Paediatrics

Glycaemic targets set by national guidelines: Do they matter?

Chizo Agwu
Consultant Paediatrician, Sandwell and West Birmingham Hospital Trust, Birmingham

The importance of good glycaemic control in reducing the risks of long-term diabetes complications is well established. In a large cohort study, de Beaufort et al (2007) found major differences in the HbA_{1c} levels achieved by children treated at different centres. These differences were not related to the type of insulin regimen used and appeared to persist over time despite the attempts by many institutions to improve their outcomes. A subsequent study of the same cohort showed that adolescents were more likely to achieve a lower HbA_{1c} in centres where healthcare professionals set lower glycaemic targets, suggesting that the aggressiveness with which institutions pursue metabolic outcomes may be important in explaining such differences (Swift et al, 2010).

In a new study (summarised alongside), Maas et al compared the metabolic outcomes of 2622 children aged <6 years who were enrolled in the US T1DX (Type 1 Diabetes Exchange) registry or the German and Austrian DPV (*Diabetes Patienten Verlaufsdokumentation*; Prospective Diabetes Follow-up Registry). They found that the children in the DPV achieved an HbA_{1c} concentration that was an average of 0.8% (8.4 mmol/mol) lower than those in the T1DX registry. The children in the two registries had many similarities in clinical characteristics and management factors. A greater proportion used insulin pumps in the DPV but this did not appear to fully explain the differences in HbA_{1c} observed between the two cohorts, as the biggest discrepancy in metabolic outcomes was seen in the children who were managed with injections.

The authors hypothesised that a major contributory factor to these differences in HbA_{1c} may have been the fact that the clinicians in the DPV followed the lower HbA_{1c} target (<58.5 mmol/mol [<7.5%]) set by the International Society for Pediatric and Adolescent Diabetes (ISPAD), whereas providers in the T1DX registry followed the higher age-specific target set by the American Diabetes Association (ADA; HbA_{1c} <69.4 mmol/mol [<8.5%]). Interestingly, there was no difference in the proportion of children who reported severe hypoglycaemia between the two cohorts.

This study has several limitations. The authors concede that the clinical outcome data from the two registries do not prove a cause-and-effect relationship. However, the findings are thought-provoking and support other studies that indicate that targets set by healthcare practitioners do influence metabolic outcomes (Clements et al, 2013). Glycaemic targets are an easily modifiable factor, and these results should lead diabetes teams to review and agree targets at their institutions. The ADA has since lowered its targets for young children to an HbA_{1c} of <7.5% (58.5 mmol/mol), similar to the ISPAD guidelines. ■

Clements SA, Anger MD, Bishop FK et al (2013) Lower A1c among adolescents with lower perceived A1c goal: a cross-sectional survey. *Int J Pediatr Endocrinol* **2013**: 17

de Beaufort CE, Swift PG, Skinner CT et al (2007) Continuing stability of center differences in pediatric diabetes care: do advances in diabetes treatment improve outcome? The Hvidoere Study Group on Childhood Diabetes. *Diabetes Care* **30**: 2245–50

Swift PG, Skinner TC, de Beaufort CE et al (2010) Target setting in intensive insulin management is associated with metabolic control: the Hvidoere Childhood Diabetes Study Group Centre Differences Study 2005. *Pediatr Diabetes* **11**: 271–8

Diabetologia

Effect of different HbA_{1c} targets on glycaemic control in children with T1D

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

1 The authors evaluated the glycaemic outcomes of 2622 young children with T1D who were enrolled in the US T1DX (Type 1 Diabetes Exchange) registry or the German and Austrian DPV (*Diabetes Patienten Verlaufsdokumentation*; Prospective Diabetes Follow-up Registry).

2 Despite many similarities in clinical characteristics and treatment, the mean HbA_{1c} was significantly lower in the DPV cohort than in the T1DX cohort (57.7 mmol/mol [7.4%] vs 66.1 mmol/mol [8.2%]; $P<0.001$).

3 Linear regression analyses, after adjustment for age, gender, T1D duration and insulin pump use, showed that the DPV cohort was more likely to achieve an HbA_{1c} of <8.5% (<69 mmol/mol; odds ratio [OR], 3.6) or <7.5% (<58 mmol/mol; OR, 4.2).

4 The authors suggest that, as differences in clinical characteristics and treatment could not fully explain the difference in glycaemic outcomes, the lower HbA_{1c} targets in the DPV (<7.5% vs <8.5%) may have been a contributor.

5 While the use of insulin pumps was more common in the DPV cohort, the difference in outcomes between the two cohorts appeared to be independent of pump use.

6 The frequency of severe hypoglycaemia was similar in the two cohorts; however, diabetic ketoacidosis was more common in the cohort with the higher HbA_{1c} target.

Maahs DM, Hermann JM, DuBose SN et al (2014) Contrasting the clinical care and outcomes of 2,622 children with type 1 diabetes less than 6 years of age in the United States T1D Exchange and German/Austrian DPV registries. *Diabetologia* **57**: 1578–85

Diabetes Care

Neurological consequences of DKA at presentation in children with T1D

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

1 The authors sought to determine the neurological and cognitive consequences of diabetic ketoacidosis (DKA) at diagnosis of T1D in children.

2 In a prospective, longitudinal cohort study, 95 children with T1D (36 with and 59 without DKA at presentation) underwent brain imaging and cognitive evaluation at diagnosis and then after 5 days, 28 days and 6 months.

3 The DKA and non-DKA groups were similar in terms of age, symptom duration, socioeconomic status and pre-existing special educational needs.

4 Compared with the non-DKA group, the children with DKA had increased white matter volume and diffusivity in the frontal, temporal and parietal cortices; this normalised by 6 months. Total grey matter volume was lower initially but also normalised at 6 months.

5 Mental state scores were lower in the DKA group at diagnosis and after 5 days. Scores increased at a similar rate in both groups, but the examinations were not performed at later time points.

6 While total and regional white and grey matter volumes normalised over the follow-up in the DKA group, they were associated with worse attention and delayed memory recall at 6 months.

7 The authors conclude that DKA in children results in widespread neurological changes and adverse cognitive outcomes in the medium term. Efforts should be made to prevent DKA and perform neuropsychological assessment if it occurs.

Cameron FJ, Scratch SE, Nadebaum C et al (2014) Neurological consequences of diabetic ketoacidosis at initial presentation of type 1 diabetes in a prospective cohort study of children. *Diabetes Care* **37**: 1554–62

J Clin Endocrinol Metab

Vitamin D levels and T1D incidence

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

1 Finland has the highest incidence of T1D in the world; however, the incidence plateaued in 2006.

2 These authors sought to determine whether this plateau coincided with increased vitamin D levels following a policy of supplementation in children and adults in 2003.

3 Serum 25-hydroxyvitamin D (25[OH]D) levels were measured repeatedly between 1998 and 2006 in 387 children.

4 Mean 25(OH)D levels were significantly lower between 1998 and 2002 compared with 2003–2006 (69.3 vs 84.9 nmol/L; $P<0.001$). Severe deficiency was more common in the earlier period (7.7% vs 2.7%; $P<0.005$).

5 The authors conclude that vitamin D supplementation had a delayed temporal association with the plateau in T1D incidence in Finland.

Mäkinen M, Simell V, Mykkänen J et al (2014) An increase in serum 25-hydroxyvitamin D concentrations preceded a plateau in type 1 diabetes incidence in Finnish children. *J Clin Endocrinol Metab* **99**: E2353–6

Diabet Med

Early-adulthood mortality risk in people with childhood-onset T1D

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

1 The authors sought to compare standardised mortality ratios (SMRs) for death in early adulthood (age 18–38 years) between people with childhood-onset T1D (n=1309) and a sample from the general population (n=6451).

2 There were 20 deaths in the T1D cohort and 30 in the comparison cohort, resulting in an SMR of 3.3 in the T1D cohort. The SMR was much higher for women with T1D than for men with the condition (10.1 vs 1.7).

3 The majority of deaths in women were a result of accidental exposure to noxious substances, cardiovascular disease, diabetic ketoacidosis or suicide.

4 Significant risk factors for death were mean HbA_{1c}, history of four or more episodes of severe hypoglycaemia and low or medium socioeconomic background.

Cooper MN, de Klerk NH, Jones TW, Davis EA (2014) Clinical and demographic risk factors associated with mortality during early adulthood in a population-based cohort of childhood-onset type 1 diabetes. *Diabet Med* **31**: 1550–8

Diabetes Technol Ther

Best injection site in preschool children

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

1 In this randomised, crossover study, the authors evaluated whether the buttock or abdomen was the best injection site in terms of glycaemic control in a group of six preschool children with T1D who received treatment with insulin pumps.

2 The six participants (mean age, 5.2 years; three boys) ate a controlled diet at regular times throughout the study and were followed for 3 days for each injection site.

3 The mean blood glucose level and measures of glycaemic variability were significantly lower when the buttock was used as the injection site.

4 These results will need replication in larger cohorts with longer follow-up, but they suggest that the buttock is a superior injection site to the abdomen.

Zanfardino A, Iafusco D, Piscopo A et al (2014) Continuous subcutaneous insulin infusion in preschool children: butt or tummy, which is the best infusion set site? *Diabetes Technol Ther* **16**: 563–6

> *"The authors conclude that diabetic ketoacidosis (DKA) in children results in widespread neurological changes and adverse cognitive outcomes in the medium term. Efforts should be made to prevent DKA and perform neuropsychological assessment if it occurs."*