

# The Pillars of Prevention: Discover, Advocate, and Educate

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■ **EDITOR'S NOTE:** This article is adapted from a speech that Ms.

Montgomery delivered as the American Diabetes Association's President of Health Care & Education at ADA's Annual Meeting and Scientific Sessions in June 2017, San Diego, Calif. A webcast of the speech can be viewed on ADA's DiabetesPro website at <https://professional.diabetes.org/webcasts-ss2017>.

*"Never believe that a few caring people can't change the world. For, indeed, that's all who ever have."* —Margaret Mead

My purpose here is to illustrate how the diabetes world was changed by the Diabetes Prevention Program (DPP) study and how the American Diabetes Association (ADA), based on the findings of the DPP, stepped in to support, disseminate information about, and advocate on behalf of the prevention of diabetes.

### Three Pillars of Prevention

The ADA is focused on three strategic imperatives, which I call the "pillars of prevention." I have organized this discussion according to ADA's strategic plan, which describes the three pillars of prevention as follows:

1. **Drive Discovery.** Through research, partnerships, and innovation on a global scale, drive discoveries to prevent, manage, and ultimately cure diabetes.
2. **Raise Voice.** Intensify the urgency around the diabetes epidemic, and mobilize bold action through advocacy and engagement.
3. **Support People.** Provide new, effective resources for individuals living with and at risk of devel-

oping diabetes and for the health care professionals serving them.

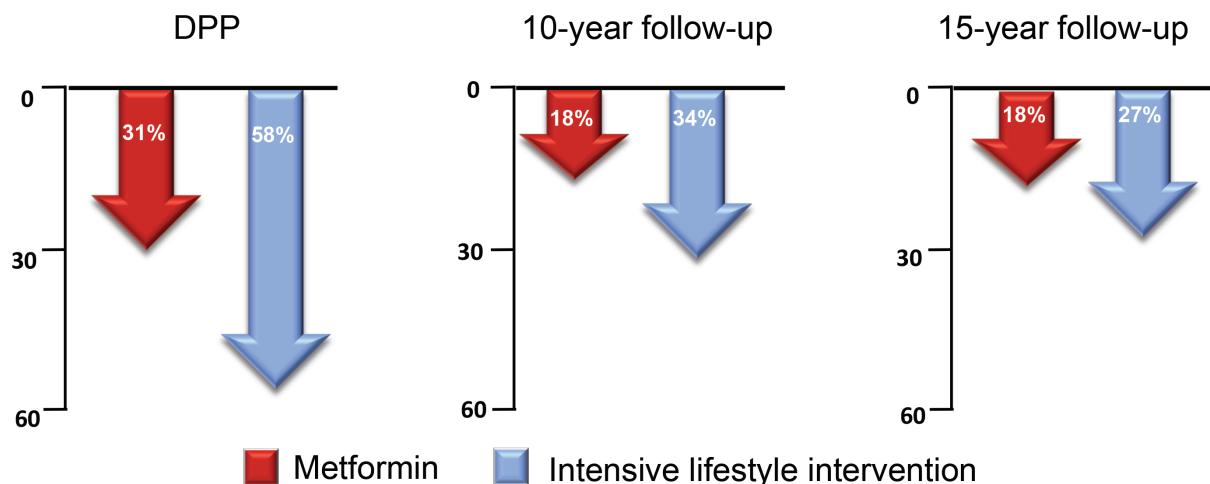
What do we know about the DPP and how its findings guide these pillars of prevention? For the first pillar, Drive Discovery, the DPP provided evidence for effective prevention approaches. Then, the follow-up DPP Outcomes Study (DPPOS) demonstrated durability of effect. The YMCA translated the DPP interventions for a real-world setting, and the DPP approach was replicated internationally. For the Raise Voice pillar, the ADA advocated for the Diabetes Prevention Act, a piece of legislation to establish a National Diabetes Prevention Program (NDPP) at the Centers for Disease Control and Prevention (CDC). The ADA also collaborated with the YMCA to advocate for the establishment and funding of the NDPP. Finally, for the third pillar, Support People, the ADA has helped to broaden access to prevention services by advocating for expanded coverage through the Centers for Medicare & Medicaid Services (CMS). The ADA has also facilitated the national scaling of prevention efforts through its Education Recognition Program, which is helping to implement the NDPP and its

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■ FIGURE 1. Long-term diabetes risk reduction from lifestyle intervention and metformin therapy in the DPP (2–4).

efforts to engage the community in diabetes prevention.

### Pillar 1: Drive Discovery

#### **DPP: Small Steps, Big Rewards**

There has been huge progress in our understanding of prevention since 1993, when the DPP was designed. The phrase “small steps, big rewards” was used in the DPP and DPPOS to stress how modest lifestyle changes can make a big difference in health. We now use it when discussing the pillars of prevention and our quest to change the world.

When DPP started in 1996, the charge was to over-recruit people disproportionately affected by diabetes: older people, women, and ethnic minorities. We did well in this regard: 20% of study subjects were  $\geq 60$  years of age, 68% were women, and 45% were from ethnic minority populations. Nearly 31,000 individuals were screened for the study, and 3,819 were randomized to one of four treatment arms: an intensive lifestyle intervention, metformin therapy, troglitazone therapy, or placebo (1). Although the troglitazone arm was halted early due to safety concerns, the DPP was still able to drive discovery by contributing information about the hepatotoxicity of this medication.

The now-familiar results of the study, and its long-term follow-up, are shown in Figure 1 (2–4). The intensive lifestyle intervention reduced the risk of diabetes by 58% and metformin reduced diabetes risk by 31% compared to placebo. There were no significant differences in results of the interventions among the various racial/ethnic groups or between sexes. We are fortunate that funding for the DPP continued, enabling it to gather and report through the DPPOS 10- and 15-year data. After 10 years, the original lifestyle intervention group continued to realize a diabetes risk reduction of 34%, and the metformin group had a continued risk reduction of 18% (3). At 15 years, risk reductions were 27 and 18%, for lifestyle intervention and metformin therapy, respectively (4).

The DPP and DPPOS attracted much scientific interest and cultivated a collaborative model of discovery in studies focusing on genetics, cardiovascular disease, diabetes complications, metformin and cancer, behavioral intervention, nutrition therapy, and other areas. Most of these efforts have been funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) or other National

Institutes of Health groups, with additional support in some cases from the ADA.

One of the most exciting things about the DPP is that it continues to this day to bear fruit. Of the more than 30 DPP-related articles that have been published in just the past 4 years, I would like to highlight three. In 2013, Herman et al. (5) reported that, at 10 years, lifestyle and metformin were cost-effective diabetes prevention measures—evidence that certainly helped make the case for a government-supported NDPP program. In 2014, Delahanty et al. (6) reported their findings that, although the degree of weight loss at 2 years was the strongest predictor of diabetes, weight cycling (defined as how many times a person gained and lost 5-lb increments) was an independent predictor of diabetes risk, with more cycles associated with an increased risk for type 2 diabetes. Finally, in 2016, Aroda et al. (7) reported that they had found an association between long-term metformin use and vitamin B12 deficiency in the DPP population. Their study had implications not only for those at risk for diabetes, but also for people already living with type 2 diabetes. This prompted the ADA

to add a new recommendation to its 2017 *Standards of Medical Care in Diabetes* (8), stating, “Long-term use of metformin may be associated with biochemical vitamin B12 deficiency, and periodic measurement of vitamin B12 levels should be considered in metformin-treated patients, especially in those with anemia or peripheral neuropathy.” This was given an evidence level B, indicating the quality of the research (8).

### **DPP Translation for the Real World**

Would the DPP intervention be translatable in real-world settings? That was a common concern after its results were published.

One of the earliest translation efforts was the YMCA DPP (YDPP) initiative, which trained YMCA wellness instructors to deliver the DPP intervention in YMCA centers in the community. The 2008 DEPLOY (Diabetes Education & Prevention with a Lifestyle Intervention Offered at the YMCA) pilot study (9) was conducted at the YMCA of Greater Indianapolis, Ind., and showed an average 6% weight loss in program participants, with persistent 5% weight loss at 28 months. Seven years later, the RAPID (Reaching Out to Prevent Increases in Diabetes) study (10), evaluated the YDPP in the same community in a large, randomized trial in which 50% of the study population was African American. It, too, showed positive weight loss results, with an average 5% weight loss among participants. Based on these promising results, the YMCA of Greater Indianapolis has shared its YDPP with YMCAs across the country.

DPP translation did not end with the YMCA effort, however. Indeed, there have been a multitude of studies evaluating real-world interventions modeled after the DPP. A 2012 meta-analysis (11) of 28 of these studies from the United States compared weight loss among the studies’ participants and looked at

whether the type of personnel delivering the interventions had any effect on results. Regardless of whether the interventions were delivered by medical or allied health professionals, lay community members, or through electronic media, subjects had positive effects of weight loss, with a consensus weight loss of ~4% at 1 year. This was good news that should ease concerns about what types of resources are required to deliver a successful lifestyle intervention in real-world settings.

The numerous studies mentioned above provided evidence that the DPP could be successfully replicated or adapted in the United States. Before, during, and after the DPP, a number of international studies also demonstrated the benefits of lifestyle and other interventions for diabetes prevention. The Da Qing study in China (12), the Finnish Diabetes Prevention Study (13), the Indian Diabetes Prevention Program (14,15), and Japanese Zensharen study (16), among others, demonstrated salutary effects in many populations and led to worldwide efforts to prevent diabetes. In 2014, Dunckley et al. (17) published a systematic review of 22 international translation studies showing a mean 1-year weight loss of ~2 kg—additional confirmation that lifestyle interventions can be successfully replicated regardless of study design or location. Indeed, many countries around the world appear to have gotten a relatively early start in these efforts. In 2008, Colagiuri et al. (18) conducted a survey of diabetes associations in 202 countries to gather information about national diabetes programs. Of the 95 responses received (47%), 58 countries (61%) had national diabetes programs; of those programs, 48 (83%) had prevention components.

### **Pillar 2: Raise Voice**

#### **The Diabetes Prevention Act**

In 2009, in partnership with the YMCA, the ADA approached U.S. Sen. Al Franken, a Democrat from

Minnesota, about the potential to successfully translate the DPP and the need for affordable group classes to offer the DPP intervention in community programs across the country. With his colleague Sen. Richard Lugar, a Republican from Indiana, Franken introduced the Diabetes Prevention Act, a bipartisan effort to establish through the CDC an NDPP for people at high risk for developing diabetes. The ADA and the YMCA together advocated in Congress for support of this important initiative, and language establishing the NDPP was included as part of the Patient Protection and Affordable Care Act (ACA), which became law in 2010.

#### **The Medicare Diabetes Prevention Act**

Building on the successful establishment of the NDPP, in 2011, the ADA began to focus specifically on translating the success experienced by seniors who had participated in the DPP study. Seniors in the DPP reduced their risk for developing diabetes by >70% (2). With this in mind, ADA worked with Franken and its YMCA partners to introduce the Medicare Diabetes Prevention Act, which would require Medicare to cover the cost of participating in an NDPP-affiliated prevention program for Medicare beneficiaries with prediabetes. Despite its establishment within the ACA, the NDPP enjoys solid bipartisan support on Capitol Hill. Iowa’s Sen. Chuck Grassley, a leading Republican on the Senate Ways and Means Committee, emerged as a key champion for Medicare coverage of the NDPP and worked closely on the bill with Franken. The following year, a corresponding version of the bill was introduced in the U.S. House of Representatives by Rep. Susan Davis, a Democrat from California’s 53rd District, and Rep. Peter King, a Republican from New York’s 2nd District.

In the meantime, the YMCA was awarded a grant from the Centers for Medicare and Medicaid Innovation

(CMMI) to test the YDPP in a senior population. In 2016, after completion of this demonstration project, CMS actuaries certified that Medicare saved \$2,650 per participant enrolled over the 15 months of the program. With that certification, the NDPP became the first innovative health program eligible for Medicare coverage through CMMI.

In July 2016, U.S. Department of Health and Human Services Secretary Sylvia Mathews Burwell announced that Medicare would take steps to cover the NDPP for seniors at high risk for diabetes. In November 2016, CMS released a final rule declaring that Medicare coverage of participation in NDPP-affiliated programs would begin in 2018. This was a groundbreaking achievement and a huge victory after years of advocacy. Fifty percent of Medicare beneficiaries have prediabetes, and one-third of all Medicare expenditures are for people with diabetes. Because of the efforts of ADA and its advocacy partners, seniors now have access to evidence-based prevention programs that will not only improve their health, but also reduce overall Medicare costs.

### **Seeking a Prevention Indication for Metformin**

We know that lifestyle intervention is particularly effective in older adults and soon will be covered by Medicare; we can check this off. But in the DPP, metformin was also effective, particularly in younger and more obese participants and in women with a history of gestational diabetes (2,19). So, where are we with the use of metformin for prediabetes?

In 2012, Fradkin et al. (20) of NIDDK wrote an article published in the *New England Journal of Medicine* titled, "What Is Preventing Us from Preventing Type 2 Diabetes?" In it, they stated that, "given its efficacy, potential for cost savings, and excellent safety profile, metformin offers another approach to diabetes prevention, particularly in people less than

60 years of age and in women with a history of gestational diabetes."

Despite this, only 3.7% of patients with prediabetes in a national sample of 17,352 working-age adults were prescribed metformin over the 3-year period from 2010 to 2012 (21). The authors suggested that this low prescription rate may be, in part, because of the lack of an approved prevention indication for metformin. Because it is a generic medication, there is no pharmaceutical company eager to invest in the work that would be involved in getting U.S. Food and Drug Administration (FDA) approval of a label change or new indication regarding diabetes prevention. However, the work of a citizen's panel was successful in petitioning the FDA for metformin label changes regarding the use of metformin in individuals with mild chronic kidney disease as determined through measurement of estimated glomerular filtration rate instead of serum creatinine levels (22). With this effort as a precedent, we now need to get metformin approved as a therapy for diabetes prevention.

Toward that end, the ADA, in conjunction with the American Association of Clinical Endocrinologists, the Endocrine Society, DPP researchers, and other experts, has initiated a citizen's petition process to secure an indication for the use of metformin in individuals with prediabetes. In September 2016, the group met with FDA representatives to present data in support of its petition. At that time, the FDA requested more data, which DPP investigators will soon provide. This continuing effort to gain FDA approval of metformin therapy for diabetes prevention is a matter of crucial public health significance. The diabetes epidemic continues, with an estimated 29 million people with type 2 diabetes and 84 million adults at high risk in the United States alone (23). Understanding how to prevent or delay type 2 diabetes and being able to intervene at the appropriate time

with the goal of reducing long-term morbidity and mortality in a cost-effective manner is perhaps the most important public health issue in diabetes today.

### **Pillar 3: Support People**

#### **Preventing Diabetes in Children**

Mayer-Davis et al. (24) recently published an article in the *New England Journal of Medicine* providing alarming updated diabetes incidence data from the SEARCH for Diabetes in Youth study. SEARCH researchers previously had reported that, between 2001 and 2009, there was a 30.5% increase in type 2 diabetes in youth (Figure 2) (25). In their update, they found the incidence of type 2 diabetes in youth continuing to increase at a rate of 7.1% annually from 2002 through 2012. Furthermore, as with diabetes in adults, there were racial/ethnic group disparities, with incidence rates of 8.6% for Native American young people, 6.3% for African-American youth, 3.1% for Hispanics, 8.5% for Asian/Pacific Islanders, and 0.6% for white youth (24). We now need to mobilize significant efforts now to reduce or delay type 2 diabetes in children.

#### **Community Engagement in Diabetes Prevention**

The NDPP is focusing on scaling up DPP-style lifestyle intervention on a national level. Initiatives to further engage communities in diabetes prevention are also needed. One exciting example of community engagement comes from Lisa Randall at Inland Northwest Health Services in Spokane, Wash. She and her colleagues there have piloted a program in two primary care clinics to identify more people at risk for type 2 diabetes. They have every patient >18 years of age complete ADA's risk test regardless of their reason for having an appointment. Those who score >5 are invited to participate in their local DPP classes.

The ADA Education Recognition Program (ERP) is also facilitating

DPP intervention across the country. Its electronic charting system has been expanded to capture data from DPP classes offered through diabetes education programs. This platform will generate CDC-required reports, as well as progress reports throughout the year-long NDPP-affiliated programs. Programs do not have to have earned ERP Recognition to use the charting system. To learn more, visit the ADA ERP website ([diabetes.org/erp](http://diabetes.org/erp)).

Finally, I want to make sure everyone knows about 1-800-DIABETES, the ADA call center. This service provides support and information for those with diabetes or at risk for developing it. The call center receives 150–200 calls every month asking about prediabetes and diabetes prevention.

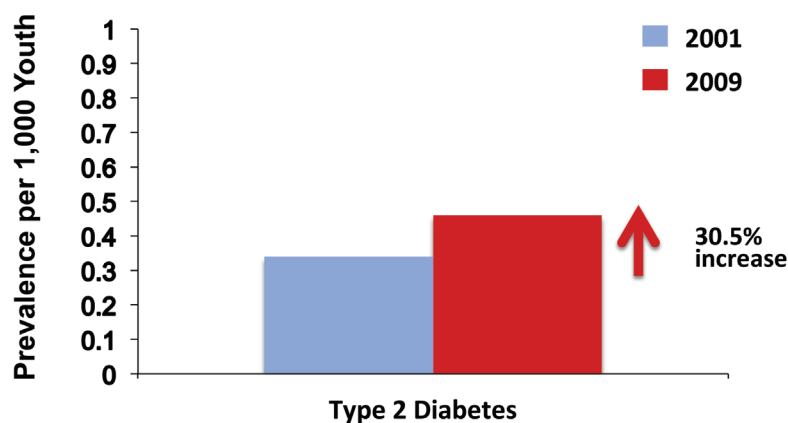
The initiatives I have described here are just drops in the bucket of advocacy and support services offered through ADA and its partners. I want to shout from the mountaintops how proud I am of the association's work. Although “small steps, big rewards” was the motto for the DPP study, I believe we now need to take larger strides or even start running toward the goal of preventing diabetes. Please join me and the ADA in our efforts to Drive Discovery, Raise Voice, and Support People.

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I began this article with a quote from Margaret Mead about changing the world. I would like to end by thanking some people who have changed the world with regard to diabetes prevention: all of the research volunteers who participated in the DPP and those who remain in the DPPOS. These people joined the study starting in 1996, long before the advent of the term “prediabetes,” and their dedication has resulted in many significant findings in diabetes prevention, early diagnosis, and treatment.

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■ **FIGURE 2.** Rates of childhood diabetes from the SEARCH for Diabetes in Youth study, 2001–2009 (25).

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### Duality of Interest

No potential conflicts of interest relevant to this article were reported.

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