Clinical Dossier

Diabetes Prevention Programs, Omada Health's Prevent Program, and August 2014 US Preventive Services Task Force Guidelines Update

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I. Executive Summary

The clinical and financial costs of the nearly 30 million Americans with type 2 diabetes are well established. Less well known is the fact that nearly 1 in 3 people in the US have prediabetes and for them, the yearly incidence of diabetes is 5%-10% compared to about 1% in the general adult population[1]. Considering the significant consequences of diabetes, delaying its onset in people with prediabetes is both clinically and economically important.

Initiated over 15 years ago, the Diabetes Prevention Program (DPP) was a large, multi-center, randomized controlled trial conducted by the National Institutes of Health (NIH). The trial examined the impact of an intensive behavioral counseling program delivered in weekly face-to-face sessions on the subsequent development of type 2 diabetes in individuals who, at baseline, had impaired glucose tolerance (prediabetes). The DPP lifestyle intervention resulted in a 58% reduction in the incidence of subsequent diabetes compared with participants who received usual care[2]. Due to the success of the DPP, influential organizations such as the American Medical Association, American Diabetes Association, and NIH have encouraged use of DPP adaptations as the standard of care for prediabetes patients and pushed for reimbursement by third-party payers. Despite the impressive results of the DPP, it has been difficult to replicate these in community settings. Broad deployment of DPP in face-to-face weekly settings has been hindered by limits in geographic accessibility, patient convenience and adherence, the ability to maintain quality while scaling, and inconsistent data collection.

The *Prevent* program was developed by Omada Health to translate the DPP into a digital format that makes evidence-based treatment of prediabetes accessible and engaging to millions of Americans. *Prevent* includes four carefully choreographed intervention components: small group support, personalized health coaching, DPP curriculum, and digital tracking tools. Prevent pricing is performanced-based and entirely determined by program completion and clinically significant weight-reduction.

A published study of 187 Prevent participants demonstrated 5.0% mean decrease in weight after 16 weeks and 4.8% mean decrease in weight after 52 weeks. HbA1c decreased from a mean 6.0% at baseline to 5.6% at 52 weeks, a regression from the prediabetes glycemic range to the normal glycemic range.

In August 2014, the US Preventive Services Task Force (USPSTF) recommended intensive behavioral counseling interventions to adults who are overweight or obese and have additional cardiovascular risk factors[4]. The majority of evidence cited by USPSTF in making their recommendation was sourced from studies of DPP, suggesting that programs structured like Omada's *Prevent* fulfill USPSTF's definition of 'intensive behavioral counseling'. Furthermore, USPSTF guidance on target population (including prediabetes as a CVD risk factor), program features, intensity, and care setting are aligned with Omada's *Prevent* program. Therefore, *Prevent* can act as a quickly-scalable, broad-coverage, highly-effective option for plans to fulfill the requirements engendered by the USPSTF recommendation.

Provisions in the Affordable Care Act (ACA) require health plans to provide coverage for Grade A and Grade B recommendations of the USPSTF with first-dollar coverage[5]. Omada's ability to scale the digital solution quickly is important given the need to comply with the ACA requirement by September 1, 2015 (one year after recommendation issue date) across a wide geographic landscape and diversity of fully-insured and self-insured groups. Deployment of *Prevent* enables health plans to meet the requirements of the ACA mandate using a proven and cost-effective solution.

II. Prediabetes

The consequences of type 2 diabetes and its complications are well known, as are the economic implications. In a study of annual medical costs, people without diabetes averaged $5,900 per year vs $13,700 for those with diabetes and $21,000 in people with diabetes and complications[6]. The annual incidence of diabetes is 5%-10% in people with prediabetes, compared to about 1% in the general adult population[1]. Thus, approximately 15-30% of people with prediabetes will progress to diabetes in as little as three years. Delaying the onset of diabetes in people with prediabetes is clinically beneficial and also economically important.

Prediabetes, also known as impaired glucose tolerance, is established when one of the following measurements is present:

- Fasting plasma glucose (FPG) between 100-125 mg/dL
- Hemoglobin A1c between 5.7% and 6.4%
- Two hour post-prandial blood glucose of 140-199 mg/dL following a 75-gram oral glucose tolerance test (OGTT)

III. Diabetes Prevention Program (DPP)

It is widely known that exercise and weight loss reduce blood sugar. Therefore, it was logical that programs offering intensive exercise and dietary counseling might delay the onset of type 2 diabetes. The landmark Diabetes Prevention Program (DPP) evaluated the outcome of a variety of approaches.

DPP was a major National Institutes of Health (NIH)-sponsored randomized controlled trial conducted at 27 centers throughout the United States[2]. Eligibility criteria for the study were:

- Age > 25
- BMI > 24 (> 22 for Asians)
- Fasting plasma glucose 95-120mg/dL or 140-199 mg /dL two hours after a 75-g oral glucose load

The 3,234 study participants were randomly assigned to three groups:

1. Lifestyle intervention group received intensive training in diet, physical activity and behavior modification. Participant goals were to eat a low-

calorie, low-fat diet, and engage in physical activity for at least 150 minutes per week in order to lose 7% of their initial body weight.

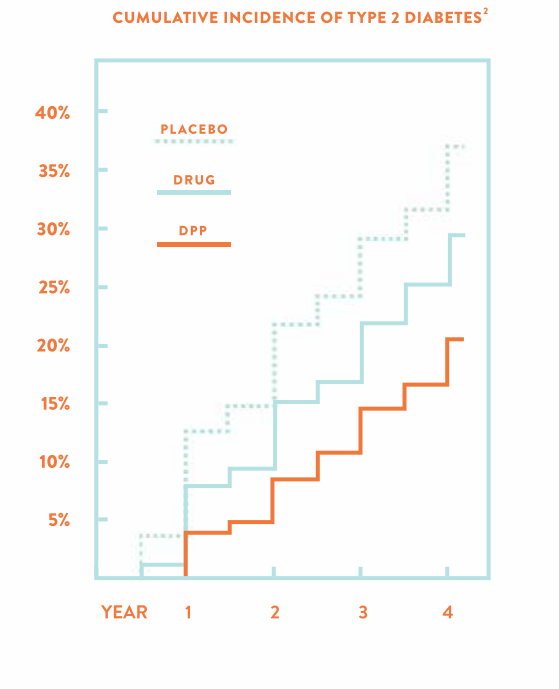
2. Medication group received metformin 850 mg twice daily.
3. Placebo group received placebo pills instead of metformin.

The medication and placebo groups also received printed information about losing weight using diet and exercise, but did not receive intensive lifestyle counseling.

Results

The mean age of the participants was 51 years and the mean BMI was 34.0; 68% were women and 45% were members of a minority group.[2]

- The average weight loss was 0.1, 2.1 and 5.6 kg in the placebo, metformin the lifestyle intervention groups, respectively (p<0.001).
- The cumulative incidence of diabetes was lower in the metformin and lifestyle-intervention groups than in the placebo group throughout the follow-up period (p<0.001).
- After 3 years, the incidence of diabetes was 58% lower in the lifestyle intervention group and 31% lower in the metformin group than in the placebo group (p<0.001).



The Finnish Diabetes Prevention Study[7] yielded similar results. The study included 522 middle-aged patients with impaired glucose tolerance (mean age 55 years & BMI 33.2 mg/k2). Patients were randomly assigned to a weight reduction exercise program or a control group receiving usual care.

- Weight loss in the intervention group was 4.2 kg at the end of 1 year vs 0.8 kg in the control group (p <0.001). At 2 years weight loss was 3.5 kg in the intervention group vs 0.8 kg in the control group (p<0.001).
- The cumulative incidence of diabetes after 4 years was 11% in the intervention group vs 23% in the control group. The risk of diabetes was reduced by 58% in the intervention group (p<0.001).

Given the compelling evidence in the landmark randomized controlled trials, many programs were subsequently implemented and follow-up studies performed to ascertain if DPP-like

programs were effective in community settings. A meta-analysis of 28 US studies concluded that the DPP lifestyle interventions could be adapted to real world settings and provide "significant and sustained benefits"[8].

IV. CDC's National Diabetes Prevention Program

In 2010 Congress authorized the CDC to establish and lead the National DPP[9]. This was in response to the growing incidence of type 2 diabetes and the substantial body of evidence of the effectiveness of DPP-like programs. The goal of the National DPP is to increase access to low cost but effective programs based on the DPP across the US. The CDC publishes the Diabetes Prevention Recognition Program (CDC DPRP) standards for delivery of real-world DPP programs[10,11]. These standards delineate what the CDC expects in community-based programs including:

Participant Eligibility

- 18 years or older
- Body Mass Index (BMI) ≥ 24kg/m2 (≥ 22kg/m2 if Asian)
- Identified high risk for type 2 diabetes:
    a. Prediabetes diagnosis via blood-based tests (i.e. FPG 100-125 mg/ dl, OGTT 140-199 mg/dl, or A1C of 5.7-6.4)
    b. Gestational diabetes mellitus (GDM) diagnosis during a previous pregnancy
    c. A high-risk score (≥ 9) on the CDC Prediabetes Screening Test (75% Positive Predictive Value compared to blood-based tests)

Health Coaches

CDC DPRP specifies that DPP programs must use a lifestyle/health coach to deliver the program to participants. Health coaches may have health care credentials (e.g. RD, RN), but they are not required. Health coaches receive initial training in line with CDC DPRP recommendations and are under ongoing supervision. Their primary responsibilities include:

- Delivering the DPP with adherence to the CDC NDPP curriculum
- Facilitating groups to optimize social interaction, shared learning, and group cohesion
- Understanding and overseeing participant safety-related issues with respect to program delivery

Program Curriculum

CDC DPRP specifies that DPP programs must base their curriculum on the original DPP clinical trial's lifestyle intervention curriculum. The CDC's own NDPP Curriculum is the recommended curriculum, which consists of a series of sessions providing health information,

assigned homework, and feedback in stages to optimize behavioral change. The curriculum must remain focused on the overarching goal of preventing type 2 diabetes (vs. purely focusing on obesity) and thus emphasize the need to make lasting lifestyle changes, rather than simply completing a one-time curriculum.

During the 'core phase' of the program, 16 sessions of curriculum are delivered within 16-26 weeks (usually weekly), with the goal of achieving weight loss in the range of 5-10% of baseline body weight. Strategies used to achieve these goals include a focus on self-monitoring of diet and physical activity, building of self-efficacy and social support for maintaining lifestyle change, and problem-solving strategies for overcoming common challenges to sustaining weight loss. The 'post core phase', occurring over the remainder of a year, includes at least six sessions of curriculum (usually monthly) focused on relapse prevention and long-term maintenance.

Program Outcomes

CDC DPRP requires DPP programs to document specific metrics related to participant engagement and outcomes, including: session attendance, documentation of body weight and physical activity, and measurement of weight loss achieved at the end of the core and post-core phases[12]. A participant is considered to be a program 'starter' by finishing 4 core sessions, and program 'completer' by finishing 9 core sessions. Key program benchmarks include starters being expected to complete an average of at least 9 sessions, and achieve an average of at least 5% weight loss after 6 and 12 months.

Performance of In-Person DPP in Real-World Settings

The CDC's National Diabetes Prevention Program has tried to disseminate DPP programs nationwide, but these efforts have been hindered by several factors:

- The brick-and-mortar DPP programs cannot scale to reach all the people it must
- Most Americans cannot consistently fit fixed, weekly meetings into otherwise busy lives
- Health coaches (who are not typically employed by the program providers) are difficult to track and manage across disparate physical sites
- It is a challenge to consistently track progress and harness insights across larger groups

V. The *Prevent* Program

Omada Health designed the Prevent program to translate the DPP into a digital format that makes evidence-based treatment of prediabetes accessible and engaging to millions of Americans.

Prevent includes 4 major intervention components: small group support, personalized health coaching, DPP curriculum, and digital tracking tools.

Small Group Support

To re-create the experience and group dynamic of an in-person program, participants are demographically matched into online groups of approximately 15 participants to maximize social relatedness (based on similar location, age, and BMI). Participants communicate with each other via a private online social network, which resembles popular social networks such as Facebook. An online group discussion board allows participants to post and reply to comments about how they are doing and progressing.

Participants can “like” and “understand” comments to express social support and empathy, which mimic key group therapeutic processes. Group discussion is asynchronous, rather than live, to make the intervention more flexible and convenient. Visual progress bars allow group members to see each other’s relative progress towards the shared 5-10% weight loss goal and provide social support and accountability to one another

Expert Health Coaching

Each group is led by a professional health coach, who is trained in a manner consistent with CDC DPRP standards for lifestyle coaches. Health coaches serve an important moderating and personalizing function by communicating with participants via online private messages or telephone calls and text messages. Health coaches keep participant discussions on track, give personalized feedback on food logs and physical activity progress, and provide individualized counseling using techniques such as motivational interviewing.

Behavior Change Curriculum

The DPP curriculum is presented in an online format that builds upon popular online learning platforms. Prevent begins with a 16-week core program phase, consisting of online weekly lessons adapted from the CDC NDPP core curriculum. Lessons are posted every Sunday morning, and participants are encouraged to complete them at their own convenience within the week. Lessons resemble an online workbook, in which individuals read curriculum content and answer relevant free response questions, which are shared with their health coach and group. A lesson is considered complete if a participant clicks through all of the pages and answers the free response questions to indicate engagement and understanding.

Health Data Tracking

Prevent participants receive several tools to help monitor their progress within the program. A no-setup wireless scale is mailed to each participant in their 'Welcome Kit' allowing for transmission of daily weights into their personal profiles. Similarly, a digital pedometer is provided to track physical activity. A food diary in the Prevent web portal and mobile app facilitates tracking of eating habits.

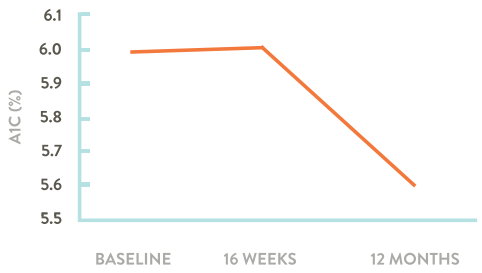
VI. Prevent Outcomes

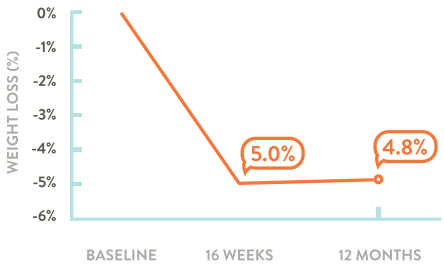
The effectiveness of the Prevent program has been assessed:

Sepah et al 2014[3]

This study enrolled 220 participants, recruited via online advertisements, with a diagnosis of prediabetes. Participants underwent the Prevent 'core' 16-week intensive lifestyle change intervention and were then offered to continue with a 'post-core' lifestyle maintenance intervention, with the entire intervention (core plus post-core) totaling 12 months. A total of 187 participants completed the core program and 144 participants completed both the core and post-core phases of the program.

- At 16 weeks the 187 core participants achieved an average weight loss of 5.0% of their body weight.
- The 187 core participants also achieved an average 12-month HbA1c reduction of 0.4%, from A1C 6.0% (prediabetes) to A1C 5.6% (normal).
- Two year data will be available on these patients shortly.





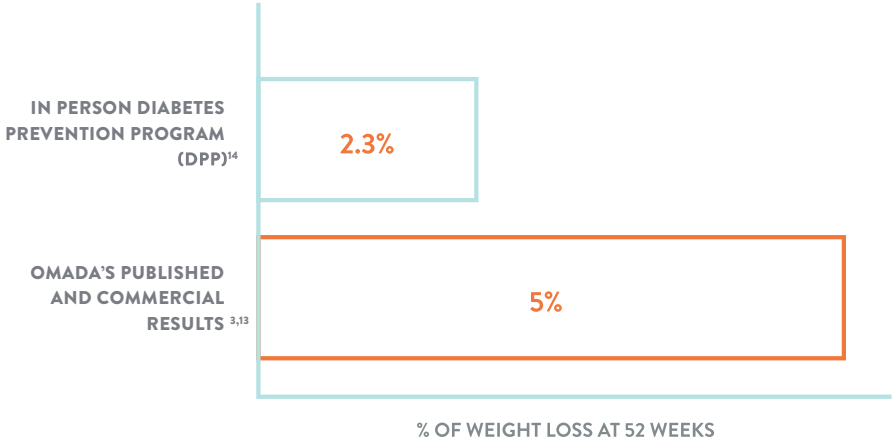
Omada Health Commercial Prevent Registry 2014[13]

- Beyond the patients treated in Omada's published study (above), several thousand individuals have participated in Prevent's core program and achieved an average weight loss of 5.1% at 16 weeks.
- One year data is available on 250 participants and they have shown an average weight loss of 5.0%.

Comparative Effectiveness

A meta-analysis of DPP-like programs confirmed, "structured lifestyle interventions tested in the Diabetes Prevention Program clinical trial and adapted to real-world use have shown 'significant and sustained benefits'"[8].

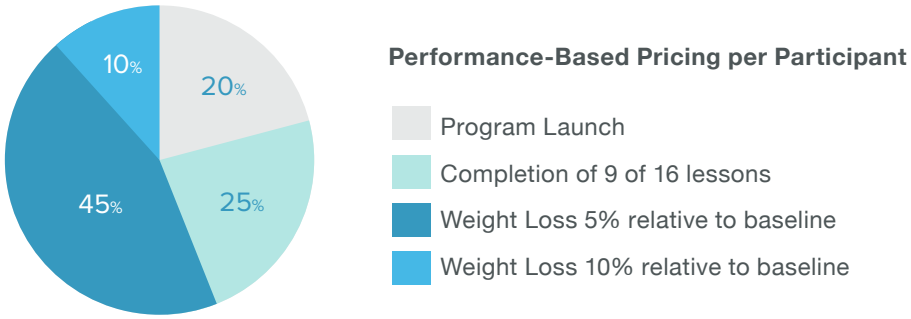
However, a more recent meta-analysis showed that DPP translational programs vary in their effectiveness with an average loss of 2.4% of body weight at 12 months[14]. Further, this analysis demonstrated that the more successful programs followed guidelines for behavioral intervention programs that feature frequent interaction and psychosocial support, aspects that have been incorporated into *Prevent.* Thus, one might predict that *Prevent* would perform well. And indeed the program has: Prevent's 5.0% average weight loss at 12 months compares very favorably with the 2.4% average in the meta-analysis.



Prevent's above-average performance may relate to the multi-modal digital and telephonic approach. The program is convenient for participants allowing for frequent interaction without disruption of their schedules or the need to travel. The social media platform allows for matched peer group support. The telephonic link to health coaches allows for qualified and experienced health coaches to be effectively leveraged to serve a larger group of participants than face-to-face meetings would allow.

VII. Performance-Based Pricing

Pricing for *Prevent* is based on the outcomes individuals achieve. Sponsors are billed only when individual participants reach pre-defined engagement and outcomes milestones—sponsors are not billed for milestones not acheived. This unique approach provides a high value and cost-effective approach to preventing diabetes onset in patients with prediabetes. It also creates alignment between Omada Health, payers, and employers since costs are only incurred once engagement and clinically meaningful weight loss outcomes are achieved. The figure below shows the percentage of potential participant fees associated with each engagement and outcomes milestone.



VIII. August 2014 US Preventive Services Task Force Recommendation

Published in the Annals of Internal Medicine in August 2014 the US Preventive Services Task Force (USPSTF) updated its recommendation for "Behavioral Counseling to Promote a Healthful Diet and Physical Activity for Cardiovascular Disease"[4]. The new recommendation states:

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. (Grade B recommendation)

The majority of evidence cited by USPSTF in making their recommendation was sourced from studies of DPP, suggesting that programs structured like Omada's *Prevent* fulfill USPSTF's definition of 'intensive behavioral counseling'. Furthermore, USPSTF guidance on target population (including prediabetes as a CVD risk factor), program features, intensity, and care setting are aligned with Omada's *Prevent* program. Therefore, *Prevent* can act as a quickly-scalable, broad-coverage, highly-effective option for plans to fulfill the requirements engendered by the USPSTF recommendation.

USPSTF recommendation	*Prevent*
POPULATION	
"This recommendation applies to adults aged 18 and over in primary care settings who are overweight or obese and have known CVD risk factors (hypertension, dyslipidemia, impaired fasting glucose or metabolic syndrome)."	The target population for Prevent is overweight or obese individuals with prediabetes who are 18 years old or over. This is aligned with the USPSTF recommendation.
EVIDENCE	
"The evidence reviewed by the USPSTF shows the effectiveness of intensive behavioral counseling interventions in making small but important changes in health behavior outcomes… diabetes incidence decreased by as much as 42% in trials reporting outcomes after 3 years."	Evidence for the effectiveness of DPP-like programs is extensive. The performance of Prevent exceeds that of the average DPP program.
INTENSITY OF INTERVENTIONS	
"Interventions involved an average of 5-16 contacts over 9-12 months depending on their intensity."	USPSTF emphasized that based on the evidence, programs need to be intensive in order to be effective. Prevent is intensive with 16 initial sessions, real-time monitoring of weight and physical activity, text messaging, one-on-one interaction with health coaches, and peer support via a social network.
PROGRAM FEATURES	
"Many types of intensive counseling were effective. However, it was not clear how the magnitude of the effect was related to the format of the intervention (for example face to face, individual, group, or telephone)."	USPSTF recognized that the evidence supported the effectiveness of a variety of intervention formats. Prevent incorporates several formats in order to maximize convenience for the participants, utilizes the power of social networking and leverages the skill of healthcare coaches.

USPSTF recommendation	*Prevent*
PRIMARY CARE	
"Because of the intensity and expertise required, most interventions were referred from primary care and delivered outside that setting." *"Multifaceted approaches with linkage between primary care practices and community resources could increase the effectiveness of the interventions"*	USPSTF recognized that the evidence involved interventions too intensive for primary care settings but that a linkage with primary care was important. Prevent is configured for an easy hand-off from primary care. The digital format allows Prevent to be available everywhere there is online access.

IX. DPP and *Prevent* Applicability to a Broader Population

Analyses of DPP data have added to the evidence that changes in diet and physical activity leading to weight loss are especially effective in helping reduce risk factors associated with both diabetes and cardiovascular disease, including high blood pressure and metabolic syndrome[15]. A person with metabolic syndrome has several of the risk factors for developing diabetes and heart disease, such as having excess fat deposited around the waist, high triglyceride levels, and high fasting blood glucose levels.

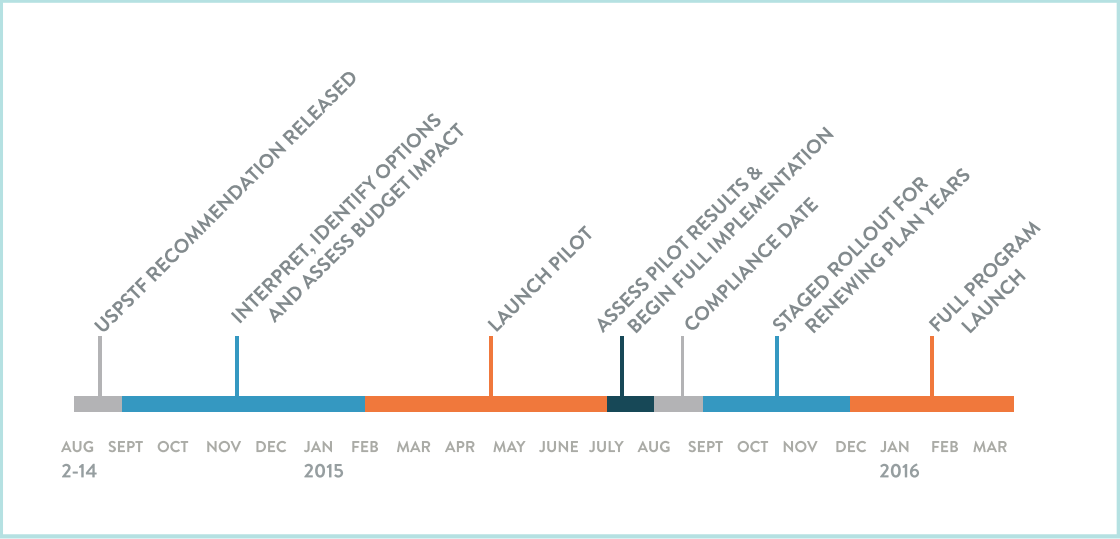
One analysis found that DPP participants in the lifestyle intervention group who did not have metabolic syndrome at the beginning of the study (approximately half of the participants) were less likely to develop it than those in the other groups. Another analysis of DPP data found that the presence of high blood pressure in DPP participants decreased in the lifestyle intervention group but increased in the metformin and placebo groups over time. Measures of triglyceride and HDL cholesterol levels also improved in the lifestyle intervention group. A third analysis found that levels of C-reactive protein and fibrinogen (risk factors for heart disease) were lower in the metformin and lifestyle intervention groups compared to the placebo group, with a larger reduction in the lifestyle intervention group. The DPP cohort entered the study with prevalence of hypertension of 30%, hypertriglyceridemia of 29%, and hypercholesterolemia of 44%. Annual assessment of these outcomes demonstrated progressive increases in prevalence of hypertension and dyslipidemia in the placebo and metformin groups with attenuation by intensive lifestyle intervention[16].

X. Affordable Care Act Required Coverage

The Affordable Care Act includes a mandate that health plans provide coverage for Grade A and Grade B recommendations of the USPSTF (5). When the USPSTF adds a new recommendation, the compliance date is one year after the recommendation or guideline is issued. This means that for plans whose plan year starts on January 1, compliance with

USPSTF guidance must occur by January 2016. Omada has obtained a memorandum from Hooper, Lundy, & Bookman, P.C. that addresses Prevent eligibility for "first dollar coverage" and applicability to the USPSTF recommendation[17].

XI. Template Timeline for Guideline Implementation



- DPP translational programs have been shown to substantially reduce the incidence of subsequent diabetes development in people with prediabetes compared with usual care.
- *Prevent* was designed to comply with CDC standards for DPP translational programs. Moreover, *Prevent* includes DPP program features known to be particularly effective.
- *Prevent* has been shown to be more effective than the average DPP translational program.
- *Prevent's* digital design improves convenience and access for participants, leverages the skills of health counselors, and allows for the establishment of social media support.
- USPSTF relies heavily on evidence from DPP translational programs as the basis for its guidance and thus, DPP programs likely meet ACA mandated coverage requirements.
- *Prevent* provides a scalable, performance-based, single vendor solution for health plans to improve outcomes, reduce medical claim costs, and meet ACA preventive coverage requirements.

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