

COMMENTS AND RESPONSES

Response to Rodríguez-Segade et al. and Leslie and Kilpatrick

Rodríguez-Segade et al. (1) question the clinical usefulness of the estimated average glucose (eAG) developed by the A1C-Derived Average Glucose (ADAG) Study (2). They note that although the study met the a priori-specified criterion for acceptability ($\geq 90\%$ of subject values within 15% of the regression line between A1C and calculated mean glucose), the variability of the estimate makes the equation clinically useless. Furthermore, they state, without any supporting evidence, that the assumption that “A1C depends exclusively on average plasma glucose—is not justified.”

Leslie and Kilpatrick (3) remarkably resort to the Heisenberg uncertainty principle of quantum physics (which states the uncertainty of simultaneously measuring the position and momentum of a particle, owing in part to the perturbation of the particle as part of the measurement) to point out the variability of the ADAG average glucose levels. They cite the consensus of “18 professional organizations” in the U.K. that decided, 6 months before the ADAG study was published, to reject the use of eAG (4). The U.K. consensus group didn’t reject the “conceptual benefits” of translating A1C into eAG but recommended against the use of eAG at that time based, at least in part, on “insufficient information regarding entry criteria, study design, and data analysis” (4). We assume that these concerns would have been allayed if they had read the ADAG study when it was published. The U.K. consensus group recommended “further research into the individual utility of eAG and of its use in all groups of individuals with diabetes.”

The rationale that we used in select-

ing the acceptability criterion is worth reviewing. The calibration of A1C by average glucose required us to consider the variability of the measures that would go into the comparison. Average glucose was calculated from a combination of self-monitoring of blood glucose (SMBG) and continuous glucose monitoring (CGM), each of which has variability (5,6). Although the performance of SMBG and CGM has improved over time, the accuracy of SMBG, which accounted for the majority of the calculated average glucose, is substantially worse than the “internationally accepted maximum error” of 10% cited by Segade et al. (5,6), because patients, rather than technicians, perform the monitoring. Moreover, other factors such as temperature and humidity, which varied widely in our multicenter study, can influence SMBG results (although we purposely chose an SMBG device that is relatively stable in varying conditions) (7). CGM is also subject to variability that approaches 15%.

Of course, we agree with both respondents that it would be naïve to express any measured biological variable, and especially a mean value, without considering its variability (which is one reason why we use the word “estimated” to express the translated “estimated average glucose”). Given the variability of the measures that went into the calculation of eAG, not to mention the variability of the A1C assay, we chose the criterion that 90% of subjects be within 15% because it was realistic and one that we thought would be acceptable to clinicians. Clinicians and patients have already accepted the relative (in)accuracy and (im)precision of SMBG and CGM; the eAG translation of A1C reflects these measurements in a real-world setting. We point out that all measured clinical analytes have associated variability; however, few clinical results, if any, are expressed as a range.

The intention of the ADAG translation is to supplement the current reporting of A1C with an estimate of average glycemia presented in the same units as patients encounter in their daily monitoring. Hopefully, this will improve patients’ understanding of chronic glycemia (8) and facilitate better diabetes management.

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DOI: 10.2337/dc08-1752

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

References

- Rodríguez-Segade S, Rodríguez J, Paz JM, Camiña F: Translating the A1C assay into estimated average glucose values (Letter) *Diabetes Care* 32:e10, 2008
- Nathan DM, Kuenen J, Borg R, Zheng H, Schoenfeld D, Heine RJ, the A1c-Derived Average Glucose (ADAG) Study Group: Translating the A1C assay into estimated average glucose values. *Diabetes Care* 31: 1473–1478, 2008
- Leslie RDG, Kilpatrick ES: Translating the A1C assay into estimated average glucose values (Letter). *Diabetes Care* 32:e11, 2008
- Barth JH, Marshall SM, Watson ID: Consensus meeting on reporting glycosylated haemoglobin and estimated average glucose in the UK: report to the National Director for Diabetes, Department of Health. *Ann Clin Biochem* 45:343–344, 2008
- Alto WA, Meyer D, Schneid J, Bryson P, Kindig J: Assuring the accuracy of home glucose monitoring. *J Am Board Fam Pract* 15:1–6, 2002
- Skeie S, Thue G, Nerhus K, Sandberg S: Instruments for self-monitoring of blood glucose: comparisons of testing quality achieved by patients and a technician. *Clin Chem* 48:994–1003, 2002
- Bimenya GS, Nzarubara GR, Kiconco J, Sabini S, Byaragaba W: Accuracy of self-monitoring blood glucose meter systems in Kampala Uganda. *Afr Health Sci* 3:24–32, 2003
- Heisler M, Piette JD, Spencer M, Kieffer E, Vijan S: The relationship between knowledge of recent HbA1c values and diabetes care understanding and self-management. *Diabetes Care* 28:816–822, 2005