

# Time for a Victory Lap or Time to Raise the Levees: A Perspective on Complication Reduction and New-Onset Diabetes

The Mississippi River is a small piddling stream as it leaves Lake Itasca, Minnesota. As it meanders southward along its 2,300 mile journey, it is joined by 250 different tributaries that ultimately drain one-third of the continent. These widen the river, increase the flow, and strain the system of levees and spillways that contain the “Big Muddy.” It then passes on to the Gulf of Mexico.

There is a striking analogy between the U.S. diabetes population and the Mississippi River. Early in life the prevalence of diabetes is small as is the Mississippi at its origin. The population increases in number, age, and girth, and is enriched with high-risk minorities. Over time, many people with prediabetes transition to diabetes and develop one or more of its complications. The 2010 U.S. Census cites improvements in overall longevity, particularly in males, meaning people with diabetes are living longer and contributing to the expanding diabetes prevalence. Tributaries of people with undiagnosed, newly diagnosed, and established diabetes join the rush of the river. Increased volume and velocity put pressure on the levees and strain the system of locks and dams that regulate the river and protect the communities along its banks. The river finally passes on to the Gulf of Mexico.

U.S. 40-year diabetes population projections by Boyle et al. (1) are sobering. Using census, birth, death, and net migration data, plus estimates and standard errors for the U.S. adult population aged 18–79 years, the authors developed a matrix to transition people from having no diabetes, prediabetes, undiagnosed, diagnosed diabetes, and mortality by glycemic and diabetes state. They used a logistic curve to project low, middle, and high diabetes incidence (new cases per 1,000 person-years). These incidence projections and other population-based data are used to project prevalence (all diabetes cases). According to the estimates, adult diabetes prevalence will rise from the current 1 in 10 to between 1 in 5 and 1 in 3 by 2050 (1). This two- to three-fold increase in diabetes prevalence is a

conservative estimate since it excludes individuals  $\geq 80$  years who have a diabetes prevalence approaching 18% and grew by 22% in the last decade (2,3).

In this issue of *Diabetes Care*, Kytö et al. (4) describe the 20- to 30-year decline in cumulative incidence of laser photocoagulation to prevent blindness in cohorts of patients with type 1 diabetes. The authors attribute these reductions in complications to the no-cost or low-cost glucose testing and insulin available in Finland. Even more striking are the reductions in type 1 diabetes complications found in the Epidemiology of Diabetes Interventions and Complications (EDIC) cohort that followed the Diabetes Control and Complications Trial (DCCT) population. Complication rates fell in the group with tight glycemic control including peripheral neuropathy (5), autonomic neuropathy (6), retinopathy (7,8), and nephropathy (9).

The May issue of *Diabetes Care* reports a secular trend showing a 34% reduction in the age- and sex-standardized incident lower-limb amputation rates in the U.S. Department of Veterans Affairs (VA) from 2000 to 2004 (10). This parallels a 37% reduction in the age-adjusted rates of lower-limb amputation reported for the U.S. population between 1998 and 2006 (11), and a 26% reduction in age- and sex-adjusted total amputation rates reported for the Medicare population between 1992 and 2001 (12). Another approach to analyze trends over time is to use quality improvement methods of statistical process control. According to Wheeler (13), any eight data points below the mean represent a shift in the direction or a change in the system. Thus, the U.S. amputation rates from 1988 to 2006 (14) (Fig. 1) represent a systematic reduction in this complication despite not having met the national goals of Healthy People 2010 (15) or benchmark approaches (16). These improvements came with effort. The VA mandated diabetes foot care performance measures in primary care clinics that included foot screens and referrals. Electronic medical records, electronic

alerts, and improvements in stand-alone foot care clinics were available and may be a factor in the lower amputation rates (17,18). In addition to the impressive reduction in amputations, evidence shows reductions in other major complications of type 2 diabetes (19).

The question is whether we should build more levees downstream to manage the two- to threefold growth of the diabetes population, or can we work further upstream to change the magnitude and flow of people with diabetes?

There is strong evidence for upstream action from the Diabetes Prevention Program (DPP). Three randomized groups were followed for 2.8 years. The lifestyle intervention group achieved a 7% weight loss and  $\geq 150$  min of physical activity/week and reduced their diabetes development by 58%, and the metformin group (850 mg twice daily) reduced their diabetes onset by 31% compared with the placebo group (20). The DPP follow-up study offered the participants in all three groups the lifestyle intervention using a group format. Metformin was continued at the same dosage as in the original metformin group, and additional lifestyle support was available to the original lifestyle support group. During the 5.7 years of the follow-up study, new-onset diabetes rates were similar across the treatment groups: 5.9 per 100 person-years for lifestyle, 4.9 for metformin, and 5.6 for placebo. The striking finding was diabetes incidence was reduced in the 10 years following DPP randomization by 34% in the lifestyle group and 18% in the metformin group compared with the original placebo group (21). Thus in both the DPP and the DCCT/EDIC, the benefits are extending  $\geq 10$  years from initial study randomization (5–9,21).

The National Diabetes Prevention Program at the Centers for Disease Control and Prevention (CDC) is coordinating with community partners who demonstrate they are willing and ready to support a less costly, community-based translation of the DPP for at-risk individuals in their communities. A pilot cluster-randomized



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