical activity and dietary changes to reduce their risk. Participants in the control group were waitlisted to start the Alive-PD program in six months. The characteristics of the participants were balanced at baseline. Follow-up was 86% complete at six months and similar in the two groups. At six months, the Alive-PD group had lost more weight (3.6% versus 1.3%, p<0.001) and had greater reductions in fasting plasma glucose (-7.4 versus -2.2 mg/dL, p<0.001) and in HbA1c (-0.26% versus -0.18%, p<0. 001). The decrease in HbA1c was modest but twice that observed in the DPP Trial.

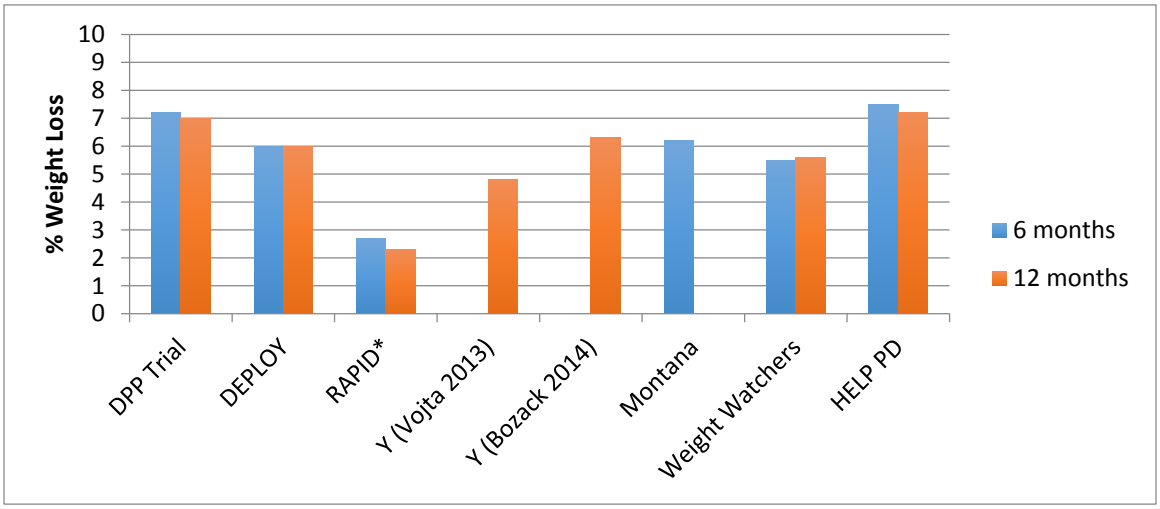
Clinical Benefits

Weight Loss

Weight was measured objectively in most studies either during in-person visits or via an automated electronic scale (Appendix Table H8). There is one exception: the large observational study using administrative data in the Y (Vojta 2013)[32] that did not report how weight was measured. The average percentage weight loss at six and 12 months follow up is summarized in Figures 5-7. The first set of bars in each figure represents the results from the original DPP Trial to serve as a reference. Figure 5 summarizes the weight loss results for the programs using in-person group coaching to deliver the diabetes prevention intervention. Weight loss was consistently in the 5-7% range across the studies with the DPP and the HELP-PD studies at the upper end of the range, with one exception. In the RAPID trial, a DPP-based study in the Y system, weight loss was only in the 2-3% range (estimated from other results because percentage weight is not reported), though this was greater than that observed in the control group (p<0.001). This likely reflects the design of the

study, which was an "invite to participate design." In the DPP lifestyle arm of the study, 37% of participants did not attend any sessions. Among those who completed at least nine of the 16 core group sessions, the weight loss was 5.3 kg or approximately 5% of baseline weight.

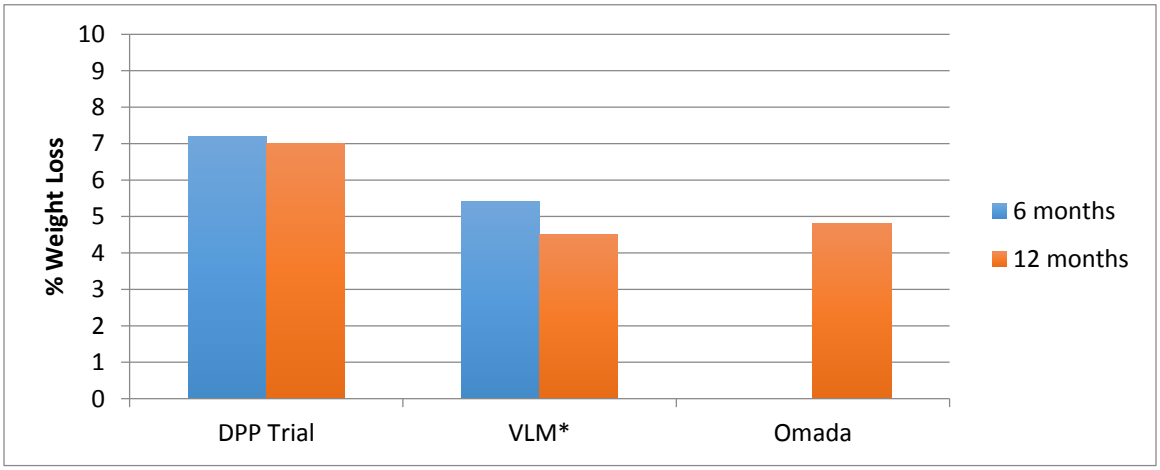
Figure 5. Percentage Weight Loss at Six and 12 Months for In-person Group Coaching compared with the DPP Trial



* Estimated from results in publication

The weight loss results for the two programs using a digital with human coaching design are summarized in Figure 6. The VLM study did not report percentage weight loss overall or in the eight participants with prediabetes. The average weight loss for the 45 trial completers was 4.8 kg at 12 months, which was about a 4.5% of the initial weight of the participants (estimated from data and figures in the published results). In the Omada trial, the average weight loss at 12 months was 4.8%.

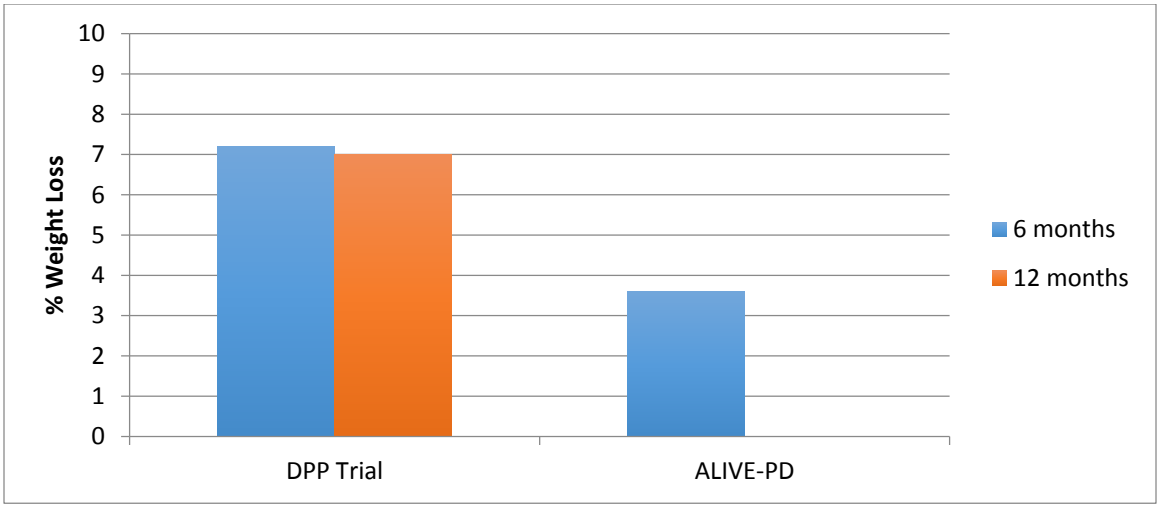
Figure 6. Percentage Weight Loss at Six and 12 Months for Digital with a Human Coach compared with the DPP Trial



* Estimated from results in publication

The weight loss results for the one program using a digital with fully automated coaching design are summarized in Figure 7. The Turnaround Health Alive-PD study reported a 3.6% weight loss at six months, which is only about half the weight loss reported in the DPP Trial at six months. This may reflect the lack of a mandatory weight loss goal-setting component in their program. Participants using Alive-PD may also continue to lose weight after six months, though this pattern of weight loss has not been observed in the DPP Trial or the other translations of the DPP.

Figure 7. Percentage Weight Loss at Six and 12 Months for Digital with Fully-automated Coaching Compared with the DPP Trial



Half of the available studies reported some measure of change in glycemic control during follow-up (see Appendix Table H9). In the original DPP Trial study, there was only a small reduction in HbA1c (~-0.1% versus ~+0.1%, p<0.001) and in FPG (~-5 mg/dL versus ~+1 mg/dL, p<0.001) at one year in the lifestyle group. In the DEPLOY and Weight Watchers studies, no significant differences were noted between intervention and control subjects in measures of glycemic control. However, the HELP-PD study reported changes in FPG (-4.5 mg/dL versus -0.6 mg/dL control, p<0.001) at 12 months.

Among the digital with a human coach programs, only the Omada study reported results, but the change in HbA1c (-0.4% at 12 months, no control) was the largest reported of any program including the original DPP Trial.

Interestingly, even though the Alive-PD program (digital with fully automated coaching) reported a relatively low percentage weight loss at six months (3.6% versus 1.3%, p<0.001), the reduction in HbA1c (-0.3% versus -0.2%, p<0.001)) and FPG (-7.4 mg/dL versus -2.2 mg/dL, p<0.001) were greater than in most of the other studies. This may reflect the greater focus on diabetes prevention and control as the primary goal of their dietary intervention rather than weight loss.

Diabetes Incidence

Most of the studies were of too short a duration to assess incident diabetes. The HELP-PD study (in-person with group coaching) reported that the diabetes incidence at two years was non-significantly lower in the lifestyle group than in the usual care group (3.0% versus 8.7%, p=0.10). The study did not have sufficient statistical power to detect a difference in diabetes incidence, though the greater than 50% observed reduction is likely to be clinically significant. In the DPP Trial, the cumulative incidence of diabetes was approximately 4% in the lifestyle intervention group and 13% in the usual care group.[34]

Other Cardiovascular Risk Factors

The DPP Trial reported reductions in blood pressure and improvements in total and HDL-cholesterol levels (Appendix Table H10). These improvements, though small, could contribute to an overall reduction in cardiovascular disease independent of the reduction in diabetes incidence. Among the in-person group coaching programs, the DEPLOY study reported greater improvements in cholesterol than those reported in the DPP Trial. The Weight Watchers study reported similar reductions in blood pressure compared with the DPP Trial and a greater increase in HDL-cholesterol, but also a small increase in total cholesterol.

Finally, the VLM study (digital with human coaching) reported twice the reduction in systolic blood pressure compared with the DPP Trial, but a slight increase in diastolic blood pressure. None of the other digital programs reported changes in blood pressure or cholesterol levels.

Harms

There was no excess rate of adverse events or serious adverse events in participants randomized to the lifestyle intervention in any of the randomized trials. The DPP Trial and other RCTs specifically assessed myalgias, arthralgias, fractures, and other musculoskeletal complaints potentially arising from lifestyle interventions, and no significant increases were observed for participants in the lifestyle group.

Subgroup Analyses

The original DPP Trial did not find any difference in the efficacy of the intensive lifestyle intervention by sex, race, ethnicity, body mass index, or initial FPG or OGTT level. Older participants in the lifestyle group appeared to have greater weight loss and a greater reduction in incident diabetes than younger participants. In the DPP Trial, the reduction in diabetes comparing the lifestyle intervention to placebo was 48% for participants ages 25-44 years, 59% for those 45-59 years, and 71% for those ages 60 years and older. This finding was consistently reported in the subsequent implementation trials. Older participants tend to attend more sessions and lose more

weight. This is likely to translate into a greater reduction in incident diabetes. This is particularly relevant for the Medicare population, which may benefit disproportionately from such lifestyle interventions.

Controversies and Uncertainties

The original DPP Trial clearly demonstrated that an intensive lifestyle intervention is more effective than both a drug (metformin) and usual care at preventing or delaying the onset of diabetes and that weight loss was the primary mediator of diabetes prevention/delay, not physical activity. Subsequent translational studies, including those summarized above, have demonstrated that real-world lifestyle interventions can deliver significant weight loss that is sustained for a year. However, the degree of weight loss is somewhat less than that attained by participants in the DPP Trial, and long-term sustained weight loss has not yet been demonstrated in these translational studies. The primary uncertainty is whether the one-year weight loss observed in these studies will lead to a significant reduction in the incidence of diabetes in these patients and whether the reduction (or delay) in the diagnosis of diabetes will result in meaningful reductions in the complications of diabetes for these patients.

At 15 years of follow-up, there was no reduction in either microvascular disease or cardiovascular disease in the DPP Trial despite ongoing weight loss maintenance classes. Between-group differences between the lifestyle and placebo groups of the DPP Trial may be diluted because the lifestyle intervention was offered to participants in all three groups at the end of the initial three years of the trial, although it was delivered in a group setting rather than individually. The lifestyle intervention was delivered to 57% of the original placebo group, 58% of the original metformin group, and 40% of the original lifestyle group. In the Chinese Da Qing study, it took 23 years before a reduction in cardiovascular mortality was observed.

A second uncertainty arises from the definition of prediabetes. In clinical practice, patients with prediabetes are usually diagnosed by measurement of FPG. In the US, the ADA defines an FPG of 100-125 mg/dL as prediabetes, but the WHO definition requires an FPG of 110-125. Patients with an FPG of 100-109 mg/dL are at lower risk for progression to diabetes and may receive less benefit from intensive lifestyle interventions.

In addition, critics of the term “prediabetes” have raised concerns about the adverse effects of labeling patients given that those with prediabetes are at high risk for diabetes but do not yet have a diagnosed disease. A 2014 criticism published in *The BMJ* asserted that “pre-diabetes could be defined as a risk factor for developing a risk factor.”[35] The WHO recognizes this concern and recommends that the health care community use the term “intermediate hyperglycemia” rather than prediabetes.[55] Since estimates suggest that approximately one-third of US adults (86 million people) have prediabetes and the majority of those individuals will not go on to develop diabetes, the impact of even small individual harms of labeling could be substantial on a population basis.

Summary

The 10 studies of CDC-recognized programs reviewed above consistently demonstrate that intensive lifestyle interventions produce 4% to 6% weight loss, which should translate into a 40% to 50% reduction in type 2 DM over a three-year time horizon based on the DPP Trial results. In addition, the lifestyle interventions produce small improvements in blood pressure and cholesterol, which may reduce cardiovascular events. The majority of the translational programs used an in-person group coaching approach to deliver the content of the core DPP lessons, and group support may enhance the efficacy of the intervention. However, the digital approaches reported similar reductions in body weight and improvements in cardiovascular risk factors. There is not clear evidence that one approach is more efficacious than another at either weight loss or diabetes prevention.

It is also important to point out that the different types of DPP implementation that are now being used may have differential effectiveness in various groups of patients. Some patients may be more willing to enroll and stay engaged with online programs, while others may respond more positively to in-person group-based programs. A priority for the prevention community should be research into the potential for segmentation of the at-risk population and targeting of different styles of DPP, to maximize effectiveness and minimize the costs of delivering DPP in broader settings.

We judge the evidence for the CDC-recognized intensive lifestyle programs using an in-person group coaching design to provide an incremental or better (B+) net health benefit when compared to usual care for patients with prediabetes. There is no question that these programs yield modest weight loss in the short term compared with usual care. However, there is moderate certainty of a net benefit because of the uncertainties about the long-term durability of weight loss and the long-term improvements in health from the modest weight reductions demonstrated after one to two years of follow-up in the published studies.

We also judge the evidence for the CDC-recognized intensive lifestyle programs using a digital with human coach design to provide an incremental or better (B+) net health benefit when compared to usual care for patients with prediabetes. There is more uncertainty in this judgment than that for in-person group coaching because the number of studies is smaller (two) and because there are no good quality trials. However, there is clearly modest weight loss with these programs through two years compared with usual care that is similar in magnitude to that observed with the in-person group coaching programs. There is uncertainty about the long-term durability of weight loss and subsequent long-term health improvements similar to that described for the in-person group counseling programs.

We judge the evidence for the CDC-recognized intensive lifestyle programs using a digital with fully-automated coaching design to provide comparable or better (C+) net health benefit when compared to usual care for patients with prediabetes. There is greater uncertainty of a net benefit

for the fully-automated approach because there is only one trial, it only reported six-month outcomes, and the weight loss was qualitatively less than that observed in the original DPP Trial and the majority of the other translational programs. However, it was a high-quality randomized trial that showed statistically significant improvements in body weight and glycemic control compared with usual care.

We judge that there is Insufficient Evidence (I) to distinguish the efficacy of any one approach (in-person group counseling; digital with a human coach; digital with fully-automated counseling) from the others. There are no randomized trials or cohort studies that directly compare any two of the approaches, and the evidence base is currently too sparse to perform a network meta-analysis.

5. Other Benefits or Disadvantages

Our reviews seek to provide information on other benefits or disadvantages offered by the intervention to the individual patient, caregivers, the delivery system, other patients, or the public that would not have been considered as part of the evidence on comparative clinical effectiveness. Examples include but are not limited to:

1. Methods of administration that improve or diminish patient acceptability and adherence
2. A public health benefit, e.g., reducing new infections
3. Treatment outcomes that reduce disparities across various patient groups
4. More rapid return to work or other positive effects on productivity (if not considered a benefit as part of comparative clinical effectiveness)
5. New mechanisms of action for treatments of clinical conditions for which the response to currently available treatments varies significantly among patients for unknown reasons (substantial heterogeneity of treatment effect)

The primary additional benefit would be the public health benefits that may result from decreasing the weight and increasing the physical activity of a large segment of the population. In addition to the likely reductions in diabetes and cardiovascular disease described above, there may be reductions in some of the many complications of obesity, including arthritis, sleep apnea, and esophageal reflux disease. In addition, exercise has been proposed to improve mental health and quality of life, and to decrease long-term disability. Further, the availability of DPPs in a variety of formats (in-person, digital) and increasingly, using culturally-appropriate curricula, that can be selected to best meet an individual participant's needs may help to reduce disparities by improving access to DPPs.

6. Comparative Value

6.1 Overview

We reviewed the published literature for analyses that have examined the economic impact of diabetes prevention programs in the US with full or pending recognition from the CDC DPRP. This included studies of the cost to initiate and operate DPPs and/or specific components of such programs, analyses of the costs that are potentially offset through the use of such programs (e.g., reduced downstream medical costs), and cost-effectiveness analyses (CEAs). This section of the report summarizes what is currently known in the literature about the economic impact of DPPs and specific components of those programs, the strength and validity of that evidence, and where gaps in knowledge still exist.

We also explored the potential health system budget impact of DPPs over a shorter-term time horizon, utilizing published or otherwise publicly-available information on program planning, implementation, and ongoing treatment costs; any cost offsets; and the potential population eligible for such programs. These budget impact analyses assumed a specific program "uptake" rate over a five-year period for specific populations of interest, based on the availability of relevant data. Our analysis estimates the potential budget impact of broader implementation of DPPs and allows assessment of any need for managing the cost of such interventions. More information on ICER's methods for estimating product uptake and calculating potential budget impacts can be found at: http://icer-review.org/wp-content/uploads/2016/02/Slides-on-value-framework-for-website-v4-13-16.pdf.

6.2 Prior Published Evidence on Costs and Cost-Effectiveness of Diabetes Prevention Programs

Cost-Effectiveness Analyses

Li et al. conducted a systematic review of economic analyses of "diet and physical activity promotion programs with at least two sessions over at least three months delivered to persons at increased risk for type 2 DM."[36] This was an update of an earlier review by Li and colleagues that compiled published CEAs of ADA-recommended interventions to prevent, delay the development of, and control diabetes, from 1985 through May 2008.[103] Cost-effectiveness of these programs was assessed in 22 studies (eight of which were US-based). Overall, the median cost per quality-adjusted life-year (QALY) gained for the eight US-based analyses was $9,824, with an interquartile range of $1,930 to $41,982 per QALY gained. However, the authors noted that few studies included information on recruitment costs, or on the cost to implement and scale up these programs. In

addition, only two studies had examined the “cost-effectiveness of translational programs implemented in community and primary care settings” in the US.

Most of the cost-effectiveness analyses of DPPs in the US have been performed by the DPP Research Group that was involved with the original DPP Trial, using a simulation model based on data from the DPP Trial and other sources, though economic evaluations of several other DPP implementations have also been published. We have summarized the results of economic evaluations of the DPP Trial and other DPP types from a health care system perspective in Table 5 and in the text below. Further details, including cost-effectiveness results from a societal perspective, are reported in Appendix Table I1.

Table 5. Overview of Evaluations of DPP Cost-Effectiveness, Health-Care System Perspective

Reference	Name	Comparator	Time Horizon	Population	ICER ($/QALY)
In-person, Individual Coaching					
DPP Research Group 2003	DPP Trial	Placebo	3 years	DPP Trial	$32,000
	Metformin	Placebo	3 years	DPP Trial	$102,200
DPP Research Group 2012	DPPT/DPPOS	Placebo	10 years	DPP Trial, DPPOS	$13,000
	Metformin	Placebo	10 years	DPP Trial, DPPOS	Cost-saving
	DPP Trial/DPPOS	Metformin	10 years	DPP Trial, DPPOS	$14,900
Herman 2005	DPP (simulation)	Placebo	Lifetime	Age ≥ 25 with IGT	$1,100
	Metformin	Placebo	Lifetime	Age ≥ 25 with IGT	$31,300
Hoerger 2007	DPP for IGT+IFG	No screening	Lifetime	Age 45-74, BMI ≥ 25 kg/m^2	$8,200
	DPP for IGT or IFG	No screening	Lifetime	Age 45-74, BMI ≥ 25 kg/m^2	$9,500
	DPP for IGT or IFG	DPP for IGT+IFG	Lifetime	Age 45-74, BMI ≥ 25 kg/m^2	$10,200
Eddy 2005 (Archimedes)	DPP	No prevention	30 years	Adults at high risk for diabetes	$143,000
In-person, Group Coaching					
DPP Research Group 2003	DPP Trial as group	Placebo	3 years	DPP Trial	$9,000
DPP Research Group 2012	DPP Trial as group	Placebo	10 years	DPP Trial, DPPOS	$1,500
Herman 2005	DPP as group (simulation)	Placebo	Lifetime	Age ≥ 25 with IGT	Cost-saving
Hoerger 2007	DPP group for IGT+IFG	No screening	Lifetime	Age 45-74, BMI ≥ 25 kg/m^2	Cost-saving
	DPP group for IGT or IFG	No screening	Lifetime	Age 45-74, BMI ≥ 25 kg/m^2	$267
Eddy 2005 (Archimedes)	DPP group ($217/yr)	No prevention	30 years	Adults at high risk for diabetes	$27,000
Hinnant 2016 claims analysis	DEPLOY	Usual care	2 years	Medicare beneficiaries with prediabetes	Cost-saving
Spitalnic 2016 budget impact	DEPLOY (Medicare expansion)	No Medicare expansion	Lifetime	Medicare beneficiaries age 65-75	Cost-saving*
Digital, Human Coaching					
Su 2016 ROI analysis	Omada	Usual care	10 years	Adults with prediabetes & BMI ≥25kg/m^2	Cost-saving (positive ROI)
Smith 2016	VLM	Usual care	10 years	Prediabetes (BMI ≥ 25 kg/m^2 and ≥ 1 CVD risk factor)	$7,800
Digital, Fully Automated Coaching					
(No published cost-effectiveness analyses identified)					

*Cost-saving if mortality effects excluded (as for Medicare certification); approximately cost-neutral if included

BMI: body mass index, CVD: cardiovascular disease, IFG: impaired fasting glucose, IGT: impaired glucose tolerance, ILI: inventive lifestyle intervention, ROI: return on investment

In-person, Individual Coaching

DPP Trial

The DPP Research Group has conducted multiple analyses based on the DPP Trial. In summary, from a health system perspective, the cost per QALY for the intensive lifestyle intervention decreased as the time horizon increased, from $32,000/QALY at three years,[37] to $13,000/QALY at 10 years,[38,39] and $1,100/QALY using a lifetime time horizon.[40] Further details on these studies are provided below.

The DPP Research Group conducted a within-trial CEA of the DPP Trial,[37] comparing lifestyle intervention and metformin to placebo over a three-year time horizon. From a health system perspective (i.e., including only direct medical costs), the DPP Trial intervention was estimated to cost approximately $2,300 more and provide approximately 0.07 additional QALYs than placebo, or approximately $32,000 per QALY gained. From a societal perspective (direct medical, direct non-medical, and indirect costs included), the DPP Trial intervention was found to cost $52,300 per QALY gained. In contrast, the metformin intervention was estimated to cost approximately $102,000 per QALY gained from both the health system and societal perspectives.

In 2012 (with a 2013 erratum), the DPP Research Group conducted a 10-year within-trial CEA of the DPP and subsequent Outcomes Study (DPPOS), comparing lifestyle intervention and metformin to placebo.[38,39] From a health system perspective, the DPP Trial intervention was found to cost approximately $13,000 per QALY gained compared with placebo. From a societal perspective, the DPP Trial intervention was found to cost approximately $19,800 per QALY gained. Metformin was cost-saving compared to placebo for both perspectives. The discounted incremental cost-effectiveness ratios for the DPP Trial intervention compared to metformin were approximately $14,900 and $45,900 per QALY for the health system and societal perspectives, respectively.

Herman and colleagues[40] in the DPP Research Group modeled the lifetime cost-effectiveness of the DPP intervention compared to placebo in individuals age 25 and older with impaired glucose tolerance (IGT) using a Markov simulation model with inputs from data collected for the DPP Trial as well as published data. Cost-effectiveness ratios for the DPP Trial intervention were estimated to be approximately $1,100 per QALY gained from a health care perspective, and approximately $8,800 per QALY gained from a societal perspective. Cost-per-QALY ratios for the metformin intervention were approximately $31,300 and $29,900 for the health system and societal perspectives, respectively. The major limitation of this analysis is that it required the assumption that the DPP Trial intervention's costs and effectiveness persisted over a lifetime horizon.

Hoerger et al. (2007)[104] used the DPP Research Group simulation model to evaluate the lifetime cost-effectiveness of different screening strategies for prediabetes in adults age 45-74 who were overweight or obese (BMI ≥25 kg/m^2) for enrollment in the DPP Trial intervention. They compared

three strategies from a health system perspective: no screening; screening followed by the DPP Trial intervention for individuals with IGT plus IFG; and screening followed by the DPP Trial intervention for individuals with IGT and/or IFG (the latter category represents broader eligibility for enrollment). They reported a cost per QALY gained of $8,181 for the strategy treating IGT plus IFG compared to no screening, and $9,511 for the strategy treating IGT and/or IFG compared to no screening. The incremental cost-effectiveness ratio for the latter strategy compared to the former was $10,167 per QALY gained. If the DPP Trial intervention was provided to groups (i.e., at lower cost), the IGT plus IFG screening strategy was estimated to be cost-saving and the IGT and/or IFG strategy to cost $267 per QALY gained.

In contrast to the above analyses, Eddy et al. conducted another CEA of the DPP Trial intervention using the Archimedes model, which simulates detailed anatomic and physiologic components of several diseases.[41] This analysis compared no prevention to the DPP Trial intervention, lifestyle intervention after diagnosis of diabetes, and metformin. Over a 30-year time horizon, they estimated that the DPP Trial intervention would cost approximately $143,000 per QALY gained from a health system perspective, and approximately $62,600 per QALY from a societal perspective, and that metformin and delaying lifestyle intervention until diabetes diagnosis would be more cost-effective (at $35,500/QALY and $24,500/QALY using a health system and societal perspective, respectively). The incremental cost-effectiveness of the DPP Trial intervention compared to delayed lifestyle intervention was estimated to be approximately $201,800/QALY. In sensitivity analyses, they concluded that the DPP Trial intervention would be cost-effective (i.e., <$50,000/QALY) relative to the alternative strategies only if the program cost could be reduced to approximately $210 per person per year.

There are several explanations for the differing results found in the DPP Research Group and Eddy et al. analyses.[105,106] In addition to using different types of simulation models and assumptions, Eddy et al. assumed that the clinical benefits of the DPP would diminish over time and that there would also be a lower rate of glycemic progression over time (i.e., slower progression from prediabetes to diabetes, and from diabetes diagnosis to complications). Their health system perspective analysis also assumed turnover in health plan enrollment over time, which would lead to higher estimated cost-effectiveness ratios than in the DPP Trial evaluations. This may also explain why Eddy et al. found lower cost-effectiveness ratios from a societal vs. health system perspective, as health plan turnover rates are not relevant in a societal analysis.

In-person, Group Coaching

DPP Trial

As part of the DPP Research Group's within-trial CEA of the DPP Trial,[37] the DPP as "might be implemented in routine clinical practice" (i.e., as a group rather than individual intervention, and with lower costs but equal effectiveness) was estimated to cost $4,500 per diabetes case prevented

and $9,000 per QALY gained from a health system perspective; from a societal perspective, the intervention was estimated to cost $13,200 per diabetes case delayed or prevented, and $29,100 per QALY gained. A similar group assumption was made in their 10-year evaluation of the DPP Trial/DPPOS,[38,39] with resulting cost per QALY ratios of approximately $1,500 from a health system perspective and $8,400 from a societal perspective. In their evaluation of the lifetime cost-effectiveness of the DPP Trial intervention, Herman and colleagues[40] also estimated the impact if costs could be reduced by implementing the lifestyle intervention in groups of 10 participants rather than one-on-one coaching, assuming equal clinical effectiveness. In that scenario, they estimated that the program would be cost-saving over a lifetime, even if effectiveness were reduced by 50%, as downstream savings from reduced diabetes incidence would still be greater than the cost of the group intervention. Finally, Eddy et al.[41] also evaluated a scenario where the DPP was provided as a group intervention costing $217 per year; they estimated a cost/QALY gained of $27,000 from a health care perspective and $12,000 from a societal perspective.

Y DPP

RTI International[42] conducted an evaluation of the Y DPP as part of an assessment of CMS' Health Care Innovation Awards. The initiative aimed to provide a DPP to Medicare beneficiaries with prediabetes in community settings (17 Y centers across the US), with the objective of at least 5% weight loss and 150 minutes of physical activity per week for at least half of participants. Eighty-three percent of recruited participants enrolled; of those enrolled, 37% completed fewer than 9 sessions, 37.5% 9-16 sessions, and 25.4% 17 or more sessions. In a claims analysis using CMS's Chronic Conditions Data Warehouse through 2014, 1,679 participants were compared to propensity score-matched Medicare beneficiaries diagnosed with prediabetes. The authors found statistically significant differences in spending (lower for the treatment group) in the first five calendar quarters of the program, with no significant differences in subsequent quarters. The overall weighted average quarterly spending differential was calculated as $455 per member per quarter. Limitations of this preliminary analysis include the reliance on ICD-9 codes in claims data to identify beneficiaries with prediabetes. In addition, it was discovered that 34% of the DPP participants actually had a previous diabetes diagnosis recorded in claims data.

Because of the lack of long-term results for most DPP implementations, the CMS Office of the Actuary developed a model to project net costs per beneficiary over a lifetime horizon of expanding the DPP to Medicare beneficiaries with BMI ≥ 25 kg/m^2 and fasting plasma glucose of 110-125 mg/dL, as detailed in a Certification of Medicare DPP memorandum.[43] They assumed that the program would have mean payments per participating beneficiary of $300 in year one, $150 in years two and three, and $100 in subsequent years. The model estimated net costs or savings per year from lowering the probability of progression to diabetes and thus delaying diabetes-related costs, and it assumed that the Medicare DPP expansion would be somewhat less effective than the DPP Trial because it was less intensive. Specifically, the model assumes 50% diabetes risk reduction

in year one, with a steady decrease to 20% risk reduction in years 7 and following. Their analysis estimated that near-term savings would be offset by higher Medicare spending due to lower mortality, making it unclear whether the DPP expansion would break even over a lifetime horizon. Ignoring the mortality improvement (as required in the certification process) suggested that the DPP would reduce Medicare expenditures.

Digital, Human Coaching

Omada (Omada Health)

A recent analysis examined the return on investment (ROI) of the Omada digital DPP (previously called the Prevent program).[44] A Markov-based model with a 10-year time horizon was used to compare Omada DPP participants with propensity score-matched community controls with prediabetes. Their simulation found a break-even point at three years, with a positive ROI of $1,565 at five years. One limitation of this study is that it relied on only 26 weeks of weight loss data from Omada participants, which required assumptions about longer-term weight loss.

VLM (Canary Health)

Smith et al. have assessed the cost-effectiveness of the VLM DPP using a Markov model with a 10-year time horizon.[45] Costs and changes in weight came from a pre-post study of the VLM intervention, which estimated an incremental cost of $458 and incremental gain of approximately 0.06 QALYs compared to usual care in a hypothetical cohort without diabetes. They estimated that the intervention would cost approximately $7,800 per QALY gained from a health system perspective and approximately $18,300 from a societal perspective. Using a $100,000 per QALY threshold, the intervention was found to be cost-effective in over 95% of model iterations in a probabilistic sensitivity analysis. However, it should be noted that these results are based on data from one study using a one-year before/after design in only 50 patients, 14 of whom already had diabetes.

Digital, Fully-automated Coaching

We were unable to locate any publicly-available CEAs or detailed costing studies examining digital DPPs with fully-automated coaching.

6.3 Potential Budget Impact

We also estimated the potential budget impact of different types of DPPs among candidate populations for such treatment in the US. Our estimates are based on those found in the published and grey literature. In general, relevant cost data were most robust for in-person individual and group programs, coming from published articles with measured costs; results for digital human-

coached programs came from a combination of models and claims-based analyses reported in published articles and conference abstracts. No published or publicly-presented data on diabetes incidence or cost offsets were available for digital fully-automated DPPs, so we used unpublished data provided by one such program in a separate scenario analysis. We combined estimates of the mean cost per participant with estimates of the prediabetes population potentially eligible for DPPs, as well as different assumed levels of uptake of such programs.

Potential Budget Impact Model: Methods

Potential budget impact was defined as the total incremental cost of DPPs for the enrolled population, calculated as the incremental health care costs of DPPs minus any health care costs that were offset in enrolled participants. All costs were undiscounted and estimated over one- and five-year time horizons. The five-year timeframe was of primary interest, given the potential for cost offsets to accrue over time. The potential budget impact analysis included the entire candidate population for DPPs in the US, which was considered to include adults with prediabetes, using the ADA definition of individuals with IFG (i.e., between 100 and 125 mg/dL). We also considered the case where prediabetes was defined using the WHO criterion of 110-125 mg/dL.

To estimate the size of the potential candidate population for DPPs, we used estimates of the prevalence of prediabetes in US adults aged 20 and older that were generated from National Health and Nutrition Examination Survey (NHANES) 2009-2010 data.[46] These prevalence estimates were applied to the projected US adult population in 2016 to estimate the total number of people with prediabetes. This resulted in a candidate population size of approximately 93.7 million individuals in the US using 100 mg/dL as the cutoff, or of approximately 31.2 million individuals using 110 mg/dL.

In estimating potential budget impact, we recognized that not all individuals with prediabetes would have access to DPPs, and that not all those with access would be interested in enrolling in such programs. Therefore, our calculations assume that the utilization of such programs reaches only a relatively small fraction of the eligible population. To estimate the population size that would use DPPs, we assumed that some percentage of the eligible population would enroll in each year and that this percentage would stay constant over time (years one through five). Our assumed base case was that 10% of those eligible would enroll in and complete a DPP; we also varied these percentages to examine the potential budget impacts if 25% or 50% of eligible individuals were to utilize DPPs (see Figure 8).

The resulting population size after five years, assuming an estimated 10% uptake, was approximately 9.4 million using the 100 mg/dL criterion, and 3.1 million using the 110 mg/dL criterion. We assumed that it may take some time to ramp up the implementation of and recruitment into DPPs and assumed this would occur in equal proportions across the five-year timeframe (i.e., a 20% increase in capacity per year). For example, in the population estimated to have a 10% five-year uptake, 2% of individuals would be assumed to participate in a DPP each year.

Individuals participating in a program in year one would accrue all program costs and cost offsets over the full five years, but those initiating in other years would only accrue a proportional amount of these costs and cost offsets.

Next, we estimated the cost per participant of various types of DPPs compared to usual care. Specifically, we tabulated the average costs for DPPs that use in-person individual coaching (i.e., the original DPP Trial), in-person group coaching, and digital programs with human coaching. Preliminary estimates for digital fully-automated programs, supplied by the vendor, are reported separately, as no published data were available. Where available, annual costs and annual cost offsets for individual programs for years one through five were collected, and then an average within each of the four program types was calculated. Cost offsets included reductions in non-DPP related health care costs from any cause, including reduced diabetes incidence. The mean costs by program type, inflated to 2015 dollars, are shown in Appendix Table I2, along with sources.

The net cost per participant per year was then multiplied by the population assumed to be eligible at each uptake rate, and this was used to calculate the total potential budget impact of each type of DPP at various levels of uptake.

Potential Budget Impact Model: Results

Table 6 presents the potential budget impact at one year and five years of each DPP type in the candidate population, assuming implementation of a DPP for 10% of the eligible population at the end of five years.

Results from the potential budget impact analysis showed that, with the uptake assumptions mentioned above, approximately 1.9 million individuals would participate in a DPP in the first year. After one year, net annual costs per participant are estimated to be $1,902 for in-person individual and $117 for digital human-coached programs, with total one-year potential budget impact estimated to be approximately $3.6 billion for in-person individual and $220 million for digital coached programs. In contrast, in-person group programs were found to be cost-saving, with annual savings of $455 per person. Total one-year savings were $850 million for in-person group programs.

Over the entire five-year time horizon, 10% uptake would lead to approximately 9.4 million persons enrolled in a DPP for one or more years. Across this timeframe, the weighted potential budget impact (i.e., adjusted for differing periods of utilization and associated cost-offsets) is approximately $2,800 per participant for in-person individual programs, leading to an average annual potential budget impact of approximately $5.2 billion. Estimated savings from enrollment in in-person group programs continue to accrue over five years, resulting in estimated savings of $2.1 billion per year.

In contrast to the one-year horizon, where digital coached programs were estimated to increase budgets by $220 million, these programs became cost-saving over the longer term due to lower

program costs and higher cost offsets in subsequent years. Over five years, digital human-coached programs would generate net savings of approximately $600 per participant enrolled, leading to annual cost savings of approximately $1.2 billion. Net costs for the full five-year time horizon are described in detail in Appendix Table I3.

Table 6. Total Potential Budget Impact (BI) of DPPs Based on 10% Uptake at One and Five Years Using FPG of 100-125 mg/dL (n=9,366,203)*

DPP Type	Analytic Horizon = 1 Year			Analytic Horizon = 5 Years		
	Number Enrolled (millions)	Annual BI per Participant ($)†	Total BI (billions)	Number Enrolled (millions)	Weighted BI per Participant ($)*	Average BI per year (billions)
In-person, Individual Coaching	1.87	$1,902	$3.56	9.37	$2,793	$5.23
In-person, Group Coaching	1.87	-$455	-$0.85	9.37	-$1,146	-$2.15
Digital, Human Coaching	1.87	$117	$0.22	9.37	-$618	-$1.16

* Preliminary estimates for digital fully-automated programs are reported separately, as no published or publicly-presented data were available.

†Weighted budget impact calculated by subtracting cost offsets from DPP costs for one-year horizon. For five-year horizon, DPP costs and cost offsets apportioned assuming 20% of patients in uptake target initiate therapy each year

In the absence of robust, published results for digital automated DPPs, we performed a projection using unpublished six-month results for decreased diabetes incidence to estimate cost offsets from preventing or delaying cases of diabetes.[107,108] If decreases in HbA1c are used as the criterion for determining diabetes prevention or delay, digital fully-automated DPPs would be estimated to be cost-saving, with annual savings of $24 per person (annual program costs of $66 with a cost offset of $90 per person), and total one-year savings of approximately $40 million. Over a five-year time horizon, estimated potential budget savings would be approximately $130 million per year. If diabetes status was determined using FPG measures rather than HbA1c, there would be a greater reduction in diabetes incidence at one year and therefore a larger estimated cost offset of $455 per participant (for a net annual savings of $389 per person). Under this scenario, the estimated budget impact of digital automated DPPs would be similar to that of in-person group DPPs, with one-year cost savings of approximately $728.7 million and savings of approximately $2.2 billion per year over five years. The wide range of potential budget impacts estimated using these two measures emphasizes the uncertainty around the financial impact of digital automated DPPs.

Table 7 shows the potential budget impact at one year and five years for each DPP type in the candidate population using the 110 mg/dL criterion, with the assumption that 10% of the prediabetic population would participate in a DPP at the end of five years. We estimated that approximately 624,000 individuals would participate in a DPP in the first year. After one year, total

potential budget impact is estimated to be approximately $1.2 billion for in-person individual and $70 million for digital human-coached programs. Total one-year savings of approximately $280 million with in-person group programs were estimated.

Over the entire five-year time horizon, 10% uptake in the 110 mg/dL population would lead to approximately 3.1 million persons in a DPP for one or more years (i.e., approximately one-third the population size using the 100 mg/dL threshold). Over five years, average potential budget impact per year is approximately $1.7 billion for in-person individual programs. Estimated savings from enrollment in in-person group and digital human-coached programs over five years resulted in estimated annual savings of approximately $720 million and $390 million, respectively, reflecting the smaller candidate population size using the 110 mg/dL threshold. Net costs for the full five-year time horizon are described in detail in Appendix Table I4. Using the projection methods described above for digital automated programs, average potential cost savings over five years would be approximately $45 million and $729 million based on the HbA1c and FPG approaches, respectively.

Table 7. Total Potential Budget Impact (BI) of DPPs Based on 10% Uptake at One and Five Years Using FPG of 110-125 mg/dL (n=3,122,068)*

DPP Type	1-year Analytic Horizon			5 -year Analytic Horizon		
	Number Enrolled (millions)	Annual BI per Participant ($)†	Total BI (billions)	Number Enrolled (millions)	Weighted BI per Participant ($)*	Average BI per year (billions)
In-person, Individual Coaching	0.62	$1,902	$1.19	3.12	$2,793	$1.74
In-person, Group Coaching	0.62	-$455	-$0.28	3.12	-$1,146	-$0.72
Digital, Human Coaching	0.62	$117	$0.07	3.12	-$618	-$0.39

*Preliminary estimates for digital fully-automated programs are reported separately, as no published or publicly-presented data were available.

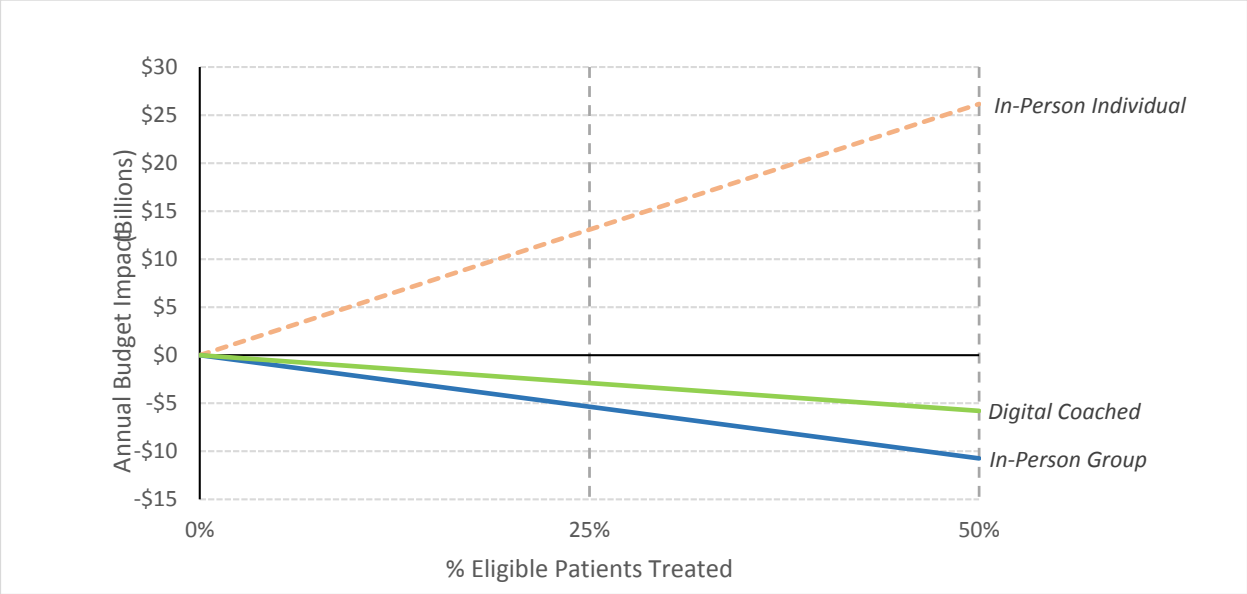
†Weighted budget impact calculated by subtracting cost offsets from DPP costs for one-year horizon. For five-year horizon, DPP costs and cost offsets apportioned assuming 20% of patients in uptake target initiate therapy each year

Figure 8 shows the relationship between varying uptake patterns and potential budget impact for each DPP type for the US population with FPG 100-125 mg/dL. The vertical axis shows the annualized potential budget impact, and the horizontal axis represents the percentage of eligible individuals participating over a five-year period. The colored lines demonstrate how quickly the annual potential budget impact changes with increasing percentages of individuals enrolled in the four different DPP types.

As can be seen in Figure 8, for the US population with FPG 100-125 mg/dL, the annualized potential budget impact is positive for individual in-person programs, and would increase to just over $25

billion with 50% of eligible individuals participating. In contrast, annual savings for digital human-coached and in-person group programs accumulate at much higher rates, reaching approximately $5.8 billion and $10.7 billion, respectively. Assuming 50% uptake in the US population with FPG 110-125 mg/dL would result in a similar pattern (see Appendix Figure I1), but with smaller annualized cost for individual in-person programs ($8.7 billion) and smaller annualized savings for digital coached ($1.9 billion), and in-person group programs ($3.6 billion).

Figure 8. Potential Budget Impact Graph for DPPs Provided to Varying Proportions of the US Population with FPG 100-125 mg/dL



Note: Colored lines represent the annualized potential budget impact of different uptake patterns (percent of eligible population enrolled) for each type of DPP.

6.4 Summary and Comment

With one exception,[41] the consensus in the literature is that findings for the cost-effectiveness of an in-person DPP at the individual level are well below commonly-accepted thresholds ($50,000 - $150,000 per QALY gained). Providing the program in a group setting appears to be cost-saving over time, with little or no apparent loss in effectiveness relative to individual coaching. Delivering the DPP via digital adaptations with human coaches also appears to be cost-effective or cost-saving, although these findings are based on fewer studies with only short-term effectiveness data. We were unable to find any published evaluations of the cost-effectiveness of digital fully-automated programs for delivery of a DPP. While online adaptations are less costly than in-person DPPs, longer-term studies are needed to determine whether online versions of the DPP will provide comparable effectiveness over time. In addition, it should be noted that analyses sometimes differed in how they defined program participation (e.g., enrollment vs. completion) and to the

relationship with program costs; more standardized definitions would make comparisons across program types more comparable.

Our estimates of the short-term potential budget impact of these programs were more variable and depended on using averages across relatively sparse data, especially for the digital programs. Using averages of the available data within program type and the assumptions in our analysis, in-person individual DPPs had positive annual budget impacts over five years, while in-person group and digital coached programs appear to be cost-saving in the short-term. We estimated that a digital fully-automated program was appeared to be cost-saving based on clinical extrapolations, but no published data were available for this category of programs.

A limitation of this analysis is that there was wide variation in 1) the sources of data and 2) the number and types of analyses performed, which may influence the comparability of results across program types. In addition, the definition of prediabetes introduces uncertainty into potential budget impact calculations. For one, the candidate population size is three times larger using the 100-125 mg/dL range of FPG. However, we would also expect diabetes incidence to be higher using the WHO definition (i.e., 110-125 mg/dL). While we were able to test the impact of differences in candidate population size on estimates of potential budget impact, there were unfortunately no data to distinguish program costs and performance between the two definitions of prediabetes.

It should also be noted that this analysis was based on annual program costs that did not include development or start-up costs for these programs, which may be substantial. One area where further research would be helpful is the tabulation of such costs, as well as detailed cost and cost-offset data from implementations of DPPs in different settings.

Furthermore, our estimates of levels of DPP uptake in the health care system by five years were based on arbitrary assumptions, so actual uptake may reach these levels more or less quickly. In addition, the costs used in our analysis came from a specific set of programs, and so may not be representative of the costs for such programs in other settings in the US.

Finally, further data on the long-term effectiveness of these programs in maintaining weight loss and diabetes risk reductions would confirm whether these programs will actually be cost-effective or cost-saving over time. This would be especially useful for the newer, digital adaptations of the DPP. There is also a need for data on the efficacy of maintenance modules of the digital programs, and a need to measure the efficiency of extending these programs to lower-risk groups.

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This is the first CTAF review of diabetes prevention programs.

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APPENDICES

Appendix A. Search Strategies and Results

Table A1. PRISMA 2009 Checklist

	#	Checklist item
TITLE		
Title	1	Identify the report as a systematic review, meta-analysis, or both.
ABSTRACT		
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.
INTRODUCTION		
Rationale	3	Describe the rationale for the review in the context of what is already known.
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).
METHODS		
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.

Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.
RESULTS		
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).
DISCUSSION		
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.
FUNDING		
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.

From: Moher D, Liberati A, Tetzlaff J, Altman DG. The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

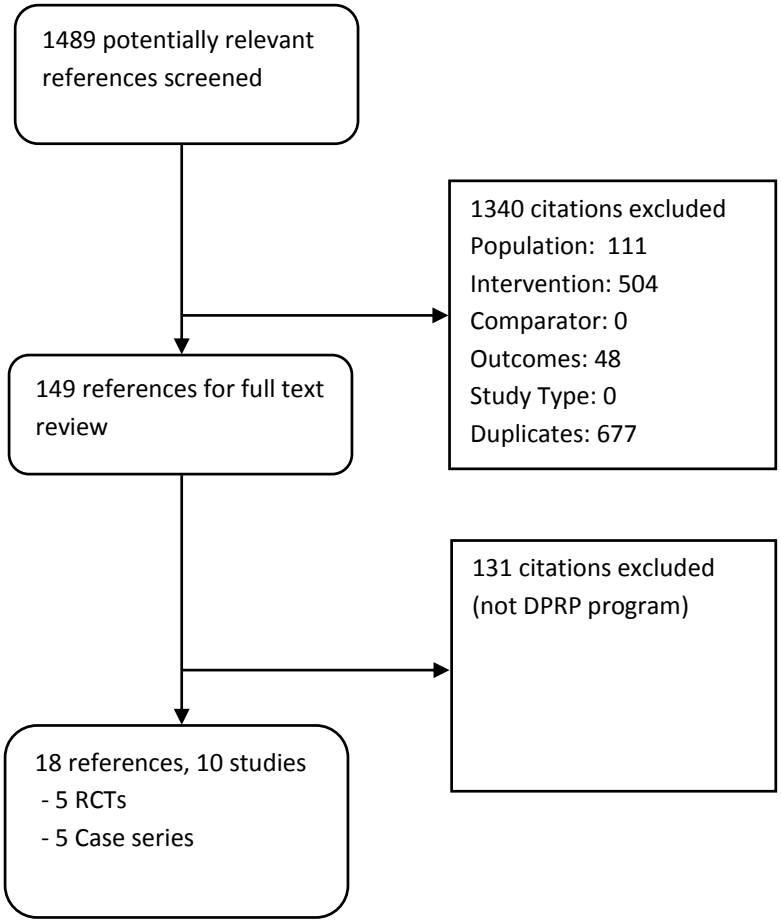
Table A2. Search Strategies for MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials, April 7, 2014 through April 7, 2016

The search strategy for this review was reproduced from the Balk et al., 2015 systematic review commissioned by the CDC.[15]

1	("pre-diabetes" or pre-diabet* or prediabet*).af.
2	exp prediabetic state/
3	(impaired and (fasting glucose or glucose tolerance)).af.
4	(impaired and fasting blood sugar).af.
5	("diabetes risk" or (risk adj6 diabetes)).af.
6	or/1-5
7	(((behaviour or behavior) and modification) or behavior therapy or lifestyle or lifestyle intervention or healthy eating or diet or weight loss or physical activity or resistance training or exercise or life style or healthy-living).af.
8	exp diet/ or diet therapy.sh. or exp exercise/ or exp exercise therapy/ or exp lifestyle/ or exp weight loss/ or exp behavior therapy/
9	*"Diabetes Mellitus"/pc [Prevention & Control]
10	or/7-9
11	(diabetes prevention program* or diabetes prevention study*).af.
12	randomized controlled trial.pt.
13	controlled clinical trial.pt.
14	randomized controlled trials/
15	Random Allocation/
16	Double-blind Method/
17	Single-Blind Method/
18	clinical trial.pt.
19	Clinical Trials.mp. or exp Clinical Trials/
20	(clinic$ adj25 trial$).tw.
21	((singl$ or doubl$ or trebl$ or tripl$) adj (mask$ or blind$)).tw.
22	Placebos/
23	placebo$.tw.
24	random$.tw.
25	trial$.tw.
26	(randomized control trial or clinical control trial).sd. or program evaluation.af.
27	(latin adj square).tw.
28	Comparative Study.tw. or Comparative Study.pt.
29	exp Evaluation studies/
30	Follow-Up Studies/
31	Prospective Studies/
32	(control$ or prospectiv$ or volunteer$).tw.
33	Cross-Over Studies/
34	or/12-33
35	exp cohort studies/ or exp prospective studies/ or exp retrospective studies/ or exp epidemiologic studies/ or exp casecontrol studies/

36	(cohort or retrospective or prospective or longitudinal or observational or follow-up or followup or registry).af.
37	case-control.af. or (case adj10 control).tw.
38	ep.fs.
39	or/35-38
40	((6 and 10) or 11) and (34 or 39)
41	(((Non-alcoholic or nonalcoholic) and Fatty Liver Disease) or hepatitis).af.
42	40 not 41
43	remove duplicates from 42
44	meta-analysis.pt.
45	systematic$ review$.mp. [mp=ti, ab, ot, nm, hw, ps, rs, ui, tx, kw, ct]
46	(systematic$ adj9 overview$).mp.
47	(meta-analys$ or meta analys$ or metaanalys$).mp. [mp=ti, ab, ot, nm, hw, ps, rs, ui, tx, kw, ct]
48	evidence review$.mp. [mp=ti, ab, ot, nm, hw, ps, rs, ui, tx, kw, ct]
49	or/44-48
50	"pre-diabetes".af.
51	prediabetes.af.
52	impaired glucose tolerance.af.
53	impaired fasting glucose.af.
54	insulin resistance.af.
55	or/7-11
56	6 and 12
57	remove duplicates from 13
58	43 or 57

Figure A1. PRISMA flow Chart Showing Results of Literature Search for Diabetes Prevention Programs



Appendix B. Key Informant Interviews

Table B1. List of Key Informant Organizations

Category	Organization
Payer	Anthem
	America's Health Insurance Plans
	Blue Shield of California
	California Department of Health Care Services
	Connecticut Department of Social Services
	UnitedHealth Group
Provider	Black Women for Wellness (Los Angeles)
	Canary Health
	Kaiser Permanente
	Noom, Inc.
	Omada Health
	Turnaround Health
	University of California, San Francisco
	YMCA of San Francisco
	YMCA of the USA
	Weight Watchers
Intermediary Organizations	Solera
Public Health	California Health Care Foundation
	California Department of Public Health
	Centers for Disease Control and Prevention, Division of Diabetes Translation
	Diabetes Advocacy Alliance
	Diabetes Coalition of California
	Integrated Healthcare Association
	National Association of Chronic Disease Directors
	Los Angeles Department of Public Health, Division of Chronic Disease and Injury Prevention
Purchaser	California Public Employees' Retirement System (CalPERS)
	Lowe's
	Pacific Business Group on Health
	Silicon Valley Employers Forum
Professional Society	American Diabetes Association
	American Association of Diabetes Educators

To develop a list of potential interviewees, we reviewed the policy literature and identified key groups of stakeholders relevant to diabetes prevention efforts. When conducting interviews with initial contacts, we sought recommendations for additional regional and national experts to include as part of our assessment. We conducted 34 30- to 60- minute telephone interviews using a semi-

structured guide (some key informant organizations participated in multiple calls). To help ensure that key barriers and solutions were included in our assessment, we performed a scan of the existing policy literature. Participation in the stakeholder interviews should not be construed as an endorsement of ICER's findings, and interviewees are not responsible for the final contents of this report.

Appendix C: Topic in Context Supplemental Information

Table C1. CDC Prediabetes Risk Assessment Questionnaire

Question	Yes	No
Are you a woman who has had a baby weighing more than 9 pounds at birth?	1	0
Do you have a sister or brother with diabetes?	1	0
Do you have a parent with diabetes?	1	0
Find your height on the chart (see table C2). Do you weigh as much as or more than the weight listed for your height?	5	0
Are you younger than 65 years of age and get little or no exercise in a typical day?	5	0
Are you between 45 and 65 years of age?	5	0
Are you 65 years of age or older?	9	0
Total points for all "yes" responses		

Reproduced from http://www.cdc.gov/diabetes/prevention/pdf/dprp-standards.pdf

Scores of nine or higher indicate high risk for prediabetes. Individuals with scores of three to eight points are not likely at risk for prediabetes, but are recommended to eat healthily, not smoke, be active, and lose weight if overweight.

Table C2. CDC Prediabetes At-Risk Weight Chart

Height	Weight (pounds)	Height	Weight (pounds)
4'10"	129	**5'8"**	177
4'11"	133	**5'9"**	182
5'0"	138	**5'10"**	188
5'1"	143	**5'11"**	193
5'2"	147	**6'0"**	199
5'3"	152	**6'1"**	204
5'4"	157	**6'2"**	210
5'5"	162	**6'3"**	216
5'6"	167	**6'4"**	221
5'7"	172		

Reproduced from http://www.cdc.gov/diabetes/prevention/pdf/dprp-standards.pdf

Table C3. Overview of Prevent T2 Curriculum

Reproduced from http://www.cdc.gov/diabetes/prevention/pdf/curriculum_toc.pdf

Topics Covered in First 6 Months

- Welcome to the Program
- Be a Fat and Calorie Detective
- Three Ways to Eat Less Fat and Fewer Calories
- Healthy Eating
- Move Those Muscles
- Being Active - A way of Life
- Tip the Calorie Balance
- Take Charge of What's Around You
- Problem Solving
- Four Keys to Healthy Eating Out
- Talk Back to Negative Thoughts
- The Slippery Slope of Lifestyle Change
- Jump Start Your Activity Plan
- Make Social Cues Work for You
- You Can Manage Stress
- Ways to Stay Motivated

Topics Covered in Second 6 Months

- Fats - Saturated, Unsaturated, and Trans Fat
- Food Preparation and Recipe Modification
- Healthy Eating - Taking it One Meal at a Time
- Healthy Eating with Variety and Balance
- More Volume, Fewer Calories
- Staying on Top of Physical Activity
- Stepping up to Physical Activity
- Balance Your Thoughts for Long-Term Maintenance
- Handling Holidays, Vacations, and Special Events
- Preventing Relapse
- Stress and Time Management
- Heart Health
- A Closer Look at Type 2 Diabetes
- Looking Back and Looking Forward

Appendix D. Clinical Guidelines

American Academy of Clinical Endocrinologists (AACE) / American College of Endocrinology (ACE), 2016[109]

Adults with prediabetes (i.e., FPG 100-125 mg/dL, OGTT 140-199, or with metabolic syndrome) should be provided behavioral counseling on diet, physical activity, sleep, behavioral support, and smoking cessation. The guidelines note that while weight loss is the primary goal of prediabetes therapy, patients with prediabetes should also work to bring lipid and blood-pressure levels to appropriate targets through behavioral change and pharmacotherapy. Medication-assisted weight loss may be appropriate for patients who meet more than one prediabetic criteria, and the guidelines recommend metformin or acarbose as low-risk options. If neither metformin nor acarbose are effective, thiazolidinedione (TZD) or a glucagon-like peptide-1 (GLP-1) receptor agonist should be used. In some cases, bariatric surgery may be appropriate to prevent or delay the progression of prediabetes to type 2 DM.

American College of Obstetricians and Gynecologists (ACOG), 2013[110]

All pregnant patients should be screened for gestational diabetes mellitus (GDM). All patients who test positive should begin nutrition therapy, and medication should be used when clinically appropriate. Women with GDM should be screened for prediabetes and type 2 DM six to 12 weeks post-pregnancy, and those who test positive should be referred to preventive therapy. Follow-up screenings at least every three years are recommended for women who have had GDM and a normal screening result for post-partum prediabetes or type 2 DM.

American Diabetes Association (ADA), 2016[111]

Adults who are overweight or obese (BMI ≥ 25 kg/m^2 or ≥ 23 kg/m^2 in Asian-Americans) and all adults over age 45 should be tested for prediabetes, which is defined as HbA1c of 5.7-6.4%, impaired glucose tolerance demonstrated by OGTT levels of 140-199 mg/dL, or FPG 100-125 mg/dL. Individuals who are diagnosed with prediabetes should participate in a diet and lifestyle modification program that follows the tenets of the DPP, namely 7% body weight loss and a minimum of 150 minutes of moderate-intensity physical activity each week. Physicians should monitor their patients with prediabetes at least once per year, and should screen for and treat any modifiable risk factors for cardiovascular disease. Third-party payers are encouraged to cover DPPs due to their demonstrated cost-effectiveness. In addition, the ADA suggests that digital versions of the DPP be considered alongside in-person implementations, noting that the CDC has recently begun to recognize these electronic offerings.

The guidelines recommend that women be tested for undiagnosed type 2 DM at the first prenatal visit, and for GDM at 24 to 28 weeks of pregnancy. The ADA recommends using either a 75g OGTT or a 50g non-fasting screen followed by a 100g OGTT for those who screen positive, and notes that the latter option is easier to administer as it does not require fasting. Women with a history of GDM should be tested for prediabetes or type 2 DM at least every three years, and individuals found to have prediabetes should be referred to a lifestyle intervention program or be prescribed metformin.

The ADA notes that evidence supports the use of metformin for individuals under the age of 60 with high risk for developing type 2 DM (e.g., individuals with a history of GDM, BMI ≥ 35, increasing HbA1c despite lifestyle intervention, with severe or progressive hyperglycemia).

American Heart Association (AHA) / American College of Cardiology (ACC) / The Obesity Society (TOS), 2013[112]

All adults who are obese or overweight should be counseled that high BMI and waist circumference increase the risk of developing cardiovascular disease, type 2 DM, and all-cause mortality. Physicians should advise adults who are overweight or obese with cardiovascular risk factors (e.g., hyperglycemia, hypertension, and hyperlipidemia) that sustained weight loss of 3-5% reduces the risk of developing type 2 DM. To achieve this goal, physicians should refer these patients to a high-intensity (i.e., ≥ 14 sessions in six months) comprehensive lifestyle management program of at least six months' duration to improve diet and physical activity. These programs should include counseling delivered by a trained professional at the individual or group level.

The AHA/ACC/TOS guidelines note that electronically-delivered programs may result in less weight loss compared to in-person programs, but that digital offerings are superior to no or minimal intervention. The guidelines recommend that commercially-available weight-loss programs be prescribed only if they have published, peer-reviewed evidence that demonstrates safety and efficacy. Individuals who successfully lose weight through lifestyle modification should participate in a long-term, comprehensive weight-loss maintenance program of at least one year's duration with in-person or telephonic guidance once or more per month to promote greater than 200 minutes of physical activity per week, weight monitoring, and a reduced-calorie diet.

Canadian Diabetes Association (CDA), 2013[113]

Individuals over the age of 40 or at high risk should be screened for diabetes every three years, with more frequent screening recommended for individuals at very high risk or with additional risk factors. Risk factors include, but are not limited to, a family history of type 2 DM, history of prediabetes or GDM, membership in a high-risk racial or ethnic group, dyslipidemia, and hypertension. The CDA defines prediabetes as IFG demonstrated by FPG of approximately 110-124 mg/dL, IGT demonstrated by two-hour OGTT of approximately 140-198 mg/dL, or HbA1c of 6.0-

6.4%. Individuals with IFG and IGT should enter a lifestyle modification program that promotes weight loss and regular physical activity, and the use of metformin or acarbose may be appropriate for individuals with IGT.

The Endocrine Society, 2008 and 2013[114,115]

Providers should screen patients for metabolic syndrome at least every three years by taking measurements of blood pressure, waist circumference, fasting lipid profile, and FPG.[115] Patients with prediabetes should be screened for type 2 DM every one to two years through FPG or OGTT tests. Lifestyle modification should be the first-line treatment offered to patients at increased risk for metabolic syndrome, and patients should be referred to a clinical program to reduce weight by 5-10% through a minimum of 30 minutes of physical activity five days per week, reduced caloric intake, and behavioral modification.

The Endocrine Society's 2013 guidelines for the treatment of GDM recommend that all pregnant individuals be screened for the condition through measurement of FPG, HbA1c, or an untimed random plasma glucose test before 13 weeks of gestation and again between weeks 24 and 28.[114] Women who have had GDM should take an OGTT six to 12 weeks post-pregnancy to detect prediabetes or DM, and women who receive normal results should repeat the test periodically and before subsequent pregnancies. All women who have had GDM should be counseled on lifestyle modifications to reduce the risk of developing type 2 DM.

Institute for Clinical Systems Improvement, 2014[116]

The Institute for Clinical Systems Improvement (ICSI) guidelines define prediabetes as one or more of HbA1c of 5.7-6.4%, FPG of 100-125 mg/dL, or OGTT of 140-199 mg/dL. Individuals who meet these criteria should be referred to a health professional (e.g., clinician, dietitian, nurse, pharmacist) for education and lifestyle modification therapy. Achievable goal-setting is encouraged, as is weight loss of 5-10% and 150 minutes per week of physical activity; ICSI recommends metformin for some patients, at least annual monitoring for the development of DM, and screening/treatment for modifiable risk factors of cardiovascular disease. Individuals found to have prediabetes should be screened for progression to type 2 DM annually.

National Institute for Health and Care Excellence (NICE, United Kingdom), 2012[117]

Validated, computer-based risk assessment should be conducted in all adults over the age of 40 excepting pregnant women; individuals aged 25-39 from high-risk ethnic or racial populations, again excepting pregnant women; and adults with conditions that increase the likelihood of developing type 2 DM. Health care professionals should administer FPG, OGTT, or HbA1c tests for adults who score highly on these questionnaires, and the guidelines list FPG of approximately 100-125 mg/dL or HbA1c of 6.0-6.4% as ranges indicative of high risk. Individuals with low to moderate risk should be

counseled to improve lifestyle factors to reduce risk, with brief interventions and referral to weight loss programs indicated for those with moderate risk. Those at high risk should be referred to a nearby evidence-based intensive lifestyle modification program. NICE recommends that individuals at low risk be tested every five years, those at moderate risk every three years, and those at high risk every year.

Lifestyle modification programs should include groups of 10 to 15 individuals at high risk; be developed in collaboration with communities to ensure content is delivered in a culturally-appropriate manner; ensure face-to-face contact (group, individual, or a combination) at least eight times over nine to 18 months for at least 16 cumulative hours; and should deliver lessons in a logical progression. Follow-up sessions are recommended for at least two years, and should occur at regular intervals. In terms of content, lifestyle modification programs should encourage at least 150 minutes of moderate-intensity physical activity each week, gradual weight loss to a BMI under 25 kg/m^2 or under 23 kg/m^2 for individuals of South Asian or Chinese descent, and a healthy diet. Metformin is considered appropriate for adults who continue to progress toward type 2 DM despite lifestyle modification or for individuals who are unable to participate in lifestyle modification programs due to disability or other medical reasons.

Primary Care Diabetes Europe (PCDE), 2010[118]

Screening is recommended for prediabetes or type 2 DM in Caucasians over the age of 40 and in individuals over the age of 25 from ethnic or racial groups at high risk for DM who also have at least one of the following risk factors: family history of DM, BMI greater than 25 kg/m^2, large waist circumference, and treated or untreated hypertension or dyslipedemia. In addition, screening is recommended in individuals with a history of GDM or temporary diabetes, cardio- and cerebrovascular disease, severe mental health problems, a history of impaired glucose tolerance or FPG, and women with polycystic ovary syndrome and a BMI ≥ 30 kg/m^2. Referral to treatment should be determined based on level of risk, and individuals with sufficient risk should enter an intensive lifestyle modification program that promotes sustained weight loss of 5-7%, at least 30 minutes of physical activity per day, and a healthy diet. Pharmacological treatment with metformin, acarbose, or orlistat is recommended as a second-line treatment for individuals with impaired glucose tolerance, and bariatric surgery may be considered for patients at high risk for type 2 DM or cardiovascular disease with a BMI ≥ 35 kg/m^2.

United States Preventive Services Task Force (USPSTF), 2014[69,70]

Adults aged 40 to 70 who are overweight or obese should be screened for abnormal blood glucose levels as part a cardiovascular risk assessment. Abnormal glucose levels are defined as HbA1c from 5.7-6.4%, FPG from 100-125 mg/dL, or OGTT from 140-199 mg/dL. Individuals who screen positive for glucose abnormalities should be referred to a behavioral counseling program to improve diet

and physical activity, and the USPSTF notes that there is insufficient evidence to demonstrate that pharmacological treatment produces the same wide-ranging benefits as behavioral modifications.

In a separate recommendation on behavioral counseling, the USPSTF recommends that all adults who are overweight or obese and have cardiovascular risk factors (e.g., impaired fasting glucose, hypertension, dyslipidemia, metabolic syndrome) be referred to intensive behavioral counseling for diet and physical activity, noting that this intervention reduces the incidence of DM.[69]

United States Department of Veterans Affairs (VA) / Department of Defense (DoD), 2009 and 2010[119,120]

Screening for prediabetes and DM is recommended in adults over age 45 and in all adults who are overweight or obese with additional risk factors (e.g., hypertension, dyslipidemia, history of GDM, sedentary lifestyle). Prediabetes is defined as FPG 100-125 mg/dL or HbA1c of ≥ 5.7% that is subsequently confirmed through FPG measurement. Individuals with prediabetes should be counseled on the implications of prediabetes and should be referred to a lifestyle modification program that promotes physical activity and weight loss of at least 5% of body weight through a reduced-calorie diet. If lifestyle modification therapy is unsuccessful, treatment with metformin or acarbose may be appropriate to delay the development of type 2 DM.

The 2009 VA/DoD guidelines for the management of pregnancy recommend that pregnant women be screened for GDM between weeks 24 and 28 of gestation via a 50g OGTT followed by a blood draw. Individuals with glucose levels between 130 and 140 mg/dL should take a three-hour, 100g OGTT to confirm the findings of the initial test. The guidelines do not include recommendations on postpartum care for women with GDM.

Appendix E. Public and Representative Private Insurer Coverage Policies

Few insurers currently cover CDC-recognized DPPs across all lines of business. While many commercial payers and self-insured employers offer some form of reimbursement for wellness programs that aim to achieve some of the same goals as DPPs, we have limited our survey of coverage policies to prevention programs that are recognized by the CDC or that deliver the CDC DPP curriculum. Given the rapidly changing landscape for coverage of DPPs, the following sections should be viewed as a "snapshot" of the status at the time of the report's publication.

Public Payers

Centers for Medicare & Medicaid Services (CMS)

We were unable to find any National Coverage Determinations or Local Coverage Determinations pertaining to California that relate to coverage of DPPs. However, on March 23, 2016 the Secretary of Health & Human Services announced that the CMS Office of the Actuary certified that the Y's DPP reduces Medicare costs without degrading quality of care, a step that paves the way for CMS to expand coverage of the program to Medicare beneficiaries nationwide.[43] The proposed rule will be available for public comment for several weeks and will likely go into effect in late 2016.[121] These efforts are based on the results of a demonstration funded by a nearly $12 million CMS Health Care Innovation grant to the Y to test a DPP model based on the CDC DPP curriculum.[43] This proposal closely follows the *Medicare Diabetes Prevention Act of 2015* (S. 1131/H.R. 2102), which was originally introduced in March 2013 by Senator Al Franken and Representative Susan Davis to expand coverage for DPPs to eligible seniors enrolled in Medicare.[122]

Medi-Cal, California's Medicaid agency, does not specifically cover DPPs using federal or state funds. The Montana Department of Public Health and Human Services is currently the only state Medicaid program to offer an adapted version of the DPP for individuals at high risk of CVD and diabetes. Results of a pre-post clinical trial demonstrated that older (>65 years) participants were significantly more likely than younger participants (<65 years) to remain active in the program, but the RR rates for CVD outcomes were similar between groups.[123] Other states, including Colorado, Kentucky, Louisiana, Maine, Minnesota, New Hampshire, Ohio, and Washington, offer DPPs through employee benefits programs.[72]

National Private Payers

Aetna

Aetna began a pilot DPP funded by the CDC in the fall of 2013 for 500 high-risk employees with metabolic syndrome.[124] The pilot program is part of a cooperative agreement with America's Health Insurance Plans (AHIP), along with other member organizations including EmblemHealth, Florida Blue, and Molina Healthcare, to implement the NDPP in four states over four years.[125]

Anthem

Anthem launched a DPP in collaboration with Solera Health, Inc. (formerly Viridian Health Management) in April 2015 to offer the program as a preventive benefit for its members in Colorado enrolled in ACA-compliant plans.[126,127]

Cigna

Cigna does not specifically cover any CDC-recognized DPPs. However, in 2013 Cigna launched a pilot program in partnership with BodyMedia, a company that produces an armband that tracks physiological data, to study the use of a fitness tracker as a tool to help prevent or delay the development of type 2 DM. An RCT will also be conducted, though we could not identify an associated trial on clinicaltrials.gov.[128]

Humana

Humana does not specifically cover any CDC-recognized DPPs. However, in partnership with Omada Health, Humana sponsored a study of 490 Medicare Advantage beneficiaries enrolled in the digitally-based Omada program,[129] which was designed to help patients reduce their risk of chronic diseases, including diabetes and heart disease.

UnitedHealth Group

UnitedHealth Group (UHG) was the first health plan to offer a DPP as a nationally covered preventive benefit. Beginning in 2010, UHG and the Y partnered with the CDC to test whether the Y's DPP could be delivered to a larger number of participants, at a lower cost, and with comparable outcomes to the DPP Trial. The program is a group-based lifestyle management intervention that is offered free-of-charge to eligible participants in both in-person and online formats.

Building on lessons learned from this experience and in partnership with Comcast and NBC, UHG developed its own DPP (Real Appeal®) that is delivered via a reality-based program format in which participants were filmed going through the program. Individuals who are overweight with a prediabetes risk factor or obese are eligible for the program (i.e., they do not need to have

prediabetes as determined by a risk survey or blood glucose results). Once participants are enrolled in the program, those who have prediabetes receive a full curriculum, while those who are not receive a less-intensive program.[130]

Regional Private Payers

Health Net

Health Net of California, Inc. offers the Omada program in partnership with Omada Health as a preventive service benefit for select plan members, including CalPERS (which covers public employees, retirees, and their families) and Aon Active Health Exchange participants.[131,132]

Blue Shield of California (BSCA)

We were unable to find any publically available information that mentioned BSCA's coverage of programs specifically intended to prevent or delay the development of type 2 DM.

Appendix F. Previous Systematic Reviews and Technology Assessments

We found three technology assessments and 11 previous systematic reviews evaluating DPPs, and have summarized the publications most relevant to this review below. Systematic reviews were restricted to those primarily reviewing the effectiveness of US-based DPPs subsequent to the passing of legislation in 2010 granting the CDC authority to manage the implementation and evaluation of these programs. The majority of these reviews were concerned with the real-world applications of the DPP Trial, some of which were strictly qualitative in nature.

Technology Assessments

US Preventive Services Task Force (USPSTF)

Lin JS, O'Connor E, Evans CV, Senger CA, Rowland MG, Groom HC. Behavioral counseling to promote a healthy lifestyle in persons with cardiovascular risk factors: A systematic review for the US Preventive Services Task Force. Annals of Internal Medicine. 2014;161(8):568-578.

The **Agency for Healthcare Research and Quality (AHRQ)** expanded on a prior systematic review for the USPSTF to update recommendation statements on the benefits of lifestyle behavioral counseling for individuals with one or more cardiovascular risk factors, including metabolic syndrome, dyslipidemia, obesity, hypertension, and impaired blood glucose. The authors concluded that medium- (between 30 minutes to six hours of total contact with providers) and high-intensity (>6 hours of contact) behavioral counseling which includes diet and physical activity consistently reduced important CVD risk factors for up to two years. In the longer term, high-intensity lifestyle change interventions also reduced the incidence of diabetes.

National Institute for Health and Care Excellence (NICE)

Johnson M, Jones R, Freeman C, et al. Can diabetes prevention programmes be translated effectively into real-world settings and still deliver improved outcomes? A synthesis of evidence. Diabetic Medicine: A Journal of the British Diabetic Association. 2013;30(1):3-15.

A NICE-funded systematic review evaluated studies that included interventions based on the DPP Trial and the Finnish Diabetes Prevention study. The primary objective was to determine the real-world applicability of DPPs outside of RCTs. Of the 17 translational studies included, 16 showed greater weight loss of at least 4% in the intervention groups across all study types; differences in blood glucose and weight circumference were inconsistent, however. Although the authors acknowledge that there is limited evidence of sustainable weight loss beyond three years, those

programs that followed the aims and content of the US or Finnish DPP can achieve significant weight loss for participants with less intensity (i.e., reducing the number of contacts) to increase accessibility in a range of settings.

National Institute for Health Research (NIHR)

Gillett M, Royle P, Snaith A, et al. Non-pharmacological interventions to reduce the risk of diabetes in people with impaired glucose regulation: A systematic review and economic evaluation. Health technology assessment (Winchester, England). 2012;16(33):1-236, iii-iv.

A systematic review of nine RCTs found that in patients with intermediate hyperglycemia, defined as having IFG or IGT, non-pharmacological interventions that focused on diet and exercise were more effective than standard lifestyle advice. Those studies with the highest compliance also showed the greatest benefit with lifestyle intervention. An economic assessment of structured lifestyle change interventions demonstrated that these programs are highly cost-effective and may be cost-saving in some situations.

Systematic Reviews

Ali MK, Echouffo-Tcheugui J, Williamson DF. How effective were lifestyle interventions in real-world settings that were modeled on the Diabetes Prevention Program? Health Affairs. 2012;31(1):67-75.

A systematic review and meta-analysis conducted by Ali et al. evaluated 28 studies that applied the DPP curricula in real-world settings. After 12 months, the mean weight loss was 4-5%, which was considered clinically significant, and these results were consistent across studies with nonmedical staff, including nutritionists, behavioral psychologists, and exercise physiologists, or untrained members of the community. Importantly, the authors noted that for every additional session attended, weight was further reduced by 0.26% (95% CI, −0.54 to 0.01; p=N/R). Six of the identified studies also evaluated costs associated with the intervention; differences in costs of providing these programs were primarily attributable to staffing differences (i.e., clinically trained versus lay educators).

Aziz Z, Absetz P, Oldroyd J, Pronk NP, Oldenburg B. A systematic review of real-world diabetes prevention programs: Learnings from the last 15 years. Implementation Science: IS. 2015;10:172.

Aziz et al. focused their systematic review on identifying those components of DPPs that may be associated with successful implementation in real-world settings according to the PIPE (Penetration, Implementation, Participation, and Effectiveness) Impact Matrix elements. All 32 studies identified reported implementation (i.e., program intensity), the majority of which also included data on program adherence. Although higher-intensity programs may be associated with better weight loss

outcomes, those low-intensity programs with high participation rates can still have an impact on lowering diabetes risk.

Cardona-Morrell M, Rychetnik L, Morrell SL, Espinel PT, Bauman A. Reduction of diabetes risk in routine clinical practice: Are physical activity and nutrition interventions feasible and are the outcomes from reference trials replicable? A systematic review and meta-analysis. BMC Public Health. 2010;10:653.

A systematic review of RCTs, pre-post evaluations, cohort studies, and grey literature evaluated programs that primarily focused on preventing diabetes in high-risk patients with the objective of determining if lifestyle change interventions could be adapted in routine clinical practice settings, including outpatient hospital or health clinics. Of the 12 studies identified, four RCTs were meta-analyzed; these results demonstrated that the mean weight loss in both the DPP Trial (5.6kg) and Finnish DPS (4.2kg) trial were superior to the pooled results for weight loss in the DPP cohorts across these studies (1.82kg) after 12 months of follow-up. Although all 12 included studies demonstrated significant effects of modified DPPs on weight loss across all study types, the authors concluded that DPPs in routine clinical practice may not produce clinically-meaningful weight loss in high-risk patients with IGT, metabolic syndrome, or obesity, alone or in combination; these results were limited by the short duration of follow-up in most studies. Longer-term studies need to be conducted in order to determine if achieving clinically significant weight loss is possible in routine clinical care settings beyond one year of follow-up.

Eaglehouse YL, Kramer MK, Rockette-Wagner B, Arena VC, Kriska AM. Evaluation of physical activity reporting in community Diabetes Prevention Program lifestyle intervention efforts: A systematic review. Preventive Medicine. 2015;77:191-199.

In a systematic review evaluating the role that physical activity plays in modified DPPs, Eaglehouse et al. identified 57 translational interventions for adults with prediabetes or at high risk of developing CVD. Although increasing physical activity to a minimum of 150 minutes per week was a primary objective of the DPPs, only 60% of studies reported these outcomes. Among those studies providing physical activity results, only 26% included the number of patients meeting this goal. Given that increasing physical activity has been shown to improve metabolic health, the authors suggested that future research needs to focus on reporting physical activity results to fully comprehend how translational programs impact health outcomes.

Neamah HH, Kuhlmann AK, Tabak RG. Effectiveness of Program Modification Strategies of the Diabetes Prevention Program: A Systematic Review. The Diabetes Educator. 2016;42(2):153-165.

In an effort to characterize the more frequently implemented modifications of DPPs, Neamah et al. examined five program components of 28 modified interventions using bivariate analyses to determine the odds of their influencing particular outcomes. Among those modification types,

including format, timeline, or dosage (i.e., reducing the number of sessions or timeline for delivery), implementation staff, contents, or implementation setting, none were individually associated with reductions in weight or BMI. However, the authors noted the programs with fewer modifications overall were associated with significantly greater weight loss after 12 months ($p<0.01$) or at the last point of follow up ($p=0.02$). There were also significantly better results for weight loss for programs that included a maintenance component at the last point of follow-up ($p=0.02$).

Whittemore R. A systematic review of the translational research on the Diabetes Prevention Program. Translational Behavioral Medicine. 2011;1(3):480-491.

Among the 16 translational studies identified for this systematic review, four different settings could be identified among programs implementing a modified DPP curriculum: primary care, community, hospital outpatient, and work or church. The populations in all studies were considered heterogeneous, with the most diversity being represented in the work or church setting. A majority of the programs included specialized providers, including exercise physiologists, health coaches, and diabetes educators. Across all translational studies, percent weight loss ranged from 2.7% to 6%. Weight loss appeared to the be greatest in hospital outpatient (7.7kg) and primary care programs (8.7kg), which also had the highest attendance rates (80–96%); there was otherwise no association between the number of sessions attended and outcomes across the other settings.

Appendix G. Ongoing US Studies

Title/ Trial Sponsor	Study Design	Comparators	Patient Population	Primary Outcomes	Estimated Completion Date
Diabetes prevention programs					
Getting in Balance: A Workplace Diabetes Prevention Intervention Trial (GIBW) **Kaiser Permanente** **NCT02589873**	RCT	In-person DPP (YMCA) Online DPP (Canary Health VLM)	N = 240 Age ≥ 18 Men and women BMI ≥ 25 kg/m^2, ≥23 kg/m^2 if of Asian descent Score of ≥ 9 on CDC prediabetes risk assessment screen Must be able to speak, read, and understand English Internet access required No type 1 or 2 DM No systolic blood pressure (BP) ≥ 180 mm/Hg or diastolic BP ≥ 100 mm/Hg on 1+ occasions in previous year No inability to exercise No concurrent use of appetite- or weight-affecting medications, enrollment in weight loss program No plans for bariatric surgery during study period	Percent and amount of body weight loss on average over 12 months and at 6 and 12 months compared to baseline	July 2017
Evaluation of Prevent in Underserved Populations (PUP) **Omada Health, Inc.** **NCT02664064**	Non-RCT	Online DPP (Omada, formerly called Prevent) No intervention (matched control)	N = 300 Age 18-75 Men and women Prediabetes confirmed through lab test Uninsured, Medicaid insured, or safety-net health plan insured Ability to speak, read English or Spanish at 5th grade level BMI ≥ 24 Internet access required No inability to exercise No type 1 or 2 DM No concurrent insulin, metformin, or hypoglycemic agent use No current pregnancy or plans for pregnancy	Percent weight loss from baseline at 6 and 12 months	April 2017

Title/ Trial Sponsor	Study Design	Comparators	Patient Population	Primary Outcomes	Estimated Completion Date
A Pharmacist-Coordinated Implementation of the Diabetes Prevention Program **University of California, Los Angeles** **NCT02384109**	Open-label RCT	Pharmacist referral to YMCA DPP or metformin prescription Usual care	N = 700 Age ≥ 18 Men and women BMI > 24 kg/m^2, > 22 kg/m^2 if of Asian descent Prediabetes defined as IFG of 100-125 mg/dL, HbA1c 5.7-6.4%, or ICD-9 billing code of 790.21 or 790.22 No HbA1c values > 6.5% No ICD-9 billing codes of 250.xx No use of antiglycemic medication No current or past DPP participation	Uptake of evidence-based diabetes prevention intervention (metformin or Y DPP) Secondary Outcomes Weight change at 12 months Change in HbA1c Change in systolic blood pressure	June 2019
Minnesota Medicaid Incentives to Prevent Chronic Disease (MMIPCD) **Minnesota Department of Human Services** **NCT02422420**	Open-label RCT	YMCA DPP with individual financial incentive YMCA DPP with group financial incentive YMCA DPP with minimal financial incentive	N = 1,500 Ages 18-75 Men and women Must be enrolled in Medical Assistance, Prepaid Medical Assistance Program (PMAP), or MinnesotaCare BMI ≥ 25 kg/m^2, ≥22 kg/m^2 if of Asian decent Current prediabetes or history of GDM No type 1 or 2 DM No pregnancy at time of enrollment No gastric bypass surgery planned in next year	DPP attendance at 12 months Weight change at 12 months	September 2016

Title/ Trial Sponsor	Study Design	Comparators	Patient Population	Primary Outcomes	Estimated Completion Date
The Reach and Effectiveness of Technology-enhanced Diabetes Prevention Programs (DiaBEAT-it) **Virginia Polytechnic Institute and State University** **NCT02162901**	Hybrid preference and randomized controlled trial	Preference arm: 1. Class with interactive virtual response (IVR) calls 2. DVD with IVR calls RCT arm: 3. Class with IVR calls 4. DVD with IVR calls 5. Class only	N = 600 Age ≥ 18 Men and women BMI ≥ 25 kg/m^2 No diagnosis of DM, congestive heart failure, or coronary artery disease No pregnancy during trial No contraindication to physical activity or weight loss Must have access to telephone Must be able to read and speak English	Body weight at baseline and 12 months	February 2017
Gestational diabetes mellitus					
Lifestyle Intervention Program for Women With Gestational Diabetes of Gestational Impaired Glucose Tolerance (APPLES) **Kaiser Permanente** **NCT01489163**	RCT	Adapted online DPP curriculum Usual care	N = 350 Women ages 20-45 Pregnancy with high glucose levels No DM prior to pregnancy No uncontrolled hypertension or active thyroid disease during pregnancy No severe cardiopulmonary disease No cancer diagnosis No conditions that lead to diet change No addiction to alcohol, drugs No current corticosteroid use	Body weight 24 months postpartum	June 2016

Title/ Trial Sponsor	Study Design	Comparators	Patient Population	Primary Outcomes	Estimated Completion Date
Diabetes Prevention Strategies in Women With Gestational Diabetes Mellitus (GDM) **Kaiser Permanente** **NCT01344278**	RCT	Adapted telephonic and online DPP No intervention	N = 2,480 Age ≥ 18 Women only All women with gestational diabetes between March 2011 and 2012 Must have access to telephone or cell phone No overt diabetes prior to pregnancy	Meeting weight goals through 12 months postpartum	December 2015

Source: www.ClinicalTrials.gov (NOTE: studies listed on site include both clinical trials and observational studies)

Appendix H. Comparative Clinical Effectiveness Supplemental Information

We performed screening at both the abstract and full-text level. A single investigator screened all abstracts identified through electronic searches according to the inclusion and exclusion criteria described earlier. We did not exclude any study at abstract-level screening due to insufficient information. For example, an abstract that did not report an outcome of interest would be accepted for further review in full text. We retrieved the citations that were accepted during abstract-level screening for full text appraisal. One investigator reviewed full papers and provided justification for exclusion of each excluded study.

We used criteria published by the US Preventive Services Task Force (USPSTF) to assess the quality of RCTs and comparative cohort studies, using the categories "good," "fair," or "poor" (see Appendix Table H11).[101] Guidance for quality ratings using these criteria is presented below, as is a description of any modifications we made to these ratings specific to the purposes of this review.

Good: *Meets all criteria: Comparable groups are assembled initially and maintained throughout the study; reliable and valid measurement instruments are used and applied equally to the groups; interventions are spelled out clearly; all important outcomes are considered; and appropriate attention is paid to confounders in analysis. In addition, intention to treat analysis is used for RCTs.*

Fair: *Studies were graded "fair" if any or all of the following problems occur, without the fatal flaws noted in the "poor" category below: Generally comparable groups are assembled initially but some question remains whether some (although not major) differences occurred with follow-up; measurement instruments are acceptable (although not the best) and generally applied equally; some but not all important outcomes are considered; and some but not all potential confounders are addressed. Intention to treat analysis is done for RCTs.*

Poor: *Studies were graded "poor" if any of the following fatal flaws exists: Groups assembled initially are not close to being comparable or maintained throughout the study; unreliable or invalid measurement instruments are used or not applied equally among groups (including not masking outcome assessment); and key confounders are given little or no attention. For RCTs, intention to treat analysis is lacking.*

Note that case series are not considered under this rating system – because of the lack of comparator, these are generally considered to be of poor quality. Nevertheless, we restricted our use of case series to those that met specific criteria, including a minimum of six months follow-up, clearly defined entry criteria, and use of consecutive samples of patient

Table H1. Key Design Elements of the Diabetes Prevention Trials with Long Follow-up (20-25 years)

	US: Diabetes Prevention Program Trial (DPP Trial)	Finnish DPS	China Da Qing DPS
Inclusion Criteria	Age ≥ 25 years BMI ≥ 24 kg/m^2 / 22 if Asian FPG 95-125 mg/dL (except American Indians any FPG) OGTT 140-199 mg/dL	Age 40-65 years BMI ≥ 25 kg/m^2 FPG < 140 mg/dL OGTT 140-199 mg/dL	Age ≥ 25 years OGTT 140-199 mg/dL
Exclusion Criteria	Short life expectancy Hospitalized with CHD in past 6 months or class 2 or greater symptoms Aortic stenosis SBP > 180 mm Hg Cancer treated in past 5 years Pregnancy or planned pregnancy Major psychiatric disorder Alcoholism On medication affecting glucose Thiazide diuretic Beta blocker Niacin Corticosteroids Medications for weight loss	Life expectancy < 6 years Unlikely to follow study protocol	None
Lifestyle Intervention	Target weight reduction ≥ 7% Target exercise ≥ 150 minutes per week moderate intensity (Brisk walking) 16 lessons in 24 weeks one-on-one with trained case manager Diet Exercise Behavior modification Two supervised group exercise sessions per week 4- to 6-week group courses offered quarterly during maintenance phase	Target weight reduction ≥ 5% Target exercise ≥ 30 minutes per day moderate intensity (Brisk walking) 7 sessions one-on-one with nutritionist in 1st year, then once every 3 months Supervised, individualized, resistance exercise circuit training offered (50-85% participation)	Target BMI 23 kg/m^2 Target exercise 1-2 units per day 1 unit = 30 minutes slow walking; 20 minutes brisk walking, 10 minutes slow running. Counseling weekly x 1 month, then monthly x 3 months, then every 3 months for 6 years.

BMI: body mass index, CHD: congestive heart disease, FPG: fasting plasma glucose, OGTT: oral glucose tolerance test;

Table H2. Baseline Characteristics of Participants in the Diabetes Prevention Trials with Long Follow-up (20-25 years)

	US: Diabetes Prevention Program Trial (DPP Trial)	Finnish DPS	China Da Qing DPS
N	3234	522	577
Age, years	51 (11)	55 (7)	45 (9)
Sex, %F	68	67	47
Weight, kg	94 (20)		
BMI, kg/m^2	34.0 (6.7)	31 (5)	26 (4)
FPG	106 (8.3)	109 (14)	101 (15)
HbA1c	5.9 (0.5)		
OGTT, 2 hours	165 (17)	159 (27)	162 (16)
BP		140 (18) /86 (9)	
Total-C		215 (37)	
Triglycerides		154 (72)	
HDL-C		46 (12)	
LDL-C			
Family History DM (%)	69		
History GDM (%)	16		
Race (%)			
White	55	100	0
African American	20	0	0
Hispanic	16	0	0
American Indian	5.3	0	0
Asian	4.4	0	100
Physical activity (MET-hr/week)	16.3		

Note: Numbers in parentheses are standard deviations

BMI: body mass index, BP: blood pressure, FPG: fasting plasma glucose, GDM: gestational diabetes mellitus, OGTT: oral glucose tolerance test, Total-C: total cholesterol

Table H3. Selected Outcomes for Participants in the Lifestyle Arms of the Diabetes Prevention Trials with Long Follow-up (20-25 years)

	US: Diabetes Prevention Program Trial (DPP Trial)	Finnish DPS	China Da Qing DPS
N	1079	265	438
One year outcomes			
Retention, %	95%	97%	>94%
Weight change, kg	-6.8	-4.2	
Weight change, %	-7.2	-4.7	
At least 5% weight loss, %	>50%	43%	
At least 7% weight loss			
Change exercise (MET-hr/week)	+7		
Change FPG	-5	-4	
Change HbA1c	-0.1		
Change OGTT, 2 hours		-15	
Type 2 DM diagnosis	1%		
Diabetes diagnosis % (RRR [95% CI])			
1 year	1% (58% [48-66])	5%	
5-year	23%	27%	35% (51% [27-67])
10-year	41%	40%	53%
15-year	55% (27% [17-35])	60% (39% [21-52])	65%
20-year			73% [43% [19-59])
Microvascular disease RR [95% CI]	0.91 (0.78-1.07) p=0.28 at 15 years	N/R	
Cardiovascular disease, RR (95% CI)			
• **1st event**	N/R	N/R	0.98 (0.71-1.37)
• **Mortality**	N/R	N/R	0.59 (0.36-0.96) At 23 years

FPG: fasting plasma glucose, OGTT: oral glucose tolerance test, RR: risk ratio, RRR: relative risk reduction, MET-hr/week: metabolic equivalent task hours per week, N/R: not reported

Table H4. Overview of Studies Implementing the DPP: Study Design

Reference	Name	Organization	Design	Control	Inclusion	Exclusion	N in lifestyle group	Follow-up, months	Notes
Reference Study: In-person, Individual Coaching									
DPP Research Group 2002	DPP	NIH	RCT 27 centers	Usual care	Age ≥ 25 BMI≥ 24 OGTT 140-199	Chronic disease limiting participation	1079	180	Reference trial
In-person, Group Coaching									
Ackerman 2008	DEPLOY	Y	Cluster RCT 2 sites	Brief coaching	Adults BMI≥24 Random BG 110-199 ≥ 2 RF for DM ADA risk assessment score ≥ 10	Exercise unsafe	46	12	
Ackerman 2015	RAPID	Y	RCT 9 sites	Brief coaching	18+ BMI ≥ 24 FPG 100-125 OGTT 140-199 HbA1c 5.7-6.9	Pregnant Non-English speaking	257	12	
Vojta 2013	-	Y	Pre-post	-	Age 18+ Participating in YMCA DPP	Exercise unsafe	2369	12	Administrative data
Bozack 2014	-	Y	Pre-post	-	Age 18+ Participating in NY State YMCA DPP	Exercise unsafe	254	10	
Brokaw 2015	-	Montana DPH&HS	Pre-post 15 sites	-	Age 18+ BMI ≥ 25 A1c 5.7-6.4 GDM	Exercise unsafe	3804	10	

Reference	Name	Organization	Design	Control	Inclusion	Exclusion	N in lifestyle group	Follow-up, months	Notes
Marrero 2015		Weight Watchers	RCT	NDEP Your Game Plan	Age 18+ BMI ≥ 24 ADA Risk assessment score ≥ 5 HbA1c 5.7-6.5	Pregnancy CVD event in past 6 months Medications affecting glucose	112	12	
Katula 2011	HELP PD	Wake Forest	RCT Single center	Two individual sessions with nutritionist plus monthly newsletter	Age 21+ BMI 25-40 FPG 95-125 English speaking	Pregnancy Recent CVD events	151	24	
Digital, Human Coaching									
McTigue 2009	VLM	Canary Health	Pre-Post Single site	-	PCP referral Ages 18-80 BMI ≥ 25 1 RF CVD Internet access	Pregnancy Exercise unsafe	50	12	Web based Only 16% with prediabetes
Sepah 2014	Omada	Omada Health	Pre-Post Online	-	Ages 18+ BMI ≥ 24 Able to exercise	-	220	12	Online recruitment
Digital, Fully-automated Coaching									
Block 2015	Alive-PD	Turnaround Health	RCT Multispecialty practice	Usual care	Ages 30-69 BMI > 27 English speaking Internet access FPG 100-125 or HbA1c 5.7-6.4		163	6	Fully automated

BMI: body mass index, BG: blood glucose, BP: blood pressure, FPG: fasting plasma glucose, GDM: gestational diabetes mellitus, OGTT: oral glucose tolerance test, PCP: primary care provider

Table H5. Overview of Studies Implementing the DPP: Program Elements

Reference	Name	Organization	16 core lessons weekly	8 monthly maintenance lessons	Weight loss goal	Exercise goal minutes per week	1-on-1 health coach	Group	Web	Handheld	Scale	Pedometer
Reference Study: In-person, Individual Coaching												
DPP Research Group 2002	DPP	NIH	1-on-1, in person	1-on-1, in person	7%	150	In person	Yes	No	No	No	No
In-person, Group Coaching												
Ackerman 2008	DEPLOY	YMCA	Group	Group	5-7%	150	No	Yes	No	No	No	No
Ackerman 2015	RAPID	YMCA	Group	Group	5-7%	150	No	Yes	No	No	No	No
Vojta 2013	-	YMCA	Group	Group	7%	150	No	Yes	No	No	No	No
Bozack 2014	-	YMCA	Group	Group	5-7%	150	No	Yes	No	No	No	No
Brokaw 2015	-	Montana DPH&HS	Group	Group	7%	150	No	Yes	No	No	No	No
Marrero 2015		Weight Watchers	Group. Weight Watchers curriculum contains core content	No, weekly Weight Watchers meetings	7%	N/R	No	Yes	Yes	Yes	No	No
Katula 2011	HELP PD	Wake Forest	24 weekly groups	18 monthly groups	5-7%	180	Yes x 3 sessions	Yes	No	No	No	No
Digital, Human Coaching												
McTigue 2009	VLM	Canary Health	Online	Online	N/R	N/R	Electronic messages	Moderated chat room	Yes	No	No	Yes

Reference	Name	Organization	16 core lessons weekly	8 monthly maintenance lessons	Weight loss goal	Exercise goal minutes per week	1-on-1 health coach	Group	Web	Handheld	Scale	Pedometer
Sepah 2014	Omada	Omada Health	Yes, online	9 online	N/R	N/R	Online and phone	Virtual, asynchronous	Yes	Yes	Wireless	Yes
Digital, Fully-automated Coaching												
Block 2015	Alive-PD	Turnaround Health	Weekly tailored goal setting mapped to DPP curriculum	Yes, every 2 weeks after 1st 6 months	No	150-300	No	Team messaging option	Yes	Yes	No	No

Table H6. Overview of Studies Implementing the DPP: Baseline Characteristics

Reference	Name	Organization	Age	% F	College +, %	Family history DM,%	BMI, kg/m^2	Weight, kg	HbA1c, %	FPG, mg/dL	Race/Ethnicity
Reference Study: In-person, Individual Coaching											
DPP Research Group 2002	DPP	NIH	51	68	N/R	70	34	94	5.9	106	White: 55 AA: 20 Hispanic: 16 AI: 5 Asian: 4
In-person, Group Coaching											
Ackerman 2008	DEPLOY	Y	56	50	N/R	N/R	32	94	5.5	N/R	White: 93 AA: 4 Hispanic: 2 AI: Asian:
Ackerman 2015	RAPID	Y	51	71	N/R	57	37	102	6.0	N/R	White: 35 AA: 57 Hispanic: 3 AI: Asian:
Vojta 2013	-	Y	50% >55	76	N/R	N/R	N/R	N/R	N/R	N/R	N/R
Bozack 2014	-	Y	57	70	45	N/R	35	97	N/R	N/R	White: 78 AA: 15 Hispanic: 4 AI: Asian:
Brokaw 2015	-	Montana DPH&HS	52	82	N/R	N/R	36	N/R	N/R	N/R	N/R

Marrero 2015	-	Weight Watchers	52	83	54	N/R	37	101	5.9	108	White: 63 AA: 29 Hispanic: AI: Asian: 5
Katula 2011	HELP PD	Wake Forest	57	58	56	N/R	33	94	N/R	105	White: 74 Black: 26 Hispanic: AI: Asian:
Digital, Human Coaching											
McTigue 2009	VLM	Canary Health	52	76	68	N/R	36	~102	N/R	N/R	White: 86 AA: 8 Hispanic: 0 AI: Asian: 4
Sepah 2014	Omada	Omada Health	44	83	52	N/R	37	101	6.0	N/R	White: 50 AA: 29 Hispanic: 11 AI: Asian:
Digital, Fully-automated Coaching											
Block 2015	Alive-PD	Turnaround Health	55	32	84	N/R	31	94	5.6	110	White: 67 AA: Hispanic: 4 AI: Asian: 25

AA: African American, AI: American Indian, BMI: body mass index, FPG: fasting plasma glucose

Table H7. Overview of Studies Implementing the DPP: Retention

Reference	Name	Organization	16 weeks	6 months	12 months	% invited	≥9 sessions
Reference Study: In-person, Individual Coaching							
DPP Research Group 2002	DPP	NIH	95% all 16	97%	98%	N/R	>95%
In-person, Group Coaching							
Ackerman 2008	DEPLOY	Y	Mean 9.1 12 among n=35 attending 1 session	85%	63%	70%	N/R
Ackerman 2015	RAPID	Y	1 session 63% Mean 9.5		83%	63%	40%
Vojta 2013	-	Y	4 sessions 89% 9 sessions 73% Mean 12.4	N/R	N/R	N/R	73%
Bozack 2014	-	Y	Mean 10.6	N/R	N/R	N/R	72%
Brokaw 2015	-	Montana DPH&HS	13.7/16	4.4/6	75%	N/R	
Marrero 2015		Weight Watchers	N/R	92%	84% 21.6 meetings	NA	NA
Katula 2011	HELP PD	Wake Forest	N/R	92%	89%	92%	N/R
Digital, Human Coaching							
McTigue 2009	VLM	Canary Health	4 sessions >82 9 sessions 66% Mean 12.8	N/R	90%	N/R	66%
Sepah 2014	Omada	Omada Health	4 sessions 85% 9 sessions 70% Mean 13.8 core	N/R	74% with weight measured	N/R	70%
Digital, Fully-automated Coaching							
Block 2015	Alive-PD	Turnaround Health	4 sessions 87% 17/24 sessions in 1st 6 months	86%	N/R	N/R	NA

Table H8. Overview of Studies Implementing the DPP: Weight Loss

Reference	Name	Organization	16 weeks, % weight lost	6 months, % weight lost	12 months, % weight lost	>5% at 12 months	>7% at 12 months	Change in weight 12 months, kg	Change in BMI 12 months	>5% at 6 months
Reference Study: In-person, Individual Coaching										
DPP Research Group 2002	DPP	NIH	-6.9	-7.2	~7	N/R	50%	~-7	N/R	65%
In-person, Group Coaching										
Ackerman 2008	DEPLOY	Y	-6.0	-6.0	-6.0	N/R	N/R	-5.7	-6.7	N/R
Ackerman 2015	RAPID	Y	N/R	N/R	N/R	32%	N/R	-2.3	N/R	N/R
Vojta 2013	-	Y	N/R	N/R	-4.8	N/R	N/R	N/R	N/R	N/R
Bozack 2014	-	Y	-4.2	-	6.3	61%	48%	-6.0	N/R	40%
Brokaw 2015	-	Montana DPH&HS	N/R	-6.2	N/R	N/R	N/R	N/R	N/R	50%
Marrero 2015		Weight Watchers	N/R	-5.5	-5.6	OR 4.7	OR 5.0	-5.5	-2.1	OR 6.9
Katula 2011	HELP PD	Wake Forest	N/R	-7.5	-7.2	59%	N/R	-7.0	-2.3	N/R
Digital, Human Coaching										
McTigue 2009	VLM	Canary Health	N/R	N/R	N/R	31%	18%	-4.8 (n=45/50) -4.9 (LOCF)	N/R	
Sepah 2014	Omada	Omada	-5.0 (n=187/220) -4.1 (LOCF)	N/R	-4.8 (n=187/220) -4.0 (LOCF)	N/R	N/R	-4.9 (n=187/220) N/R (LOCF)	N/R	N/R
Digital, Fully-automated Coaching										
Block 2015	Alive-PD	Turnaround Health	N/R	-3.6	N/R	N/R	N/R	N/R	N/R	35%

All studies used an objective measure of body weight except Vojta 2013 (not described) and McTigue 2009 (self report).

LOCF: last observation carried forward, N/R: not reported, OR: odds ratio

Table H9. Overview of Studies Implementing the DPP: Glycemic Control

Reference	Name	Organization	6 months, HbA1c	12 months, HbA1c	6 months, FPG, mg/dL	12 months, FPG, mg/dL
Reference Study: In-person, Individual Coaching						
DPP Research Group 2002	DPP	NIH	N/R	~-0.1	N/R	~-5
In-person, Group Coaching						
Ackerman 2008	DEPLOY	Y	-0.1	-0.1	N/R	N/R
Ackerman 2015	RAPID	Y	N/R	N/R	N/R	N/R
Vojta 2013	-	Y	N/R	N/R	N/R	N/R
Bozack 2014	-	Y	N/R	N/R	N/R	N/R
Brokaw 2015	-	Montana DPH&HS	N/R	N/R	N/R	N/R
Marrero 2015	-	Weight Watchers	-0.22	-0.25	-5.5	-2.8
Katula 2011	HELP PD	Wake Forest	N/R	N/R	-3.9	-4.5
Digital, Human Coaching						
McTigue 2009	VLM	Canary Health	N/R	N/R	N/R	N/R
Sepah 2014	Omada	Omada Health	N/R	-0.4	N/R	N/R
Digital, Fully-automated Coaching						
Block 2015	Alive-PD	Turnaround Health	-0.3		-7.4	

FPG: fasting plasma glucose, N/R: not reported

Table H10. Overview of Studies Implementing the DPP: Change in Physical activity and Other Outcomes at 12 Months

Reference	Name	Organization	Physical activity, MET-hr/wk	SBP, mm Hg	DBP, mm Hg	Total cholesterol, mg/dL	HDL cholesterol, mg/dL
Reference Study: In-person, Individual Coaching							
DPP Research Group 2002	DPP	NIH	~+7.5	-3.4	-3.6	-4.7	+1.0
In-person, Group Coaching							
Ackerman 2008	DEPLOY	Y	N/R	-1.6	N/R	-13.5	+1.9
Ackerman 2015	RAPID	Y	N/R	N/R	N/R	N/R	N/R
Vojta 2013	-	Y	N/R	N/R	N/R	N/R	N/R
Bozack 2014	-	Y	N/R	N/R	N/R	N/R	N/R
Brokaw 2015	-	Montana DPH&HS	N/R	N/R	N/R	N/R	N/R
Marrero 2015		Weight Watchers	N/R	-3.3	-5.4	+0.4	+6.3
Katula 2011	HELP PD	Wake Forest	N/R	N/R	N/R	N/R	N/R
Digital, Human Coaching							
McTigue 2009	VLM	Canary Health	N/R	-7.3	+0.4	N/R	N/R
Sepah 2014	Omada	Omada Health	N/R	N/R	N/R	N/R	N/R
Digital, Fully-automated Coaching							
Block 2015	Alive-PD	Turnaround Health	N/R	N/R	N/R	N/R	N/R

DBP: diastolic blood pressure, MET-hr/week: metabolic equivalent task hours per week, SBP: systolic blood pressure,

Table H11. Overview of Studies Implementing the DPP: Quality Assessment*

Reference	Name	Organization	Design	Comparable at Initiation	Maintenance of comparability	Measurements equal and valid	Clear definition of intervention	Key outcomes assessed	Analysis appropriate	Quality
Reference Study: In-person, Individual Coaching										
DPP Research Group 2002	DPP	NIH	RCT	Yes	Yes	Yes	Yes	Yes	Yes	Good
In-person, Group Coaching										
Ackerman 2008	DEPLOY	YMCA	RCT	No Age, sex, race	No 37% lost F/U	Yes	Yes	Yes	Yes	Fair
Ackerman 2015	RAPID	YMCA	RCT	Yes	Yes	Yes	Yes	Yes	Yes	Good
Vojta 2013	-	YMCA	Pre-post	N/A	N/A	Unclear	Yes	No	Yes	Poor
Bozack 2014	-	YMCA	Pre-post	N/A	N/A 26% lost F/U	Self-reported	Yes	Yes	Yes	Poor
Brokaw 2015	-	Montana DPH&HS	Pre-post	N/A	N/A 25% lost F/U	Yes	Yes	Yes	Yes	Poor
Marrero 2015	-	Weight Watchers	RCT	Yes	No 28% lost F/U	Yes	Yes	Yes	Yes	Fair
Katula 2011	HELP PD	Wake Forest	RCT	Yes	Yes	Yes	Yes	Yes	Yes	Good
Digital, Human Coaching										
McTigue 2009	VLM	Canary Health	Pre-post	N/A	N/A	Self-reported	Yes	Yes	Yes	Poor
Sepah 2014	Omada	Omada	Pre-post	N/A	N/A	Yes	Yes	Yes	Yes	Fair
Digital, Fully Automated Coaching										
Block 2015	Alive-PD	Turnaround Health	RCT	Yes	Yes	Yes	Yes	Yes	Yes	Good

*Using USPSTF Quality Rating Criteria

Appendix I. Comparative Value Supplemental Information

Table I1. Overview of Studies Implementing the DPP: Evaluations of Cost-Effectiveness from Health System and Societal Perspectives

Reference	Name	Comparator	Time Horizon	Population	Net Costs	QALYS Gained	ICER (Health System)	ICER (Societal)
In-person, Individual Coaching								
DPP Research Group 2003	DPP Trial	Placebo	3 years	DPP Trial	$2,269 (2000 USD)	0.072	$32,000	$52,300
	Metformin	Placebo	3 years	DPP Trial	$2,191	0.022	$102,200	$101,700
DPP Research Group 2012	DPPT/DPPOS	Placebo	10 years	DPP Trial, DPPOS	$1,748 (2010)	0.14	$13,000	$19,800
	Metformin	Placebo	10 years	DPP Trial, DPPOS	-$105	0.01	Cost-saving	Cost-saving
	DPP Trial/DPPOS	Metformin	10 years	DPP Trial, DPPOS	$1,853	0.12	$14,900	$45,900
Herman 2005	DPP (simulation)	Placebo	Lifetime	≥ 25 yrs old with IGT	$635 (2000)	0.57	$1,100	$8,800
	Metformin	Placebo	Lifetime	≥ 25 yrs old with IGT	$3,922	0.13	$31,300	$29,900
Hoerger 2007	DPP for IGT+IFG	No screening	Lifetime	45-74 yrs old with BMI ≥ 25 kg/m^2	$329 (2001)	0.040	$8,200	$16,345
	DPP for IGT or IFG	No screening	Lifetime	45-74 yrs old with BMI ≥ 25kg/m^2	$1,122	0.118	$9,500	$18,777
	DPP for IGT or IFG	DPP for IGT+IFG	Lifetime	45-74 yrs old with BMI ≥ 25 kg/m^2	$793	0.078	$10,200	N/R
Eddy 2005 (Archimedes)	DPP	No prevention	30 years	Adults at high risk for diabetes	$9,969 (2000 USD)	0.159	$143,000	$62,600
	Metformin	No prevention	30 years	Adults at high risk for diabetes	$4,018	0.113	N/R	$35,500
	Lifestyle intervention post-diabetes	No prevention	30 years	Adults at high risk for diabetes	$3,066	0.125	N/R	$24,500
Eddy 2005 cont'd	DPP	ILI post-diabetes	30 years	Adults at high risk for diabetes	$6,903	0.034	N/R	$201,800

Reference	Name	Comparator	Time Horizon	Population	Net Costs	QALYS Gained	ICER (Health System)	ICER (Societal)
In-person, Group Coaching								
DPP Research Group 2003	DPP Trial as group	Placebo	3 years	DPP Trial	N/R	N/R	$9,000	$29,100
DPP Research Group 2012	DPP Trial as group	Placebo	10 years	DPP Trial, DPPOS	$201	0.14	$1,500	$8,400
Herman 2005	DPP as group (simulation)	Placebo	Lifetime	≥ 25 yrs old with IGT	-$3,696	0.57	Cost-saving	
Hoerger 2007	DPP group for IGT+IFG	No screening	Lifetime	45-74 yrs old with BMI ≥ 25 kg/m^2	N/R	0.040	Cost-saving	N/R
	DPP group for IGT or IFG	No screening	Lifetime	45-74 yrs old with BMI ≥ 25 kg/m^2	N/R	0.118	$267	N/R
Eddy 2005 (Archimedes)	DPP group ($217/yr)	No prevention	30 years	Adults at high risk for diabetes	N/R	N/R	$27,000	$12,000
Hinnant 2016 claims analysis	DEPLOY	Usual care	2 years	Medicare beneficiaries with prediabetes	-$1,820 (2014 USD)	Not measured	Cost-saving	N/R
Spitalnic 2016 budget impact	DEPLOY (Medicare expansion)	No Medicare expansion	Lifetime	Medicare beneficiaries 65-75 yrs old	N/R	Not measured	Cost-saving*	N/R
Digital, Human Coaching								
Su 2016 ROI analysis	Omada	Usual care	10 years	Adults with prediabetes & BMI ≥25kg/m^2	-$12,026	N/R	Cost-saving (positive ROI)	N/R
Smith 2016	VLM	Usual care	10 years	Prediabetes (BMI ≥ 25 kg/m^2 & ≥ 1 CVD risk factor)	$458 (2010)	0.0589	$7,800	$18,300
Digital, Fully Automated Coaching								
(No cost-effectiveness analyses identified)								

*Cost-saving if mortality effects excluded (as for Medicare certification); approximately cost-neutral if included

BMI: body mass index, CVD: cardiovascular disease, IFG: impaired fasting glucose, IGT: impaired glucose tolerance, ILI: inventive lifestyle intervention, ROI: return on investment, USD: United States Dollars

Table I2. Average Costs and Cost Offsets per Year by Program Type in 2015 Dollars*

Program	Costs ($)					Cost Offsets ($)				
	Year 1	Year 2	Year 3	Year 4	Year 5	Year 1	Year 2	Year 3	Year 4	Year 5
In-person, individual coaching[39]	$2,100	$1,020	$1,052	$199	$145	$198	$37	$610	$446	$461
In-person, group coaching[20,39,42,133,134]	$752	$350	$367	$127	$100	$1,207	$783	$610	$446	$461
Digital, human coaching[44,45,135,136]	$619	$362	$311	$311	$311	$501	$752	$462	$866	$866

*Unpublished data indicate annual program costs of $66 per person for one digital automated DPP, with estimated annual cost offsets from reduced diabetes incidence of $90 per year (using HbA1c criterion) or $455 per year (using FPG criterion)[107,108]

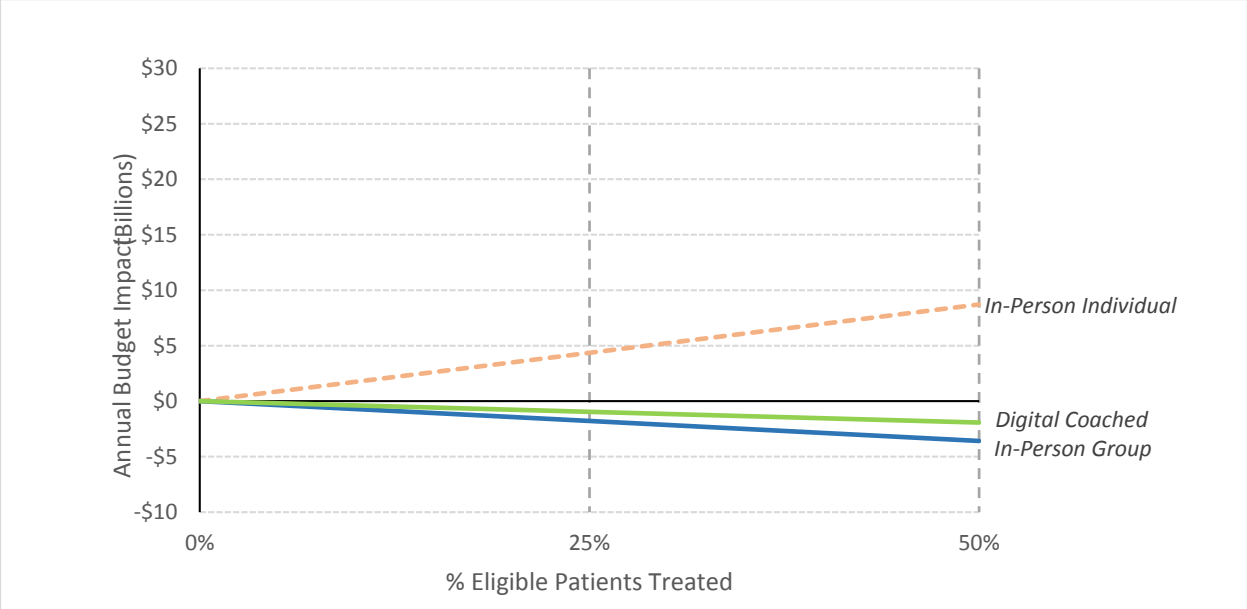
Table I3. Undiscounted Potential Budget Impact Cost per Participant from 1 to 5 years, Prediabetes defined as FPG 100-125 mg/dL: Payer Perspective

Time Horizon	In-Person Individual Coaching		In-person, Group Coaching		Digital, Human Coaching	
	Annual Total BI	Annual BI/ Participant	Annual Total BI	Annual BI/ Participant	Annual Total BI	Annual BI/ Participant
1 year	$3,563,824,621	$1,902	($851,606,567)	($455)	$219,877,054	$117
2 years	$5,406,067,698	$1,443	($1,663,498,085)	($444)	($509,824,017)	($136)
3 years	$6,235,615,751	$1,110	($2,117,394,850)	($377)	($792,509,542)	($141)
4 years	$5,772,361,644	$770	($2,714,577,187)	($362)	($1,832,628,826)	($245)
5 years	$5,179,827,320	$553	($3,390,404,989)	($362)	($2,872,748,110)	($307)

Table I4. Undiscounted Potential Budget Impact Cost per Participant from 1 to 5 years, Prediabetes defined as FPG 110-125 mg/dL: Payer Perspective

Time Horizon	In-Person, Individual Coaching		In-person, Group Coaching		Digital, Human Coaching	
	Annual Total BI	Annual BI/ Participant	Annual Total BI	Annual BI/ Participant	Annual Total BI	Annual BI/ Participant
1 year	$1,187,942,174	$1,902	($283,869,007)	($455)	$73,292,390	$117
2 years	$1,802,023,528	$1,443	($554,499,658)	($444)	($169,941,430)	($136)
3 years	$2,078,539,693	$1,110	($705,798,660)	($377)	($264,169,988)	($141)
4 years	$1,924,121,575	$770	($904,859,545)	($362)	($610,876,601)	($245)
5 years	$1,726,610,029	$553	($1,130,135,600)	($362)	($957,583,214)	($307)

Figure I1. Potential Budget Impact Graph for DPPs Provided to Varying Proportions of the US Population with FPG 110-125 mg/dL



Note: Colored lines represent the annualized potential budget impact of different uptake patterns (percent of eligible population enrolled) for each type of DPP.