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RESPONSE TO COMMENT ON AMERICAN DIABETES ASSOCIATION

Approaches to Glycemic Treatment. Sec. 7. In *Standards of Medical Care in Diabetes—2016*. Diabetes Care 2016;39(Suppl. 1):S52–S59

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We thank Giugliano et al. (1) for their comments in this issue of *Diabetes Care* on the recommendations for insulin therapy in type 2 diabetes outlined in the American Diabetes Association's *Standards of Medical Care in Diabetes—2016* (2). We agree that after basal insulin failure, there are three treatment options: continuing basal insulin and adding a rapid-acting insulin analog before the largest meal, continuing basal insulin and adding a glucagon-like peptide 1 (GLP-1) receptor agonist (GLP-1-RA), or changing to premixed analog insulin twice daily.

Figure 7.2 in the 2016 Standards reviews the approach to starting and adjusting insulin in type 2 diabetes. Basal insulin plus GLP-1-RA is a newer treatment option that is clearly outlined in Fig. 7.1 (antihyperglycemic therapy in type 2 diabetes: general recommendations). Despite the noninferiority of basal insulin plus GLP-1-RA compared with basal insulin plus a single rapid-acting insulin analog injection and the former's advantages with respect to change in body weight and hypoglycemia, there are concerns regarding both tolerability and cost. Of the four studies included in the recent meta-analysis that compared basal insulin plus GLP-1-RA with basal insulin plus a rapid-acting insulin analog, vomiting and diarrhea were more frequent among those randomized to GLP-1-RAs, and the duration of the studies was only 12 to 30 weeks (3). Although this is a promising option, longer studies are needed to assess the tolerability, effectiveness, and side effects of this combination before it can be favored as standard of care for patients with type 2 diabetes failing basal insulin therapy.

With respect to the authors' recommendations at the level of three or more injections per day, we agree that new evidence now establishes the noninferiority of up to three injections per day of premixed analog insulins compared with up to four injections per day of basal-bolus insulin with respect to efficacy, weight, and overall hypoglycemia (4). We concur that in the diabetes community, the fully intensified basal-bolus regimen is still often regarded as the "gold standard" of treatment for type 2 diabetes. This attitude likely arises from both an appreciation of the physiology of normal insulin secretion and experience treating people with type 1 diabetes. Recognizing the noninferiority of thrice-daily premixed analog insulins, we anticipate revising Fig. 7.2 in the *Standards of Medical Care in Diabetes—2017* to highlight these two options.

When type 2 diabetes has progressed to the stage at which either of these fully intensified regimens is required, it can be difficult to achieve treatment goals without unacceptable polypharmacy, side effects, and cost. Although clinical trials have demonstrated the efficacy of these regimens, misapplication of complex therapies may be harmful. Treatment must be individualized, and the American Diabetes Association's recommendations are intended to provide guidance. We continue to emphasize that if patients are not achieving treatment goals with fully intensified basal-bolus or premixed analog insulin regimens, consider switching from one fully intensified insulin regimen to the other (5,6). Changing from a failed regimen to a new regimen may be as important as the nature of the regimen itself.

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