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## Background

The effects of metabolic memory highlight the importance of good glycaemic control following diagnosis of type 1 diabetes (T1D).

There is relative insulin resistance at diagnosis, particularly in the presence of blood ketones. Local prescribing guidelines reflect this with higher insulin starting doses with ketonaemia. All children newly diagnosed with T1D are admitted to hospital for initial education, and are commenced on multiple daily injections with a basal bolus regimen following prescribing guidelines within our integrated care pathway (ICP).

## Objective and hypothesis

Insulin dosing guidance for children with newly diagnosed T1D appeared insufficient to achieve optimal glycaemic control prior to hospital discharge and this may have an impact on achieving glycaemic targets at 2 and 4 months following diagnosis (as evidenced by HbA1c). Our objective was to audit initial doses, adjust guidance for prescribing and re-audit to assess impact.

## Results: audit 1

Data was analysed from 23 children in three cohorts, determined by existing prescribing guidelines:

1. Diabetic ketoacidosis (DKA) at presentation (n=11)
2. Ketones  $\geq 1.5$ mmol/l but not in DKA (n=5)
3. Ketones  $<1.5$ mmol/l (n=7)

Starting dose of SC insulin prescribed was 0.5 - 0.7 units/kg/day (table 1).

| Patient group at presentation | Basal insulin (units/kg/day) | Bolus insulin (units/kg/day) | Total daily dose of insulin (units/kg/day) |
|-------------------------------|------------------------------|------------------------------|--|
| DKA                           | 0.4                          | 0.3                          | 0.7  |
| Ketones $\geq 1.5$ mmol/l     | 0.4                          | 0.3                          | 0.7  |
| Ketones $< 1.5$ mmol/l        | 0.2                          | 0.3                          | 0.5  |

Table 1: Total daily dose of insulin prescribed at presentation of T1D in each patient group.

The total daily dose of insulin required to be increased prior to discharge in all cohorts, but particularly those patients with elevated ketones at presentation (figure 1).

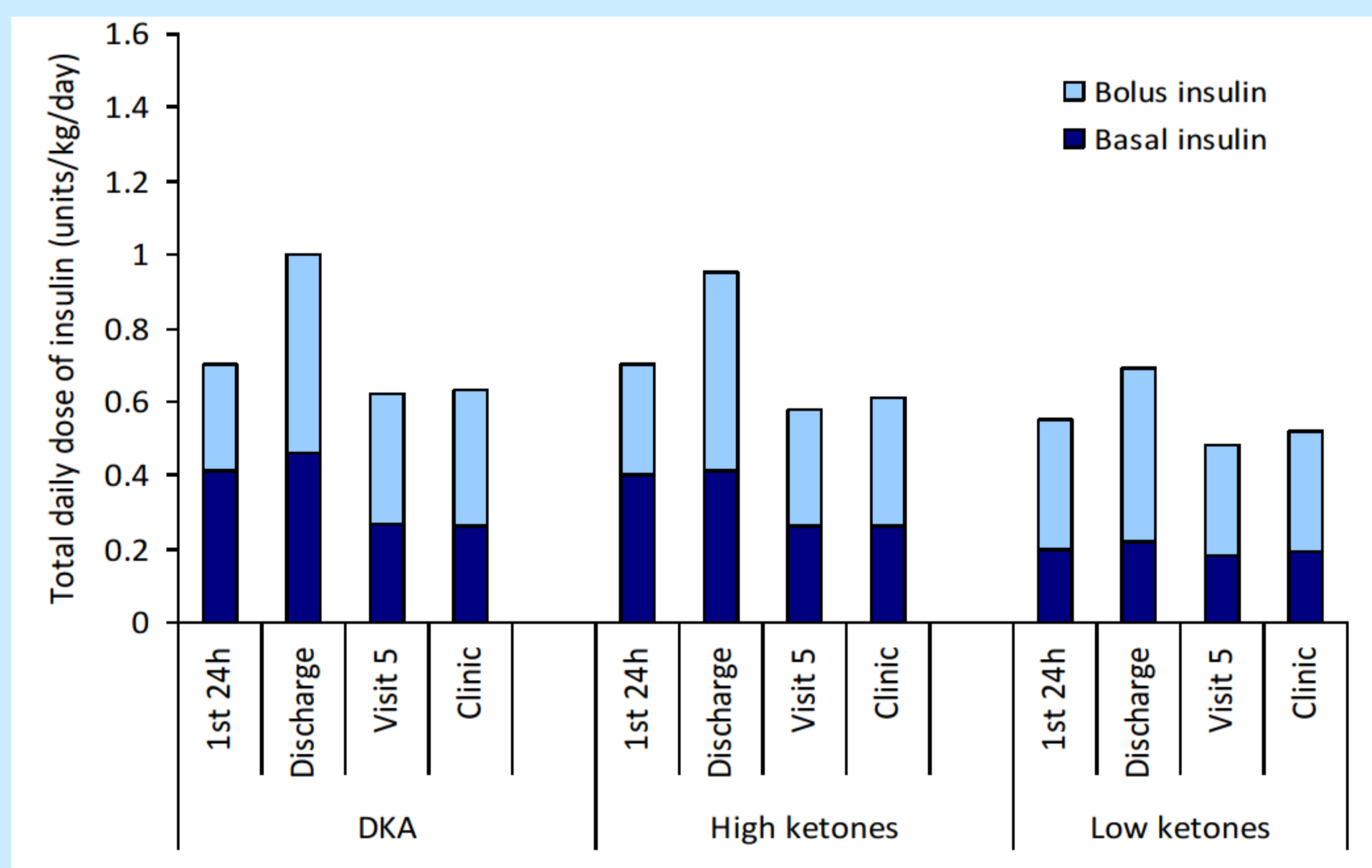


Figure 1: Total daily dose of insulin (units/kg/day) in each of the treatment groups

Despite this increase in insulin dose during the admission, mean blood glucose (BG) over the 24 hours prior to discharge was above target in all cohorts (DKA mean BG = 12.9 mmol/l, high ketones mean BG = 13 mmol/l, low ketones mean BG = 11.7 mmol/l).

## Changes to prescribing guidance

Three changes to insulin prescribing were introduced following the first audit and were incorporated into a full revision of the ICP for newly diagnosed patients:

1. Insulin starting doses were increased to between 0.55 and 1.1 units/kg/day depending on degree of ketonaemia at presentation (table 2).
2. An individualised correction factor was calculated for each patient at diagnosis.
3. Correction doses were given overnight at 00:00h and 04:00h if blood glucose was  $> 10$  mmol/l.

## Method

Medical records of children with newly diagnosed T1D presenting to our tertiary paediatric hospital over a 6 month period were reviewed. Data on blood glucose readings and insulin dosing was collected at the following time points:

- Initiation of subcutaneous (SC) insulin
- Hospital discharge or day 4, whichever was earlier
- Visit 5 of the new patient clinic follow-up process (8-13 weeks after diagnosis)
- First appointment at the diabetes review clinic (15 – 18 weeks after diagnosis)

This initial data was used to revise our integrated care pathway insulin dosing guidance.

A repeat audit was then carried out to determine if this improved glycaemic control, as determined by HbA1c and mean blood glucose.

The calculation of insulin doses is clearly explained in the integrated care pathway.

| Patient group at presentation | Basal insulin (units/kg/day) | Bolus insulin (units/kg/day) | Total daily dose of insulin (units/kg/day) |
|-------------------------------|------------------------------|------------------------------|--|
| DKA                           | 0.4                          | 0.7                          | 1.1  |
| Ketones $\geq 4$ mmol/l       | 0.4                          | 0.7                          | 1.1  |
| Ketones 1.5-3.9 mmol/l        | 0.4                          | 0.55                         | 0.95                                       |
| Ketones $<1.5$ mmol/l         | 0.2                          | 0.35                         | 0.55                                       |

Table 2: Updated insulin prescribing guidance: total daily dose of insulin prescribed at presentation of T1D in each patient group.

## Results: audit 2

20 children presented with new onset of T1D over the first 6 months of use of the new prescribing guidance. Two children were excluded from further data analysis (one commenced treatment abroad, one presented in severe DKA resulting in prolonged intensive care unit admission and an individualised care plan).

Insulin doses did not need to be escalated as significantly during the hospital admission compared to previous dosing guidelines (figure 2).

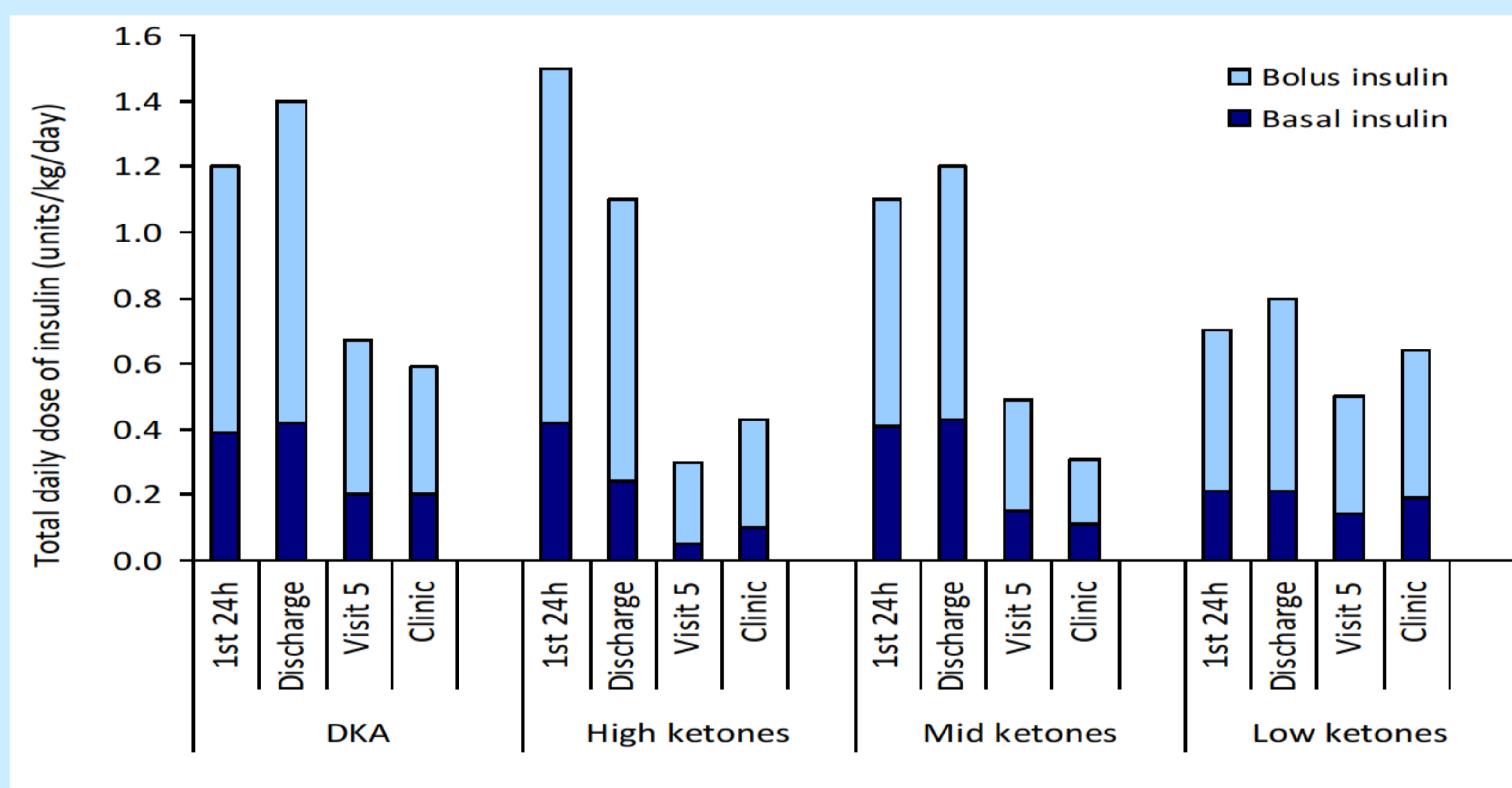


Figure 2: Total daily dose of insulin (units/kg/day) in each of the treatment groups

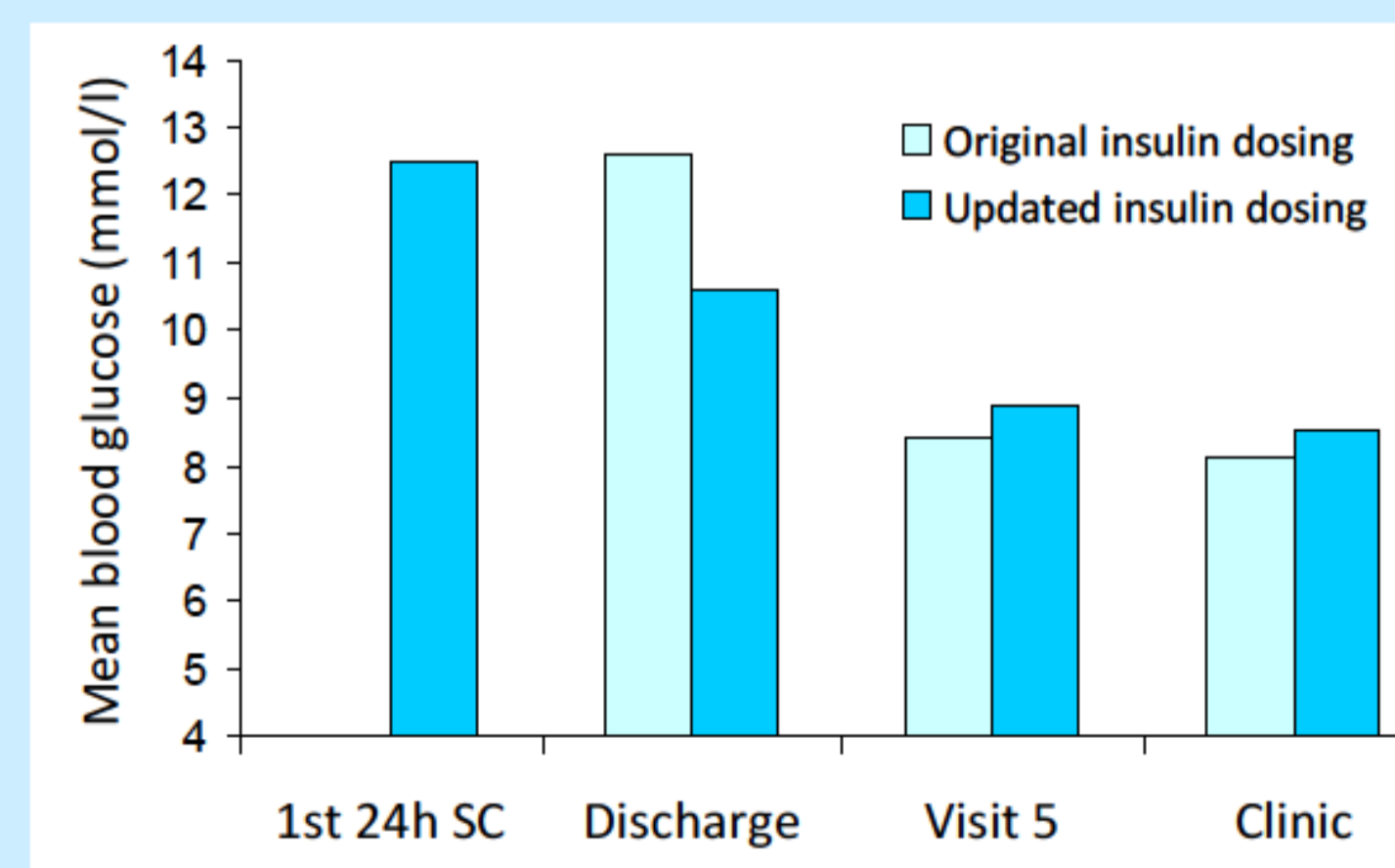


Figure 3: Mean BG pre- and post- changes to insulin dosing

Mean HbA1c was not significantly different at first clinic following the dosing change (figure 4).

There was a lower mean blood glucose at hospital discharge (figure 3). Episodes of hypoglycaemia were infrequent (n=3 in first 24h, n=1 in final 24h of admission).

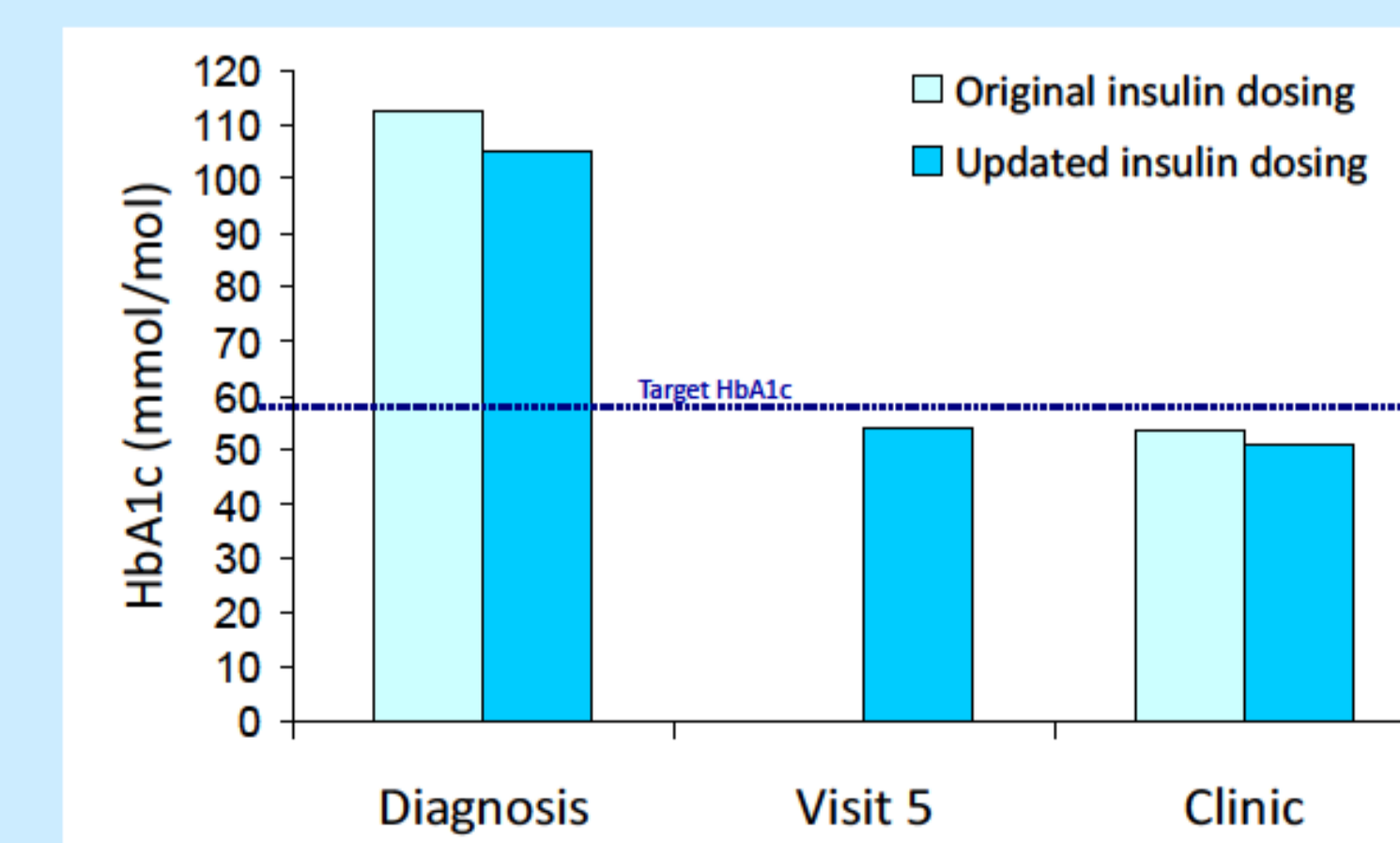


Figure 4: Mean HbA1c pre- and post- insulin dosing change

## References

- Laffel L. Ketone bodies: a review of physiology, pathophysiology and application of monitoring to diabetes, *Diabetes/Metabolism Research and Reviews* 1999; 15 (6): 412-426.
- Aschner PJ, Ruiz AJ. Metabolic memory for vascular disease in diabetes. *Diabetes Technol The* 2012, Vol. 14, No. S1: S-68-S-74.
- Danne T, Bangstad H-J, Deeb L, Jarosz-Chobot P, Mungaie L, Saboo B, Urakami T, Battelino T, Hanas R. Insulin treatment in children and adolescents with diabetes *Pediatric Diabetes* 2014; 15 (Suppl. 20): 115-134.

## Conclusion

Children with significant ketonaemia at diagnosis required more SC insulin at initiation of treatment than initially prescribed. Local ICPs were revised to provide 0.55-1.1 unit/kg/day, with improvement in glycaemic control in the early period following diagnosis.

