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Weight loss in the prevention and treatment of diabetes

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ABSTRACT

The American Diabetes Association nutrition and lifestyle recommendations for prediabetes and type 2 diabetes focus on losing 7% of body weight and increasing physical activity to at least 150 min per week. This emphasis is largely based on results of the Diabetes Prevention Program (DPP) and Look AHEAD (Action for Health in Diabetes) clinical trials. DPP demonstrated that a lifestyle intervention aimed at 7% weight loss and 150 min of activity per week reduced diabetes incidence by 58% after 2.8 years of follow-up and resulted in sustained improvements in hemoglobinA1c, blood pressure and lipid levels. After 15 years of follow-up, DPP's lifestyle intervention sustained a 27% risk reduction in progression to diabetes. Look AHEAD's lifestyle intervention significantly reduced hemoglobinA1c, blood pressure, triglycerides, and the amount and costs of medications needed to treat these conditions when compared with diabetes support and education. Other clinical and psychological benefits achieved with lifestyle intervention were greater reductions in c-reactive protein, less self-reported retinopathy, reduced risk of nephropathy, less sexual dysfunction, decreased incidence of urinary incontinence and fatty liver, remission of sleep apnea, better physical functioning, less knee pain, more remission of diabetes, reduced incidence of depression, less body image dissatisfaction and improved quality-of-life. A number of DPP translation studies have demonstrated weight losses of 4 to 7% at 6 month and 1 year follow-up which has led to Medicare coverage for CDC recognized DPP lifestyle programs starting in April 2018. Translation studies of Look AHEAD using a variety of delivery formats are underway.

When we look at the American Diabetes Association nutrition and lifestyle recommendations for prediabetes and type 2 diabetes, the main emphasis is clearly on losing 7% of body weight and increasing physical activity to at least 150 min per week. There is also advice to limit or avoid sugar sweetened beverages to reduce risk of weight gain and worsening of cardiometabolic profile, and to reduce saturated fat to <10% of calories, minimize trans fat and moderate alcohol intake (American Diabetes Association, 2016; Evert et al., 2014). This paper describes the evidence related to the role of weight loss in the prevention and treatment of diabetes and related comorbidities, highlighting major clinical efficacy trials, current translational research of these evidence-based lifestyle interventions, and implications for clinical practice.

The focus on weight loss and increased physical activity is largely based on evidence from the Diabetes Prevention Program (DPP) and Look AHEAD (Action for Health in Diabetes) lifestyle intervention clinical trials (The Diabetes Prevention Program Research Group, 2002; The Look AHEAD Research Group, 2013). The DPP was a randomized controlled trial conducted in 27 centers in the U.S. aimed at preventing type 2 diabetes in persons at high risk. Over 3000 eligible participants with impaired glucose tolerance were randomly assigned to receive either a lifestyle intervention aimed at 7% weight loss and 150 min of activity per week, 850 mg of metformin twice per day, or placebo. The lifestyle intervention focused on fat gram goals based on 25% of calories from fat and calorie targets ranging from 1200 to 2000 cal based on initial body weight. Lifestyle participants received a 16-week core curriculum via individual sessions in the first 6 months, with a minimum of at least one in-person follow up every 2 months thereafter. They also could participate in supervised activity sessions 2 times per week throughout the trial and 4–6 week refresher groups and campaigns 3 times per year after the first 6 months (The DPP Research Group, 2002; Delahanty and Nathan, 2008). The study ended one year early because after 2.8 years of follow up, when compared to placebo, the lifestyle intervention group had achieved a 58% reduction in risk of developing diabetes and the metformin group had achieved a 31% risk reduction (The Diabetes Prevention Program Research Group, 2002). This is the first time that a nutrition and lifestyle intervention was found to be more efficacious than a medication.

The lifestyle intervention group achieved a 7.2% weight loss at 6 months and a 7% weight loss at 1 year. At study end, the lifestyle intervention group sustained a 5.6 kg weight loss compared with a 2.1 kg weight loss in the metformin group and a fairly stable weight in the placebo group. The lifestyle intervention group increased their activity by ~6 MET h per week (~150 min per week) more than the other groups (The Diabetes Prevention Program Research Group, 2002). Further analyses revealed that weight loss was the dominant predictor of diabetes prevention. For every kilogram of weight loss, diabetes risk was reduced

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by 16%. If the weight loss goal was not achieved, meeting the activity goal reduced risk of developing diabetes by 44% (Hamman et al., 2006).These are important messages for clinical practice. Health care providers can tell patients with prediabetes that every pound that they lose matters and if they are not ready to lose weight, then focusing on increasing activity towards the goal of 150 min per week will help.

After 10 years of follow up, the lifestyle intervention group sustained a 34% risk reduction in development of diabetes compared to an 18% risk reduction with metformin plus lifestyle (Diabetes Prevention Program Research Group, 2009). After a mean follow up of 15 years, diabetes incidence was reduced by 27% in the lifestyle intervention group and 18% in the metformin plus lifestyle group. The lifestyle intervention group also sustained lower hemoglobin A1c levels, lower blood pressure and lipid levels with less frequent use of medications to treat these conditions, achieving better management of what we refer to as the ABCs (A1c, blood pressure, cholesterol) of diabetes control (Diabetes Prevention Program Research Group, 2015) as well as lower levels of c-reactive protein which is a risk factor for heart disease (Haffner et al., 2005; Goldberg et al., 2014). The weight losses achieved with the DPP lifestyle intervention were also associated with a lower prevalence of urinary incontinence and improvements in health-related quality of life (Brown et al., 2006; Florez et al., 2012).

The Look AHEAD trial was another weight loss efficacy trial. It was an 11 year randomized controlled multicenter clinical trial following over 5000 patients aged 45 to 74 with type 2 diabetes and a BMI ≥ 25 kg/m^2. The objective of the study was to examine in overweight or obese persons with type 2 diabetes, the long-term effects of an intensive lifestyle intervention program compared to diabetes support and education (DSE) on the primary composite outcome of fatal or non-fatal heart attacks and strokes or hospitalized angina. The lifestyle intervention had goals of 7% weight loss and 175 min of activity per week. To achieve these goals, lifestyle intervention participants had calorie targets of 1200 to 1800 cal based on initial weight with fat gram goals based on 30% of calories from fat. The lifestyle intervention program was adapted from the DPP for patients with diabetes and included the proactive use of 2 meal replacements per day for the first 4 weeks to 4 months. These meal replacements were Glucerna, Optifast, HMR or Slimfast shakes which were donated to the study. Lifestyle participants received 24 sessions in the first 6 months (3 group sessions and 1 individual session per month); 18 sessions in months 7 to 12 (2 group sessions and 1 individual session per month). In years 2 and beyond, they were offered a minimum of monthly individual sessions and could participate in 4–8 week refresher groups and campaigns 2–3 times per year (Delahanty and Nathan, 2008; Wadden et al., 2006).

After the first year of intervention, the lifestyle intervention group lost 8.6% of body weight and achieved a 20% improvement in fitness levels compared to a 0.7% weight loss and 5.8% improvement in fitness with DSE. The percent of patients meeting goals for A1c and blood pressure was greater in the lifestyle group than DSE. The percent of participants achieving LDL targets was not significantly different between the 2 treatment groups; however the lifestyle intervention group was on significantly less medication to achieve these A1c, blood pressure and lipid outcomes (The Look AHEAD Research Group, 2007).

After 4 years of intervention, while there was some weight regain, the lifestyle intervention group sustained a 4.7% weight loss compared with a 1.1% weight loss with DSE. The improvements in A1c, blood pressure and triglycerides tracked the weight loss pattern and were still significantly better with lifestyle intervention versus DSE over 4 years (The Look AHEAD Research Group, 2010).

After 11.5 years of follow up, the lifestyle intervention group had sustained a 6% weight loss vs. a 3.5% weight loss with DSE. Although, there were still differences in CVD risk factors, they were attenuated and there was no difference in the primary composite outcome of fatal and non-fatal heart attacks and strokes or hospitalized angina between the lifestyle intervention and DSE groups (The Look AHEAD Research Group, 2013).

It is important to note that there was an extensive list of other clinical and psychological benefits that the lifestyle intervention participants experienced when compared with DSE (Delahanty, 2014). They had greater reductions not only in A1c, blood pressure, and triglycerides, but also in the amount and costs of medications needed to treat these conditions (The Look AHEAD Research Group, 2007; The Look AHEAD Research Group, 2010; Delahanty, 2014; Redmon et al., 2010). They had greater reductions in c-reactive protein, less self-reported retinopathy, a 31% risk reduction in nephropathy, less sexual dysfunction, and a decreased incidence of urinary incontinence and fatty liver (Delahanty, 2014; Belalcazar et al., 2013; The Look AHEAD Research Group, 2014a; Wing et al., 2013; Phelan et al., 2012; Lazo et al., 2010). At 1 year and 4 year follow up lifestyle intervention participants had improvements in sleep apnea (Delahanty, 2014; Foster et al., 2009; Kuna et al., 2013). Despite a 50% weight regain at 4 years, there were 5 times as many patients with remission of sleep apnea in the lifestyle intervention group compared with DSE (Kuna et al., 2013). In addition, lifestyle intervention participants experienced better physical functioning with a 48% decreased risk of loss of mobility and less knee pain when compared with DSE (Rejeski et al., 2012; Foy et al., 2011). Remission of diabetes occurred in 11.5% of lifestyle intervention participants compared with 2% of DSE participants (Gregg et al., 2012). The lifestyle intervention also resulted in many psychological benefits including a reduced incidence of depression, less body image dissatisfaction and an improved quality of life (Delahanty, 2014; Faulconbridge et al., 2012; The Look AHEAD Research Group, 2014b; Stewart et al., 2011; Williamson et al., 2009). Over the course of the study, lifestyle intervention participants had fewer hospitalizations and associated medical costs (Espeland et al., 2014).

The lifestyle intervention used in the DPP and Look AHEAD clinical trials is evidence based and includes nutrition, activity and behavioral components. The nutrition component focused on achieving fat and calorie goals based on initial weight. The activity goals ranged from 150 to 175 min per week and focused on aerobic activities similar to brisk walking. The behavioral strategies used to teach lifestyle skills included goal setting; self-monitoring of weight, food and activity; stimulus control to manage cues; problem-solving to deal with barriers; cognitive restructuring to deal with negative self-talk; and relapse prevention (The DPP Research Group, 2002; Delahanty and Nathan, 2008; Wadden et al., 2006).

In both DPP and Look AHEAD, not all participants achieved the 7% weight loss target. In DPP 49% of lifestyle participants achieved the 7% weight loss goal at 6 months and 37% sustained a 7% weight loss at study-end (The Diabetes Prevention Program Research Group, 2002). Ancillary study research on 274 of the 1079 DPP lifestyle intervention participants found that the most important modifiable psychological predictor of long-term weight loss was low fat diet self-efficacy. Each unit improvement in self-confidence in following a low fat diet, predicted an almost 3-fold greater likelihood of achieving a 7% weight loss. The most important behavioral predictor of weight loss was flexible dietary restraint-the ability to respond to increases in eating or in weight by eating less to compensate and balance calorie intake. For each unit increase in flexible dietary restraint skills, there was a 4.3 fold greater likelihood of achieving a 7% weight loss long-term (Delahanty et al., 2013). These results underscore how important it is to make the diet component of lifestyle interventions doable and flexible enough so that patients experience success in approaching eating habits in a ways that are sustainable and promote lasting weight loss.

Since the DPP results were published in 2002, there has been a number of translation studies of CDC recognized DPP programs that have demonstrated a 4 to 7% weight loss at 6 month and 1 year follow up. The in-person group coaching formats achieve the greatest weight losses ranging from 5.5 to 7.5%; the digital plus human coaching programs achieve about 5% weight loss and the fully automated coaching programs achieve 3.6% weight loss (Institute for Clinical and Economic Review, 2016). The systematic reviews, meta-analyses and recent research conducted to examine the effectiveness of real world translations of DPP

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