Glycaemic tracking of HbA_1c in patients with type 1 diabetes can be modified through intensive diabetes support regardless of diabetes duration

Lauren M. Quinn[1], R. Thayakaran[2], N. Thomas[2], K. Nirantharakumar[2], P. Narendran[3,4]

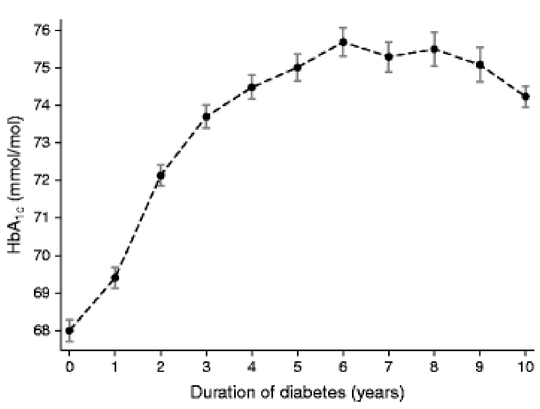
[1]Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, UK, [2]Public Health, Epidemiology and Biostatistics, Institute of Applied Health Research, University of Birmingham, Birmingham, U
[3]Institute of Immunology and Immunotherapy, University of Birmingham, Birmingham, UK, [4]Department of Diabetes, University Hospitals of Birmingham, Birmingham, UK.

UNIVERSITY OF BIRMINGHAM

Background

We have recently shown that HbA_{1c} in people with newly diagnosed type 1 diabetes gradually rises from diagnosis for the first five years, before settling into a remarkably stable plateau. This phenomenon of HbA1c stability has been referred to as glycaemic tracking.
There are a number of potential modifiable and non-modifiable factors contributing to glycaemic tracking (Table 1)

Nirantharakumar et al. 2018. Diabetologia.



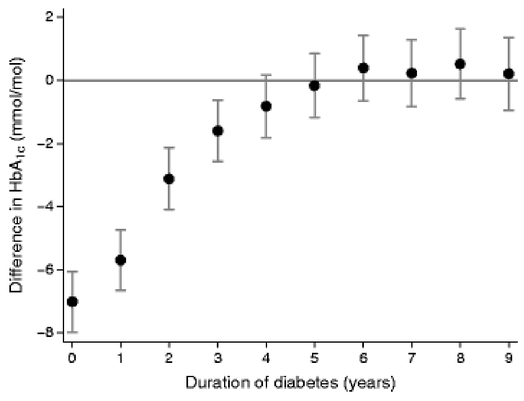


Table 1: Proposed factors that influence tracking:

Non-modifiable factors	Modifiable factors
C-peptide	Treatment regimen
Age	Lifestyle (physical activity, diet)
Gender	Presentation in DKA
Ethnicity	Psychological, social factors and socioeconomic status

Aims

We aimed to explore whether the course of glycaemic tracking is set irrecoverably early after diagnosis with type 1 diabetes or whether it can be modified.

Methods

Data was obtained from the Diabetes Control and Complications Trial (DCCT) and Epidemiology of Diabetes Interventions and Complications (EDIC) trials.

HbA_{1c} was retrospectively compared between individuals randomised to intensive treatment and usual-care using Mann Whitney and Kruskal Wallis statistical analyses. Significance level was set at $p<0.05$.

Results

A cohort of 1441 individuals with type 1 diabetes were included, of which 711 were randomised to intensive treatment, and median age was 27 years (interquartile range: 22-32 years).

HbA_{1c} at baseline was 8.68% (71mmol/mol) (7.80% (62mmol/mol)–9.90% (85mmol/mol) and median duration of diabetes was 49 months (26-108 months).

HbA_{1c} improved significantly with treatment intensification ($p<0.0005$) regardless of diabetes duration at study onset (Figures 1a-1d).

However this improvement was not sustained outside of the trial setting and HbA_{1c} returned to baseline track in the longer term (Figures 2a-2e)

Conclusions

We demonstrate that all individuals with type 1 diabetes, regardless of diabetes duration, can respond to treatment intensification. However, this improvement persists only as long as the support is made available.

We now need to explore how best to deliver long-term intensive support to people with type 1 diabetes.

Change in Hba1c from baseline to DCCT to EDIC

Figure 1a - Standard treatment
DCCT baseline to DCCT year 1

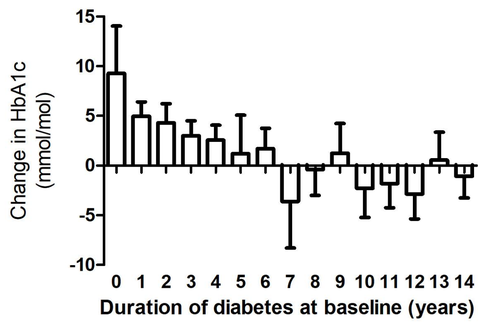


Figure 1b - Standard treatment
DCCT end to EDIC start

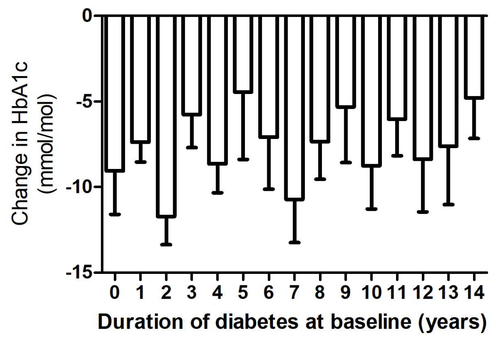


Figure 1c - Intensive treatment
DCCT baseline to DCCT year 1

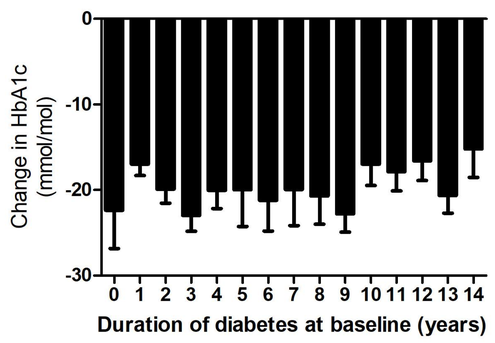
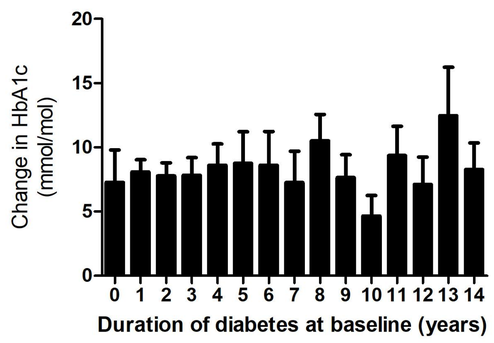


Figure 1d - Intensive treatment
DCCT end to EDIC start



Figures 1a and 1b: Change in HbA1c
Change in Hba1c from baseline to one year of DCCT in the standard treatment arm (Figure 1a, n=726) and the intensive treatment arm (Figure 1b, n=710), according to duration of diabetes at DCCT study onset.
Hba1c presented as Mean +/- Standard Error of the Mean (SEM). P>0.05.

Hba1c longitudinal trend in the DCCT and EDIC studies

Figure 2a - Standard care
0-<5 years diabetes duration

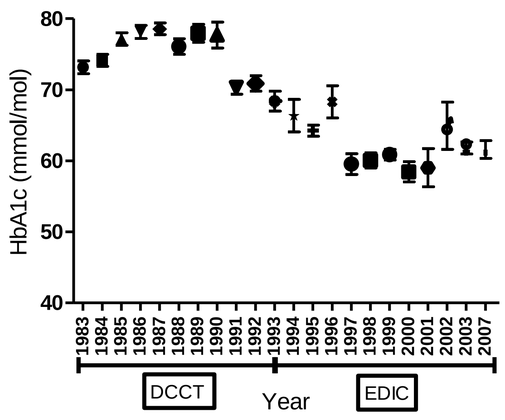


Figure 2d - Intensive care
0-<5 years diabetes duration

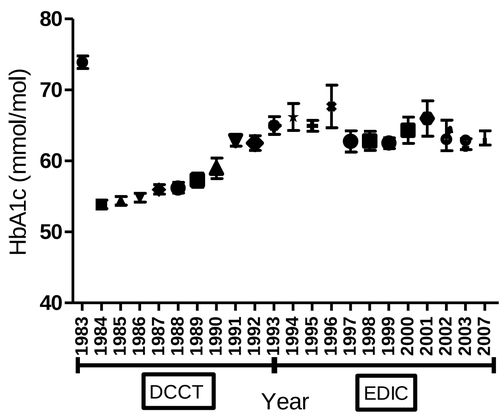


Figure 2b - Standard care
5-<10 years diabetes duration

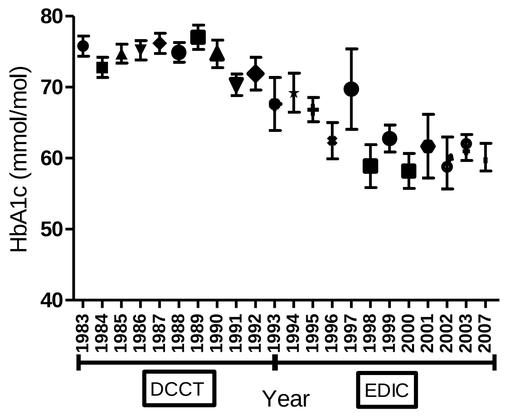


Figure 2e - Intensive care
5-<10 years diabetes duration

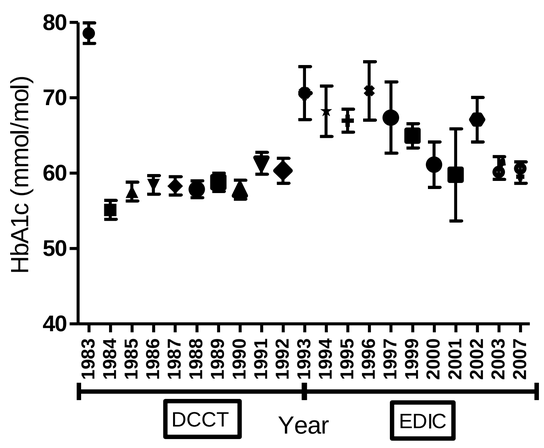


Figure 2c - Standard care
10-<15 years diabetes duration

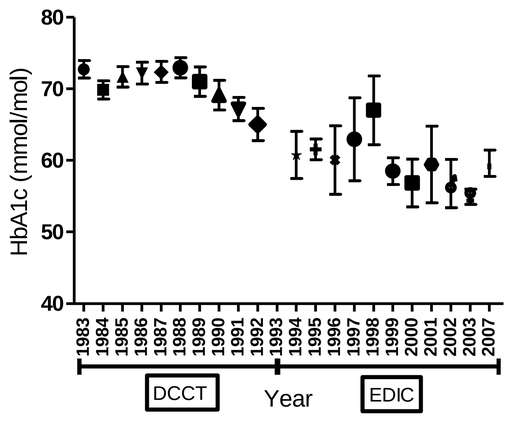
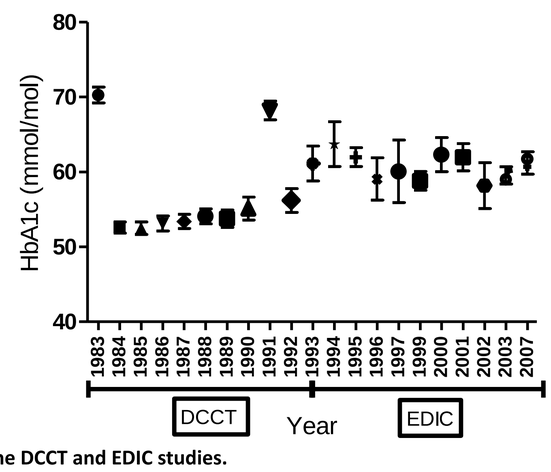


Figure 2f - Intensive care
10-<15 years diabetes duration



Figures 2a-2f: Hba1c in the DCCT and EDIC studies.
Data is mean +/- SEM. Figures 2a-2c show the changes in Hba1c across the study period (DCCT and EDIC) in the standard treatment group only and are sub-divided according to short duration diabetes at DCCT onset (Figure 2a), medium duration diabetes (Figure 2b) and long duration diabetes (Figure 2c). Figures 2d-2f show the changes in Hba1c duration diabetes from DCCT onset in individuals in the intensive care group with short duration diabetes (Figure 2d), medium duration diabetes (Figure 2e) and long duration diabetes (Figure 2f).

References

1. Nirantharakumar K, Mohammed N, Toulis KA, Thomas GN, Narendran P (2018) Clinically meaningful and lasting HbA1c improvement rarely occurs after 5 years of type 1 diabetes: an argument for early, targeted and aggressive intervention following diagnosis. Diabetologia 61(5):1064–1070. https://doi.org/10.1007/s00125-018-4574-6
2. Diabetes Control and Complications Trial Research Group, Nathan DM, Genuth S, Lachin J, Cleary P, Crofford O et al (1993) The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med 329(14):977-986. https://doi.org/10.1056/NEJM199309303291401