Testimony on **"The Economic Impact of Diabetes"**

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Good morning, Chairman Heinrich, Vice Chairman Schweikert, and esteemed Members of the Joint Economic Committee. I sincerely appreciate the opportunity to delve into the subject of emerging technologies and therapeutics available in our country, aimed at addressing the ongoing epidemics of diabetes and obesity.

Currently, I serve as the Chief of the Section of Endocrinology, Diabetes, and Metabolism at Baylor College of Medicine, where I oversee clinical and research enterprises that focus on care of individuals with obesity, diabetes, and other endocrine diseases. Prior to this, I had the privilege to work as a physician and

scientist at Duke University and Harvard Medical School. Alongside my administrative duties, I continue my hands-on role as a practicing physician, caring for patients affected by these conditions. I also direct a scientific laboratory committed to deciphering the molecular mechanisms responsible for these conditions, with the ultimate objective of identifying innovative and more effective ways to enhance the health of our citizens.

Over the past decade, we've made significant strides in understanding how obesity, diabetes, and associated cardiometabolic diseases develop in people. This understanding has been complemented by remarkable progress in the development of medications and technologies designed to treat affected individuals. Today, I'd like to spotlight three areas that showcase these advancements and their potential to improve human health:

1. The vital and revolutionary role of GLP1 Receptor Agonists (GLP1RA) and related medications in the treatment of diabetes, obesity, and associated morbidity and mortality.

2. The rapid progress in new devices and technologies, such as continuous glucose monitors and insulin pumps and advanced algorithms to integrate these technologies and facilitate diabetes treatment.

3. Our growing knowledge of the complex nature of diabetes and related complications, and what it means for the future of diabetes care. By analyzing genetic variations in large populations, we discovered that diabetes is a heterogeneous disease. The study of rare genetic variation revealed atypical types of diabetes, enriching our understanding of how diabetes develops and suggesting new avenues for treatments. These findings foresee a future of precise diagnosis and treatment of specific diabetes types and associated comorbidities.

GLP1 Receptor Agonists (GLP1RAs):

GLP1 Receptor Agonists (GLP1RAs) and related medications have emerged as a revolutionary force in the fight against diabetes, obesity, and their associated morbidity and mortality. This class of medication, which mimics the glucagon-like peptide-1 hormone (GLP-1) naturally found in our bodies, has proven vital in improving glycemic control and promoting weight loss, thereby playing an instrumental role in the management of these pervasive conditions.

GLP1RAs were initially developed based upon their ability to increase insulin secretion, thereby reducing blood glucose levels – a major goal in the treatment of diabetes[1]. However, their unexpected ability to promote satiety proved remarkably effective in helping patients reduce caloric intake and subsequently lose weight. Studies have consistently demonstrated the potency of GLP1RAs in lowering hemoglobin A1c levels, a key metric in managing diabetes, and promoting significant weight loss with recent regimens capable of producing 20% reductions in body weight [2,3]. This degree of weight loss had only previously been observed following surgical weight loss procedures.

The benefits of GLP1RAs extend beyond their ability to enhance glycemic control and promote weight loss. A growing body of evidence points to their substantial cardio-protective properties. In landmark randomized clinical trials multiple GLP1RAs have been shown to reduce the risk of major adverse cardiovascular events and cardiovascular death in patients with Type 2 diabetes at high risk for heart disease[4,5]. Furthermore, meta-analyses of these and other trials indicate that GLP1RAs reduce all-cause mortality, providing hope for enhanced life expectancy among patients with these conditions[6,7].

In the realm of obesity management, GLP1RAs offer a promising adjunct to traditional lifestyle modification and alternative to weight loss surgery. With obesity being a primary risk factor for the development of Type 2 diabetes, as well as a host of other metabolic and cardiovascular diseases, the potential of GLP1RAs to induce meaningful and sustained weight loss may represent a significant advancement in preventive care.

Until recently, it was not known whether achieving safe and significant weight loss could ever be achieved through medical intervention. In essence, GLP1 Receptor Agonists have provided proof of principle that this can be achieved. These medications have ushered in a new era in the management of diabetes and obesity, directly improving patient outcomes and extending lives. Their discovery underscores the potential of leveraging our growing understanding of endocrine physiology to create therapies that can address some of our most pressing public health challenges.

New devices and technologies to assist with diabetes treatment:

The advent of new devices and technologies, specifically continuous glucose monitors (CGMs) and insulin pumps, has transformed diabetes management, providing opportunities for a welcome shift from traditional methods. These advancements have particularly improved care for patients with diabetes by reducing hypoglycemia—a major concern, especially in children with Type 1 Diabetes[8].

CGMs represent a significant evolution in glucose monitoring. Traditional blood glucose monitoring required multiple daily fingersticks, which could be painful and inconvenient. However, CGMs provide real-time, dynamic glucose information, enabling more accurate insulin dosing decisions. They continually track glucose levels throughout the day and night, providing trends and alerts for potential hypoglycemia or hyperglycemia. This continuous tracking helps to prevent severe hypoglycemia episodes, a source of morbidity and fear in children with Type 1 Diabetes.

Similarly, insulin pumps have revolutionized the delivery of insulin, providing a more flexible approach compared to multiple daily injections. The pump delivers a continuous infusion of rapid-acting insulin, mimicking the normal background insulin production of a healthy pancreas. Additionally, patients can customize bolus doses for meals or to correct high blood sugar levels. Modern pumps can even interact with CGMs, adjusting insulin delivery in response to glucose trends, which may be especially useful in enhancing glycemic control without increasing hypoglycemic risk[9–12].

The introduction of closed-loop insulin delivery systems or "artificial pancreas" devices represents the next significant step in diabetes technology[13,14]. These systems combine CGM and insulin pump technology with a control algorithm to automate insulin delivery. Ultimately, this may further reduce the burden of disease management while improving glucose control. The cognitive demands to precisely match exogenous insulin treatment to varying levels of activity, food intake, and variable circulating glucose levels can be taxing. These novel technologies have the potential to markedly ease this burden.

Through these innovations, patients with diabetes, particularly children with Type 1 Diabetes, have seen improvements in their glycemic control and quality of life. They also experience fewer instances of hypoglycemia, improving their safety. The

integration of these technologies into patient care emphasizes the transformative power of digital health in managing chronic diseases like diabetes.

Decoding Varieties of Diabetes:

Over recent years, we've made considerable progress in understanding the complexity and heterogeneity of diabetes through advancements in genetic and other research modalities. Sophisticated studies of common genetic variation in large populations have shed light on the complex nature of this disease. We now recognize that diabetes is not a single disease but rather an umbrella term for a group of disorders with common phenotypic traits, such as hyperglycemia, but with varying underlying genetic and pathophysiological mechanisms.

By analyzing common genetic variation, scientists have identified numerous genetic loci associated with the risk of developing diabetes[15]. Analyzing these associations in conjunction with associated comorbidities and complications reveals that different subtypes of diabetes may be driven by different genetic factors and predispose to different adverse outcomes[16–19].

In parallel, examination of rare genetic variations has allowed scientists to identify unusual forms of diabetes, some of which are known as monogenic diabetes, such as Maturity-Onset Diabetes of the Young (MODY)[20]. Large scale efforts are underway to identify additional rare and atypical forms of diabetes[21]. These discoveries are essential because rare forms of diabetes, while individually infrequent, often point to underlying mechanisms that participate in the development of more common forms of diabetes. Again, defining these mechanisms can drive discovery with the potential for novel diagnostic and therapeutic strategies.

The dissection of both common and rare genetic variation has enormous implications for the future of diabetes care. By understanding the different genetic contributions to diabetes, we can move towards a more personalized and precise approach to treatment. This means we could potentially match the right treatment to the right patient based on their specific genetic profile, improving their outcomes, and reducing the risk of associated comorbidities. The investigation into the genetics of diabetes, therefore, opens a promising new frontier in our fight against this complex and heterogeneous disease.

Conclusion:

In summary, we stand on the cusp of a revolution in diabetes and obesity management, powered by scientific breakthroughs and technological advancements. The introduction of GLP1 Receptor Agonists has redefined treatment strategies, improving patient outcomes by effectively managing blood glucose levels, promoting weight loss, and reducing cardiovascular risks. Concurrently, the emergence of continuous glucose monitors and insulin pumps has significantly enhanced diabetes care, particularly in reducing the frequency of hypoglycemic events in patients, notably children with Type 1 Diabetes. Additionally, through the lens of genetic research, we are uncovering the complexities of diabetes as a heterogeneous disease with various genetic influences, paving the way for precision medicine that could lead to more effective, personalized treatment strategies. These pivotal developments inspire optimism for a future where we can more effectively combat the epidemics of obesity, diabetes, and associated cardiometabolic diseases, enhancing the health and well-being of our citizens.

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