COMMENTS AND RESPONSES

Response to Comment on: Holstein et al. Substantial Increase in Incidence of Severe Hypoglycemia Between 1997–2000 and 2007–2010: A German Longitudinal Population-Based Study. Diabetes Care 2012;35:972–975

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We thank Kerner and Völzke (1) for their interest in our study. It is correct that such population-based studies are extremely difficult to perform and need to be interpreted with caution. However, the authors neglect several crucial premises in interpreting data on frequency of severe hypoglycemia (SH).

In the cited studies from Scotland (2), Australia (3), and Germany (4,5) definitions of SH, methods of data collection, and differences in healthcare systems considerably skew the comparison. Our study, in contrast, used a precise and restrictive definition of SH as a symptomatic event requiring treatment with intravenous glucose and being confirmed by a blood glucose measurement of <50 mg/dL. Performing a sensitive regional screening for SH, all patients were recruited at a single tertiary care hospital, it being the only one in the catchment area and responsible for the inpatient and outpatient management of all emergencies. SH associated with primary care treatment was not included because these cases could not be clearly ascertained (5). DARTS (Diabetes Audit and Research in Tayside Scotland)/MEMO (Medicines Monitoring Unit) (2), for comparison, included all episodes of SH with a blood glucose of <63 mg/dL and primary care as well as emergency department and ambulance attendances. The Fremantle Diabetes Study (3) used a wider definition of SH, i.e., an episode in which *1*) a patient with subnormal blood glucose required health service use and *2*) SH was the primary diagnosis, whereas Sämann et al. (4) reexamined patients with type 1 diabetes between 1992 and 2004 from 96 hospital diabetes clinics in Germany defining SH as a condition treated by intravenous glucose or glucagon injection. However, cases of SH were only assessed by an interview (4). None of these three studies (2–4) provided blood glucose values for the respective hypoglycemic patients, unlike in our study where this was done with great care. Considering these heterogeneities, it is not surprising to see a broad range of incidences in SH. Even in the Diabetes Control and Complications Trial SH ranged enormously from 0 to 150 episodes per 100 patient-years among the 29 participating clinics, highlighting the significance of center-related quality in diabetes care (6).

As noted frankly in the discussion, our observational single center study including a catchment area with 200,000 inhabitants has the usual limitations and could have been confounded by local specifics. However, all these limitations similarly apply to the DARTS/MEMO and Fremantle Diabetes Study, including 367,051 and 120,097 inhabitants, respectively (2,3). Our restrictive definition of SH intentionally excluded cases of less severe or unclear hypoglycemia, which were included in the cited studies. We therefore believe that our stricter definition of hypoglycemia strengthens the validity of our data by eliminating doubtful cases but would naturally give rise to lower incidence rates of SH compared with the other studies.

The approach of Kerner and Völzke comparing incidence rates of SH from different countries ascertained by heterogenous methods would seem less appropriate. Our core statement of an increased regional incidence of SH in 2007–2010 compared with 1997–2000 remains unshaken.

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