

## Summary

### REPORT OF THE COUNCIL ON SCIENCE AND PUBLIC HEALTH

CSAPH Report 2-A-14

Subject: Genomic-based Approaches to the Risk Assessment, Management and Prevention of Type 2 Diabetes

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Referred to: Reference Committee E  
(R. Rodney Howell, MD, Chair)

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#### BACKGROUND

Type 2 diabetes (T2D) is a complex disease characterized by insulin resistance, impaired insulin secretion, and increased hepatic glucose production. It is a common disorder; the CDC estimates that nearly 26 million people in the United States have T2D, and that 79 million people exhibit signs of prediabetes (hemoglobin A1c or blood glucose levels higher than normal but below diagnostic levels for diabetes).<sup>1</sup> Risk factors for T2D include obesity, physical inactivity, advancing age, hypertension, hyperlipidemia and a family history of T2D. Dozens of genetic variations have been identified that also increase risk.<sup>2</sup> The progression and severity of T2D in any given individual appears to be dependent on the combination of risk factors, both genetic and non-genetic, that he or she carries.<sup>3</sup> Complications of T2D include cardiovascular disease, stroke, neuropathy, nephropathy, retinopathy, periodontal disease and foot ulcers and amputations.

T2D's serious burden of disease has led to an emphasis on early identification of individuals at high risk so that management and intervention strategies can be effectively implemented. For example, the American Medical Association's (AMA) Improving Health Outcomes group has partnered with physician practices and the Diabetes Prevention Program to identify individuals at risk and refer them for intervention.<sup>4</sup> With increasing knowledge about the genetic basis of T2D, several genomic-based strategies have been tested for their ability to improve risk assessment, management and prevention. The Council on Science and Public Health has undertaken this report to review genomic-based strategies aimed at improving T2D clinical care.

## CONCLUSIONS AND FUTURE DIRECTIONS

Genetic factors play a substantial role in the risk, onset, severity and downstream complications of T2D. Genetic discoveries are being translated into clinical tools like GRSs and genetic counseling for T2D. Although evidence thus far shows variable clinical utility of these tools, research is underway to determine which subpopulations may derive benefit from their use. Additionally, important information is being revealed about the genetic basis for differential therapeutic response to oral hypoglycemic drugs and to intervention strategies. Overall, current knowledge about the contribution of genomic factors to T2D reinforces the concept that T2D is a complex disease that can be different in every person, and that risk prediction and treatment are exceptionally challenging for health care providers.

Genomic analysis in clinical care is rapidly advancing, especially with the use of next-generation sequencing technologies and whole-genome sequencing.<sup>64</sup> A small number of studies have employed whole-genome sequencing in healthy patients as a mechanism to identify risk for future disease onset, and two have demonstrated the capability of predicting risk for T2D and other chronic diseases.<sup>65,66</sup> While the routine clinical use of whole-genome sequencing in patients that appear healthy and asymptomatic is not likely to occur for several years, the studies nonetheless demonstrate the power of the technology and potential future uses. Considering the significantly variable nature of T2D, both in the genetic and environmental risk factors and in the clinical presentation, the most immediate use of genetic information is likely to be in the characterization of individual cases of T2D, with the goal of improving each patient's outcomes, motivation for long-term lifestyle modification and therapeutic response.

## RECOMMENDATION

The Council on Science and Public Health recommends that the following recommendation be adopted and the remainder of this report be filed:

That our American Medical Association encourage continued research into the potential of genomic information to improve risk assessment, management and prevention of type 2 diabetes, and will report back on important advances as appropriate. (New HOD Policy)

Fiscal note: Less than \$500.