COMMENTS AND RESPONSES

# Response to Comment on: Rizzo et al. Reduction of Oxidative Stress and Inflammation by Blunting Daily Acute Glucose Fluctuations in Patients With Type 2 Diabetes: Role of Dipeptidyl Peptidase-IV Inhibition. Diabetes Care 2012;35:2076–2082

DeVries (1) was surprised that vildagliptin and sitagliptin groups reported different mean amplitude of glycemic excursions (MAGE) reduction because they have similar fasting and postprandial glucose levels and suggested reporting other measures of glucose variability to better understand these results.

Indeed, a previous study evaluating the role of glycemic variability in type 2 diabetic patients has demonstrated that patients with similar mean glucose and postprandial glucose have a markedly different daily glucose profile with differences both in number and duration of excursions (2). The difference in MAGE reduction found in the two study groups may be better clarified by the different glucagon-like peptide 1 (GLP-1) daily profiles of the two drugs (3) rather than by a graph showing changes in mean glucose values. In such GLP-1 profile, vildagliptin group had higher plasma GLP-1 levels not only during postprandial but also during interprandial periods.

The main aim of our study was to evaluate the effects of blunted glucose excursions on oxidative stress and inflammation parameters, which have previously been found associated with daily glucose fluctuations (4). Many different indexes have been proposed to assess glucose variability, but at the moment no "gold standard" procedure is available (5). Despite the fact that MAGE displays some significant limitations, it is the most common measure used for evaluating the association between glycemic variability and oxidative stress and inflammation parameters (4) and is the most appropriate to detect large glycemic peaks and nadirs encountered during a day (5), whereas continuous overlapping net glycemic action (defined as the SD of the differences between the current observation and the previous 2-h observation) is known to detect small glycemic swings and more appropriately describes the glycemic fluctuation of patients in optimal metabolic balance, without peak and nadir related to hypoglycemic treatment. In addition, SD, which is considered to be the simplest tool for describing glycemic variability that takes into account all excursions, has the limit of including all oscillations without a weighting of the minor or major variations (5). Several other methods such as mean absolute glucose change have been proposed but have not gained widespread use. We acknowledge that the different indexes do not seem to be interchangeable and should be used in the appropriate condition; indeed, most of these indexes are highly correlated (4) and provide the same information, making reasonable a reduction in the number of indexes that need to be considered. Whether calculating MAGE, SD, mean absolute glucose change, continuous overlapping net glycemic action, or other measures simultaneously helps to get additional insight in pathophysiological processes needs further investigation (4,5).

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DOI: 10.2337/dc12-1436



**Acknowledgments**—No potential conflicts of interest relevant to this article were reported.

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