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Type 2 diabetes—strides have been made in decreasing diabetes complications, but are they good enough?

Desmond Schatz, MD
President, Medicine and Science, American Diabetes Association, 2016
Medical Director, University of Florida Diabetes Institute
Professor and Associate Chair of Pediatrics and Associate Director of the Clinical Research Center, University of Florida
Published author (>260 manuscripts) and Principal Investigator
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Since 1990, we have come a long way in treating diabetes and have seen impressive decreases in diabetes-related morbidity and mortality. Gregg and colleagues at the Centers for Disease Control and Prevention examined this trend and found that between 1990 and 2010, acute myocardial infarction decreased by 68%, death from hyperglycemic crisis decreased by 64%, stroke decreased by 53%, amputation decreased by 51%, and end-stage renal disease decreased by 28%. However, if we examine the data more closely, the greatest improvements were seen prior to 2005. While we don’t have data from 2010 to present, we can see that from 2005 to 2010, improvement slowed or trended flat across all comorbidities.

**Figure 1.** Trend in age-standardized rates of complications related to diabetes in US adults, 1990-2010. The greatest improvements were seen prior to 2005. From 2005-2010, the improvement has slowed or trended flat, and the rates beyond 2010 are unknown. Is this plateau good enough for our patients? ESRD, end-stage renal disease.
The decline in outcome improvement can be explained by examining trends in glycosylated hemoglobin A1c (HbA1c) goal achievement (<7%) during the same time frame. According to the National Health and Nutrition Examination Survey (NHANES), the percentage of people with diabetes achieving goal (HbA1c <7%) from 2003-2006 and 2007-2010 slightly declined from 57% to 52%, and the most recent evaluation, 2011-2014, shows the percentage to goal virtually unchanged at 51%.

Data are presented as weighted percentages of survey participants.

The Healthcare Effectiveness Data and Information Set (HEDIS) paints a similar picture for the commercial HMO and Medicaid populations from 2007 to 2014. Only about 40% of the HMO population and 30% of the Medicaid population achieve treatment goal (HbA1c <7.0%), again with no improvement over time. On a percentage basis, very poorly controlled patients (HbA1c >9.0%) also remained constant in the HMO population at about 30% from 2005 to 2014. Importantly, this stasis in improvement has occurred at the same time there has been an explosion of new diabetes treatments introduced to market. During the last decade, there were >40 new type 2 diabetes (T2D) treatment options approved.

Why haven’t these many pills and injections had the impact on the percentage of patient to HbA1c <7% that we’d like to see? There are several potential reasons for this; 2 key reasons are (1) we aren’t using our best therapies aggressively enough, and (2) regardless of what therapy is being used, the HbA1c decrease that we are seeing in the real world falls far short of clinical trial efficacy due primarily to staggering rates of poor adherence.

A global survey of physicians found that GLP-1 RAs are considered among the most efficacious agents for the treatment of T2D. The 2016 AACE guidelines give a highest-strength recommendation to GLP-1 RAs as the first-line complement to metformin in patients who present with HbA1c ≥7.5%. Yet despite their efficacy and strong recommendation, GLP-1 RAs are underutilized. GLP-1 RAs are administered via injection, and barriers to injectable diabetes medications exist from both a physician and patient perspective.

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As for the second reason, a recent study examined real-world effectiveness over 1 year vs clinical trial efficacy for GLP-1 RAs and DPP-4is and found a dramatic gap. In fact, the HbA1c reduction found in the real-world setting for GLP-1 RAs was about half that seen in clinical trials. This study also calculated the contribution of various factors to the gap. Regardless of drug class, differences in baseline characteristics and additional drug therapy accounted for just 25% of the gap, while 75% of the gap was due to poor adherence. Because only 29% of real-world patients on GLP-1 RAs and 37% of patients on DPP-4is were adherent at 1 year (proportion of days covered [PDC] ≥80%), it was not surprising that poor adherence was the key contributor to the disconnect between clinical trials and the real world. Unfortunately, this is in line with other real-world data that found adherence to oral medications was <50% at the first year of follow-up, dropping to ≤40% by the second year; adherence to once-daily GLP-1 RAs was just 34% at 1 year.

At best, only about 50% of patients with T2D have HbA1c <7%, and this has remained virtually unchanged over the last decade despite >40 treatment options approved. Clinical trial outcomes are not being replicated in the real world due to staggering rates of poor adherence, and achieving meaningful and sustained HbA1c reductions remains elusive. To truly confront this chronic disease, we can’t be trapped by dogma, conventional wisdom, or the inertia of a status quo. We must challenge ourselves now to rethink type 2 diabetes.


Only new thinking can change T2D.