Management of type 1 diabetes

Ongoing confusion? HbA_{1c} units and average blood glucose

Adrian Scott
Consultant Physician in Diabetes and General Medicine, Northern General Hospital, Sheffield

When the reporting of HbA_{1c} changed from something I understood (%) to something I did not (mmol/mol), I soon found out that I was part of a big club. Patients smiled inanely when told their latest HbA_{1c} – those with a result close to 100 (mmol/mol) were particularly pleased, never having had nearly 100% in anything previously.

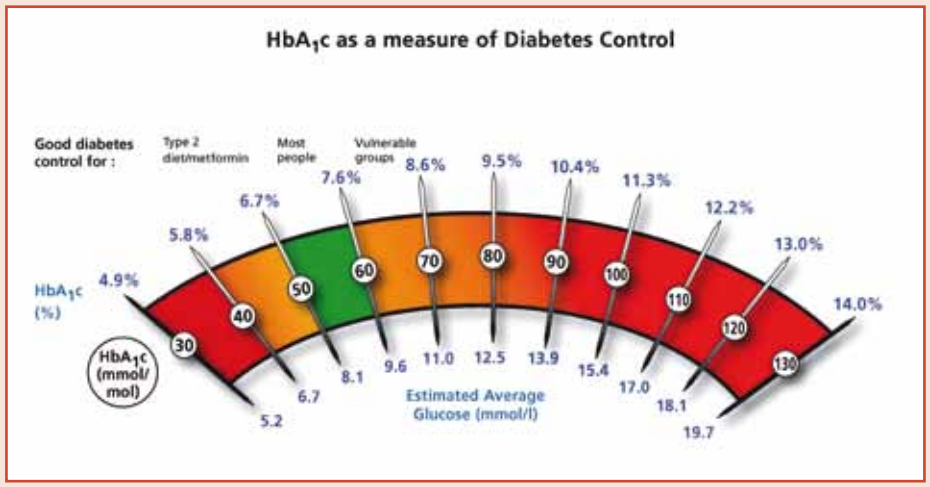
It so happened that around the same time Nathan and colleagues (2008) completed research using capillary (finger prick) blood glucose monitoring and continuous glucose monitoring to relate HbA_{1c} to an average blood glucose (ABG). Their results were challenged by some because of the wide confidence intervals and the lack of data from certain age and ethnic groups.

The paper by O'Riordan and colleagues, summarised alongside, has gone some way to address these areas of data absence by undertaking similar studies in children and young people. The results are broadly similar to those in adults, particularly for HbA_{1c} less than 80 mmol/mol (9.5%). Why does it matter what units HbA_{1c} are expressed in? For most people with diabetes, HbA_{1c} expressed as a percentage was apparently easy to understand, but completely misinterpreted because the numbers were similar (but most definitely not equal) to blood glucose values. For example, an HbA_{1c} of 5.8% is approximately equivalent to an ABG of 6.7 mmol/L, whereas an HbA_{1c} of 9.5% is equivalent to an ABG of 12.5 mmol/L. In the new units for HbA_{1c}, 5.85% and 9.5% equate to 40 mmol/mol and 80 mmol/mol respectively. In my experience, HbA_{1c} expressed in this new way remains numbers without meaning for most people with diabetes.

In the clinic where I work in Sheffield, therefore, we have used the data published by Nathan et al (2008) to create a visual interpretation of HbA_{1c} in terms of a colour spectrum (see image below). ABG values are also displayed to help with the interpretation (red is used at the lower end to emphasise the risk of hypoglycaemia).

The paper from O'Riordan et al is reassuringly in agreement with previous data, and I would urge diabetes teams to adopt estimated ABG when talking to people with diabetes about their HbA_{1c}. ■

Nathan DM, Kuenen J, Borg R et al (2008) Translating the A1C assay into estimated average glucose values. *Diabetes Care* **31**: 1473–78



A visual interpretation in terms of a colour spectrum of HbA_{1c} in % and mmol/mol, and estimated average glucose (mmol/L)

Diabetic Medicine

Paediatric estimated average blood glucose in adolescents with T1D

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓✓

1 HbA_{1c} is used to measure blood glucose over a 3-month period. A team headed by Daniel Nathan in 2008 used data from continuous glucose monitoring in adults to develop an algorithm that defines the relationship between HbA_{1c} and average glucose levels.

2 This cross-sectional study by O'Riordan et al aimed to define the algorithm for converting HbA_{1c} to average blood glucose in children and young people with T1D.

3 In total, 234 children and young people (106 male) from three centres were included in the analysis. All underwent continuous glucose monitoring over a 5-day period and provided a HbA_{1c} reading.

4 Regression analysis was used to determine the estimated average blood glucose and the new algorithm was compared to the algorithm used for adults.

5 Mean HbA_{1c} among the participants was 76 mmol/mol (9.1%) and mean continuous glucose monitoring tissue glucose was 10.4 mmol/L.

6 The paediatric equation described by the authors was: paediatric estimated average glucose=0.49 (HbA_{1c}%)+5.95 (r=0.45; P<0.001).

7 The resulting paediatric estimated average blood glucose was similar to the estimated average blood glucose calculated using the adult equation.

8 Therefore, the adult algorithm can be used in children and young people with T1D up to HbA_{1c} values of 75–86 mmol/mol (9–10%).

O'Riordan SM, Danne T, Hanas R et al (2014) Paediatric estimated average glucose in children with type 1 diabetes. *Diabet Med* **31**: 36–9

Type 1 diabetes

"In new-onset T1D, hybrid closed-loop control followed by sensor-augmented pump therapy did not provide benefit in preserving beta-cell function compared with current standards of care."

Diabetes Metab Res Rev

C-peptide: Measuring insulin secretion in established T1D

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓✓✓

1 Using C-peptide as a surrogate marker, the authors aimed to characterise insulin secretion and beta-cell function in people with varying duration of T1D.

2 Fifty-eight people with T1D for <1 year and 34 people with T1D for >2 years (20 of whom had previously participated in trials of anti-CD3 monoclonal antibody) were included. Historical data from 38 people without diabetes served as controls.

3 All participants underwent a mixed-meal tolerance test (MMTT) and C-peptide secretion was measured.

4 A decline in total insulin secretion was seen with increasing T1D duration ($P<0.0001$).

5 C-peptide was detected in 85% of people with T1D duration between 2 and 5 years, and 57% of those with T1D for ≥5 years.

6 There was no detectable difference in C-peptide between the participants who had previously been treated with anti-CD3 and those that had not.

7 There was no relationship found between the secretion of insulin and glucagon.

8 The proportion of participants with a delayed response to a meal stimulus was more pronounced with increasing disease duration.

9 In conclusion, the authors have characterised insulin secretion in subjects with established T1D, which may provide an opportunity for augmenting insulin secretion in order to improve metabolic control in people with T1D.

Sherr JL, Ghazi T, Wurtz A et al (2014) Characterization of residual beta cell function in long-standing type 1 diabetes. *Diabetes Metab Res Rev* **30**: 154–62

Diabetes Metabolism

Telemedicine: Does it work to improve glycaemic control?

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓

1 As part of a sub-analysis of the TELEDIAB-1 study, each component of a telemedicine care strategy was measured for its contribution and effectiveness to HbA_{1c} improvement over a 6-month period. The authors also wanted to build a profile for individuals who benefited most from the insulin dose advisor (IDA) function of the telemedicine care.

2 In total, 180 participants were split into three groups: group 1 received standard quarterly care; group 2 were given a smartphone with IDA function plus quarterly caregiver visits; and group 3 were given a smartphone with IDA and access to short teleconsultations every 2 weeks but no caregiver visits.

3 Participants were classified as "high users" of the IDA if the proportion of "informed" meals over the study period exceeded 67% and as "low users" if not.

4 Over the 6 months, the proportion of informed meals remained stable from baseline among the high users and decreased among the low users.

5 HbA_{1c} improved among high users in group 3 compared to group 2, and low users who received support via telecommunication showed the greatest improvement in HbA_{1c} ($P=0.084$).

6 High users tended to be older, have longer-standing T1D and be more involved with managerial activities; they were also more familiar with carbohydrate counting than the low users, who may have had greater difficulty accepting T1D and adhering to treatment.

Franc S, Borot S, Ronsin O et al (2014) Telemedicine and type 1 diabetes: is technology per se sufficient to improve glycaemic control? *Diabetes Metab* **40**: 61–6

Diabetes Care

Effectiveness of early intensive therapy in adolescents

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓

1 The aim was to assess the effectiveness of in-patient hybrid closed-loop control (HCLC) followed by out-patient sensor-augmented pump (SAP) therapy initiated 7 days after T1D diagnosis in preserving beta-cell function after 1 year.

2 Sixty-eight children (median age 13.3±5.7 years) were randomised to receive HCLC followed by SAP therapy (the intensive group[$n=48$]) or to receive multiple daily injections or insulin pump therapy (the usual-care group [$n=20$]).

3 The primary outcome was C-peptide concentrations during mixed-meal tolerance tests at 12 months.

4 In the usual-care group, insulin pump and continuous glucose monitoring (CGM) were initiated by 15 and 5 of the participants, respectively, prior to 12 months. HbA_{1c} was similar in both groups throughout the study period.

5 During out-patient SAP therapy, the use of CGM decreased over time, and, at 12 months, only 33% of intensive participants averaged sensor use ≥6 days/week.

6 At 12 months, the geometric mean of C-peptide area under the curve was not statistically different between the intensive and usual-care group.

7 In new-onset T1D, HCLC followed by SAP therapy did not provide benefit in preserving beta-cell function compared with current standards of care.

Buckingham B, Beck RW, Ruedy KJ et al (2013) Effectiveness of early intensive therapy on beta-cell preservation in type 1 diabetes. *Diabetes Care* **36**: 4030–5