Introduction to the 5th World Congress on Controversies to Consensus in Diabetes, Obesity and Hypertension (CODHy)

The 5th Congress on Controversies to Consensus in Diabetes, Obesity and Hypertension (CODHy) was held in Istanbul, Turkey, November 2015, celebrating its 10 years of cultural and educational activity. As is tradition, this supplement of Diabetes Care provides a selection of the many topics in the field of diabetes, obesity, and hypertension that were presented and debated among experts with the engagement of an active audience.

All published articles represent the collaborative effort of diabetes experts involved in the (CODHy) debates and roundtables to provide the reader with the elements of the controversy, to illustrate the basis for different points of view, and to seek points of contact that may yield consensus and agreement. In order to ensure the necessary scientific quality, all articles published in this supplement have undergone a rigorous peer-review process. Because of this, we are confident that the information included here will present a balanced and updated survey on some of the most debated issues in the field of metabolic diseases and related disorders.

The articles are presented according to topic to allow the reader to follow a rational path. First, we cover the ongoing and yet unsolved issue of prevention of diabetes and its progression, a task that has greater urgency owing to the unprecedented growth of the prevalence of diabetes in all regions of the world.

As expected, treatment of type 2 diabetes occupies a larger portion of the supplement. The introduction of new glucose-lowering agents, the expanding concept of precision medicine, and the excitement stirred by the results of recent outcome trials continue to stimulate great interest and further discussion. In the future, given the array of therapeutic opportunities, will we be able to address the individual needs of the person with diabetes? Subsequently, can the phenotype we assess, and will the genotype we determine, be able to guide our future choices for intervention? What criteria determine the start of treatment to ensure long-lasting glycemic control with minimal risk of hypoglycemia and a positive effect on weight: monotherapy, dual therapy, or multiple drug combination? And which combination of available agents should be used given the many permutations? Thus, the purpose of this supplement is to provide the reader with the most current and up-to-date views on all of these aspects.

Although emphasis has been placed on earlier intervention, even before the diagnosis of diabetes, the way to intensify treatment is still a matter of debate requiring further clinical investigation. The recent introduction of the sodium–glucose cotransporter 2 inhibitors and the results of the BI 10773 (Empagliflozin) Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients (EMPA-REG OUTCOME) have stirred much interest in this class of glucose-lowering agents. Their sequence in the treatment algorithm of type 2 diabetes needs to be determined relative to the availability of many other therapeutic options, as well as the stage of the disease. This supplement discusses the relative positioning and combination of sodium–glucose cotransporter 2 inhibitors and the incretin-based therapies along with the implications of use in the setting of reduced renal function. This is becoming an interesting topic: while it was initially shown that glucose-lowering efficacy may wane with the loss of glomerular filtration rate, more recent data demonstrated a renal protective effect even in patients with impaired kidney function.
In addition, some of the articles in this publication discuss insulin treatment in type 2 diabetes as well. In spite of an already centennial history, insulin continues to evolve. New insulin analogs have recently been introduced for the treatment of diabetes. These analogs have longer duration of action and, because of a flatter profile, are claimed to further reduce the risk of hypoglycemia. The counterpart of having available a newer analog is the higher cost, making it legitimate to ask whether the clinical benefits offset the costs. Furthermore, it may be of interest to explore whether some patients with type 2 diabetes may benefit from continuous subcutaneous insulin infusion, as recently suggested by the OpT2mise (Insulin Pump Treatment Compared With Multiple Daily Injections for Treatment of Type 2 Diabetes) trial. This question is of relevance if the alternative injectable therapies are taken into account. Injectable glucagon-like peptide 1 (GLP-1) receptor agonists are quickly evolving as well: short-acting and long-acting GLP-1 receptor analogs, fixed ratio combination with long-acting insulins, alternative means of administration, etc. The dilemma can then be when to use insulin, when to use any of these GLP-1 receptor agonists, and when it may be wiser (or better indicated) to combine the two.

The main goal of glucose lowering in diabetes is prevention of vascular complications. Although the relationship between glycemic control and microvascular complications is well established, the impact of near normoglycemia on cardiovascular (CV) outcomes remains a matter of discussion. In the most recent years, CV outcome trials have been required by the regulatory agencies to prove CV safety and potential benefit. A number of large trials have been published, and an even larger number are currently ongoing. What have we learned so far and how much can we still gain from these studies and their results? What is the contribution of hyperglycemia as opposed to hypoglycemia on CV risk? What is the benefit-to-risk ratio of individual glucose-lowering agents? How may these large and expensive CV outcome trials affect future drug development or overall treatment safety? These are just some of the major questions addressed in a series of comprehensive and detailed reviews included here.

CV disease in diabetes is the result of the concomitant effect of multiple risk factors. The need to avoid a glucocentric approach was strongly restated during the CODHy congress and is documented by the articles in this supplement that address blood pressure control in specific contexts (diabetic nephropathy and in the elderly), chronic inflammation and potential anti-inflammatory treatment, and cholesterol control with statins.

What is missing so far in the reports is the “O” in CODHy, which is obesity. Well-experienced authors cover two obesity-related topics here. The first deals with the continuous search for effective pharmacologic intervention to reduce and maintain weight loss. The second deals with bariatric surgery and its evolution into metabolic surgery.

In summary, this fifth supplement continues in the traditional spirit of CODHy, highlighting controversies while attempting to look at how to implement the most effective strategies. It is an example of how controversy based on a scientific ground and critical analysis follows the path of the Galilean scientific approach: ask the question, test the hypothesis, and reject or accept it to move to a higher level of understanding; though, often, it is also a higher level of complexity.

In the end controversy must yield some consensus. We hope the reader will appreciate the effort of the authors to interpret such spirit, as well as their contribution to the progress of clinical diabetes and related disorders.

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