Type 2 diabetes (T2D) is a complex, chronic disease with a significant quality of life burden for affected individuals, as well as socio-economic burdens on a population scale. Efforts to mitigate morbidity, mortality, and risks for other acute and chronic diseases have been compromised by a traditional chronic disease model that focuses on tertiary prevention (i.e., waiting until the disease is fully manifest and in many cases with severe complications). More specifically, the role for prevention at an earlier “prediabetes” stage has been questioned. A re-examination of the biology and clinical data on T2D pathogenesis can modulate the way we think about T2D. The new Dysglycemia-Based Chronic Disease (DBCD) model addresses these challenges by positioning T2D and prediabetes along a continuous spectrum from insulin resistance to prediabetes to T2D to vascular complications. It is hoped that by conceptualizing T2D in the DBCD framework, health care professionals can provide more efficient, cost-effective care.

Keywords
Diabetes, prediabetes, insulin resistance, dysglycemia, cardiovascular disease, chronic disease

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Do appropriate interventions mitigate risk? First, there is progression of T2D-related complications without interventions. Second, there is reduction of cardiometabolic risk with lifestyle and weight loss interventions. Third, there are decreased health care expenditures with interventions. With this emerging evidence base affirming benefits of early intervention, the next question is why are these maneuvers not more aggressively applied well before a patient is diagnosed with T2D? The key may be translating this compelling information into concrete, teachable, actionable steps that are also feasible in our very onerous health care system.
Biological basis for targeted action

Insulin resistance can be associated with abnormal adiposity (amount, distribution, and function) as described by the recently published Adiposity-Based Chronic Disease (ABCD) model. Insulin resistance is differentiated from prediabetes by the lack of any abnormalities in glycemic status (fasting, post-prandial, casual, post-challenge, or via hemoglobin A1c) in the former. Weight gain with insulin resistance can worsen adipocyte dysfunction and produce prediabetes, metabolic syndrome, T2D, and eventually CVD. Insulin resistance and pancreatic β-cell dysfunction are the main initiating events for developing T2D. Other mechanisms involve pancreatic α-cell dysfunction (hyperglucagonemia), glucose-dependent insulinotropic polypeptide, glucagon-like peptide-1, and mitochondrial methylation factors. In fact, there are 248, 138, and 24 genes from human insulinotropic polypeptide, glucagon-like peptide-1, and mitochondrial α-cell dysfunction and faster prediabetes to T2D conversion rates than Caucasians.

A dynamic driver network for the important predisease-T2D transition mechanisms was outlined by Jin et al. In this network, structured lifestyle change at critical time points can slow down disease progression and decrease T2D. Notably, in those with a high genetic risk for coronary heart disease, a healthy lifestyle was associated with nearly 50% relative risk reduction. Many of these biological and lifestyle effects vary in different ethnicities, such as Asian Indians who may have relatively more β-cell dysfunction and faster prediabetes to T2D conversion rates than Caucasians.

The dysglycemia-based chronic disease framework

Dysglycemia can be viewed as any abnormality in glycemic status associated with disease or disease risk. The American Association of Clinical Endocrinologists (AACE) has recently created a new framework to optimize the care of patients with or at-risk for T2D termed Dysglycemia-Based Chronic Disease (DBC). The impetus for this new model can be summarized as follows:

- Initial triggering by questions of whether the concept of “prediabetes” is helpful, based on concerns that notwithstanding earlier diagnosis and the potential for prevention tactics, this intervention would prove too costly for the small number of actual patients realizing benefit; this problem is solved by validating prediabetes not as an entity in isolation, but rather as a necessary event along a spectrum with antecedent drivers and downstream consequences;
- Recent AACE experience reworking chronic endocrine disease models in obesity and diabetes;
- Heightened awareness and need for a new T2D care model that is actionable and results in earlier diagnosis and prevention tactics, particularly incorporating early and pervasive structured lifestyle change.

The DBCD framework has the following structure: a continuous spectrum with four stages, preventive strategies, and specific actions:

- Stage One: molecular risk or insulin-resistance—amenable to primordial and primary prevention (emphasizing structured lifestyle change) to decrease risk for stages 2–4; requires initiative primarily with local community centers and governmental agencies for population-based programs (posted nutrition facts, distribution of educational materials, public service announcements, creation of sufficient, safe physical activity sites, tobacco cessation campaigns, etc.);
- Stage Two: biochemical cardiometabolic risk or prediabetes—continuation of primordial prevention programs in addition to secondary and primary prevention programs (structured lifestyle change and possibly medication) to decrease risk for stages 3 and 4; focused education for health care professionals (HCP), creation of comprehensive lifestyle medicine protocols with high-touch clinical settings and high-technology nudge一大早; innovative therapeutic environments that facilitate medical fitness and nutritional counseling with physician services, incorporation of sleep hygiene, community engagement, and behavioral medicine into lifestyle medicine centers;
- Stage Three: biochemical disease or T2D—continuation of primordial and primary prevention programs in addition to secondary and tertiary prevention programs (structured lifestyle change and, as needed, medication) to decrease the risk for stage 4; requires routine implementation of formal lifestyle medicine with and without pharmacotherapy, emphasis on comprehensive and complication-centric care, protocol-based tailoring of nutrition and physical activity recommendations based on specific disease severity and phenotype; and
- Stage Four: vascular complications or T2D with complications—continuation of primordial, primary, and secondary prevention programs in addition to tertiary prevention programs (structured lifestyle change with increasing medication and other procedures) to prevent further progression of disease, morbidity, and mortality; requires formal lifestyle medicine protocols that are interwoven with pharmacotherapy and procedures (e.g., renal and T2D nutritional recommendations for patients receiving hemodialysis; healthy eating counseling for patients having had bariatric surgery; comprehensive cardiac rehabilitation after coronary artery bypass surgery that also includes nutritional and behavioral counseling).

The DBCD framework will require further scientific substantiation to validate and better characterize the relative causal dependencies, perhaps in a more detailed probabilistic model. Furthermore, the major context of the DBCD is the prevention of CVD by comprehensively addressing cardiometabolic risk factors as early as possible. This framework could better inform and guide clinical decision-making in T2D care to improve outcomes at lower costs. New diagnostic coding systems for reimbursements along the entire DBCD spectrum, as also hoped for in obesity care based on the ABCD model, could be forthcoming. From a pragmatic standpoint, implementation of the DBCD framework would prompt structured lifestyle interventions in every patient, especially those in diabetogenic and obesogenic environments. Perhaps clinical practice settings will then have a higher level of preparedness with easy access to gyms, exercise physiologists, wearable technologies to monitor glycemic status, and nutritionists, behaviorists, and others who can leverage lifestyle optimization.

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