APRIL 2014

Diabetes Care

In This Issue of *Diabetes Care*

Edited by Helaine E. Resnick, PhD, MPH

Translation of Research Into Practice for Primary Diabetes Prevention

A new report in this issue of *Diabetes Care* (**p. 922**) fills a stubborn gap in the literature that took root following completion of primary diabetes prevention trials including the Diabetes Prevention Program (DPP). Once the results of the DPP and similar trials were published, the answer to a seemingly simple question remained elusive: How could the compelling results of successful lifestyle modification trials be translated into practice in a cost-effective manner that also preserved the clinical benefit? A new meta-analysis by Dunkley et al. responds to this question with a summary of findings from 22 studies whose goal was to translate the findings of lifestyle interventions into practice in the community. The observational and intervention studies in the new report all had follow-up of at least 12 months, along with information on body composition, glycemic control, and other factors. Importantly, all studies were implemented in the community and most focused heavily on primary diabetes prevention. Key findings from the pooled analysis indicated that lifestyle interventions resulted in an average weight loss of 2.12 kg and that interventions adhering more closely to recommended lifestyle modification guidelines yielded greater weight loss than those with lower levels of adherence to these recommendations. Indeed, across the studies that were included in the new report, heterogeneity in the content and delivery of the interventions explained a considerable amount of the variability in their effectiveness. The public health implications of these findings are clear: Practical approaches to primary diabetes prevention are available and they are effective. Further, interventions that adhere more closely to recommended guidelines are more likely to yield the desired benefits—a straightforward finding that provides support for the idea that diabetes prevention programs should comply with the standards set forth in international guidelines. — *Helaine E. Resnick, PhD, MPH*

Dunkley et al. Diabetes prevention in the real world: effectiveness of pragmatic lifestyle interventions for the prevention of type 2 diabetes and of the impact of adherence to guideline recommendations: a systematic review and meta-analysis. Diabetes Care 2014;37:922–933

Promising Results for Pharmacotherapy Targeting Weight Loss

Data in this issue of *Diabetes Care* (**p. 912**) provide evidence that when added to lifestyle modification, phentermine and topiramate extended release (PHEN/TPM ER) may be an effective strategy to fight obesity and prevent diabetes among high-risk individuals. The new report focuses on a subset of participants in the CONQUER trial—a 56-week, phase 3, randomized, placebo-controlled trial of PHEN/TPM ER among overweight/obese adults with two or more weight-related comorbidities. In CONQUER, three study arms were examined: once-daily oral placebo, PHEN 7.5 mg/TPM ER 46 mg, or PHEN 15 mg/TPM ER 92 mg (placebo, 7.5/46, and 15/92, respectively) plus lifestyle modification. SEQUEL was a 52-week extension of CONQUER in which participants retained their original treatment groups, yielding a total treatment period of 108 weeks. The new data in this issue of the journal focus on SEQUEL participants who had either metabolic syndrome (MetS) or prediabetes at baseline and the relationship between treatment group and both weight loss and progression to diabetes among these high-risk participants. Of the 475 participants who were eligible for the analysis, those in the placebo, 7.5/46, and 15/92 groups had average weight losses of 2.5%, 10.9%, and 12.1%, respectively. Further, relative to placebo, progression to type 2 diabetes among SEQUEL participants with MetS and/or prediabetes was reduced by 70.5% in the 7.5/46 group and 78.7% in the 15/92 group. In addition to the marked reductions in weight loss and lower risk of diabetes, participants in the PHEN/TPM ER arms also exhibited notable improvements in a number of cardiometabolic characteristics, including fasting and post-challenge glucose, triglycerides, and HDL. Consistent with these improvements and relative to placebo, a significantly larger proportion of people in the treatment arms displayed remission from MetS at study end. The encouraging findings from this new report suggest that pharmacotherapy for obesity may be a viable strategy for primary diabetes prevention in settings where lifestyle modification is not sufficient to achieve desired goals. — *Helaine E. Resnick, PhD, MPH*

Garvey et al. Prevention of type 2 diabetes in subjects with prediabetes and metabolic syndrome treated with phentermine and topiramate extended release. Diabetes Care 2014;37:912–921

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Short Telomeres Increase Odds for Periodontitis in Diabetes

Cross-sectional data from a large sample of patients with diabetes suggest that shortened leukocyte telomere length (LTL) may help explain the excess periodontal disease that has long been observed in people with diabetes and, perhaps, the higher rates of cardiovascular morbidity and mortality in people with periodontitis. The new report by Masi et al. (**p. 1140**) is based on a protocol in which 630 diabetic patients (371 with type 2 diabetes and 259 with type 1 diabetes) who were enrolled from a university-based endocrinology practice underwent a baseline visit that included both oral and physical examinations as well as a blood draw from which DNA was extracted. Of the enrolled patients, 255 (40.4%) had gingivitis and 327 (51.9%) had periodontitis. Of the 327 diabetic patients with periodontitis, 114 had moderate periodontal pockets, 213 had severe pockets, and an additional 48 patients were edentulous. Preliminary analyses indicated that diabetic patients with periodontitis had significantly shorter LTL compared with those with gingivitis, but stratified analyses revealed that this association was driven by patients with type 2 diabetes. Further analysis that controlled for a variety of potential confounding factors—including type of diabetes—showed that diabetic patients with severe periodontal pockets had significantly shorter LTL compared with their counterparts who only had gingivitis. Another key observation from the new report was that LTL was inversely related to circulating endotoxin levels but, surprisingly, not to levels of circulating inflammatory markers. Taken together, these cross-sectional data demonstrating strong interrelationships among short LTL, endotoxemia, and periodontitis may help piece together a biological pathway that explains why diabetic people with periodontitis are at especially high risk of unfavorable health outcomes. If substantiated, efforts to improve oral health among people with diabetes may prove to be an effective means of reducing diabetes-related morbidity and mortality. — *Helaine E. Resnick, PhD, MPH*

Masi et al. Association between short leukocyte telomere length, endotoxemia, and severe periodontitis in people with diabetes: a cross-sectional survey. Diabetes Care 2014;37:1140–1147

DPP Links Genetics to GDM but Not to Progression to Diabetes

Results in this issue of *Diabetes Care* (**p. 909**) show that although genetic factors are associated with history of gestational diabetes mellitus (GDM), these factors may not predict progression to type 2 diabetes. Previous findings from the Diabetes Prevention Program (DPP) showed that progression to diabetes was significantly reduced among women with a history of GDM who were treated with metformin. This observation led investigators to postulate that genetic factors may have a role in explaining this differential response to therapy. In the study presented in this issue, 34 diabetes-related genetic loci were used to calculate a genetic risk score (GRS) that was examined in women with and without a history of GDM. In addition to analyzing key indicators such as β-cell function, the GRS was also studied in relation to progression to diabetes according to GDM history. Results showed that the GRS was associated with a history of GDM, but it did not predict progression to diabetes or response to treatment, suggesting that genetic factors do not explain the earlier observation concerning favorable response to metformin treatment among women with a history of GDM. The investigators point out that additional exploration of the role of genetic factors may be warranted because the number of GDM women was relatively small in the DPP. Further, they point out that these women had an average of 12 years of diabetes-free time when they were enrolled in DPP, raising the possibility that DPP did not include sufficient numbers of women at high risk of GDM. — *Helaine E. Resnick, PhD, MPH*

Sullivan et al. Genetic risk of progression to type 2 diabetes and response to intensive lifestyle or metformin in prediabetic women with and without a history of gestational diabetes mellitus. Diabetes Care 2014;37:909–911

DOI: 10.2337/dc14-ti04