Continuous Glucose Monitoring Systems and the Improvement in Hypoglycemic Awareness Post-Islet Transplantation: A Single-Centre Cohort Study

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INTRODUCTION

- Type 1 Diabetes Mellitus (T1DM) affects >400,000 people in the UK[1]
- Intensive insulin therapy is not always effective in reducing glycemic variability[2] – this leads to an increase in hypoglycemia and impaired awareness of hypoglycemia[3]
- Islet Transplantation has been offered at the Royal Infirmary of Edinburgh to 16 patients from Scotland and Northern Ireland with the most poorly controlled T1DM
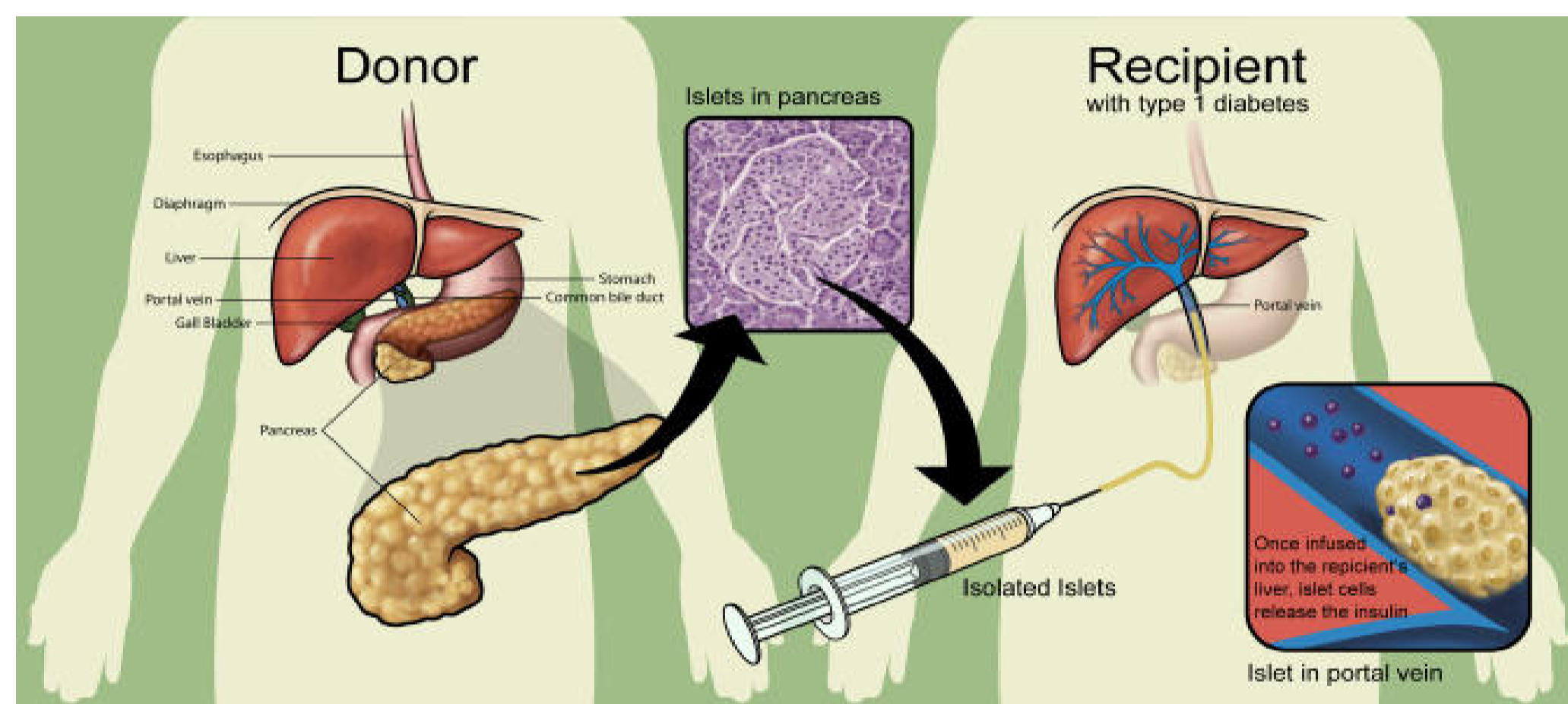

Figure 1 – Pancreatic Islet Transplantation[4]

ELIGIBILITY FOR ISLET TRANSPLANTATION[5]

- Type 1 Diabetes Mellitus
- Recurring hypoglycemia, despite:
  - Optimal insulin regimen
  - Close supervision by diabetologist
- Evidence of Impaired Awareness of Hypoglycemia (IAH)
- Willing to comply with lifetime immunosuppression and follow up

AIMS / KEY QUESTIONS

Is islet transplantation effective in patients with the most poorly controlled Type 1 Diabetes Mellitus?

a. Does glycemic control improve, as demonstrated by HbA1c and % time in hypoglycemia?

b. Does impaired awareness improve, as demonstrated by Gold & Clarke scores?

CONCLUSIONS

Islet transplantation is capable of:
- Improving glycemic control
- Reducing the hypoglycemic burden
- Improving IAH, which may continue even after graft begins to deteriorate

Findings can be combined with other UK centres to increase statistical power.

Ultimately, from research at the Edinburgh site, it can be suggested that islet transplantation offers patients with the most severe T1DM an opportunity to regain control of their condition and improve their quality of life.

METHODS

A retrospective analysis of data collected between January 2011 and March 2014 from the 16 patients who have undergone islet transplantation in Edinburgh.

1. Measure Glycemic Variability using Continuous Glucose Monitoring Systems (CGMS)
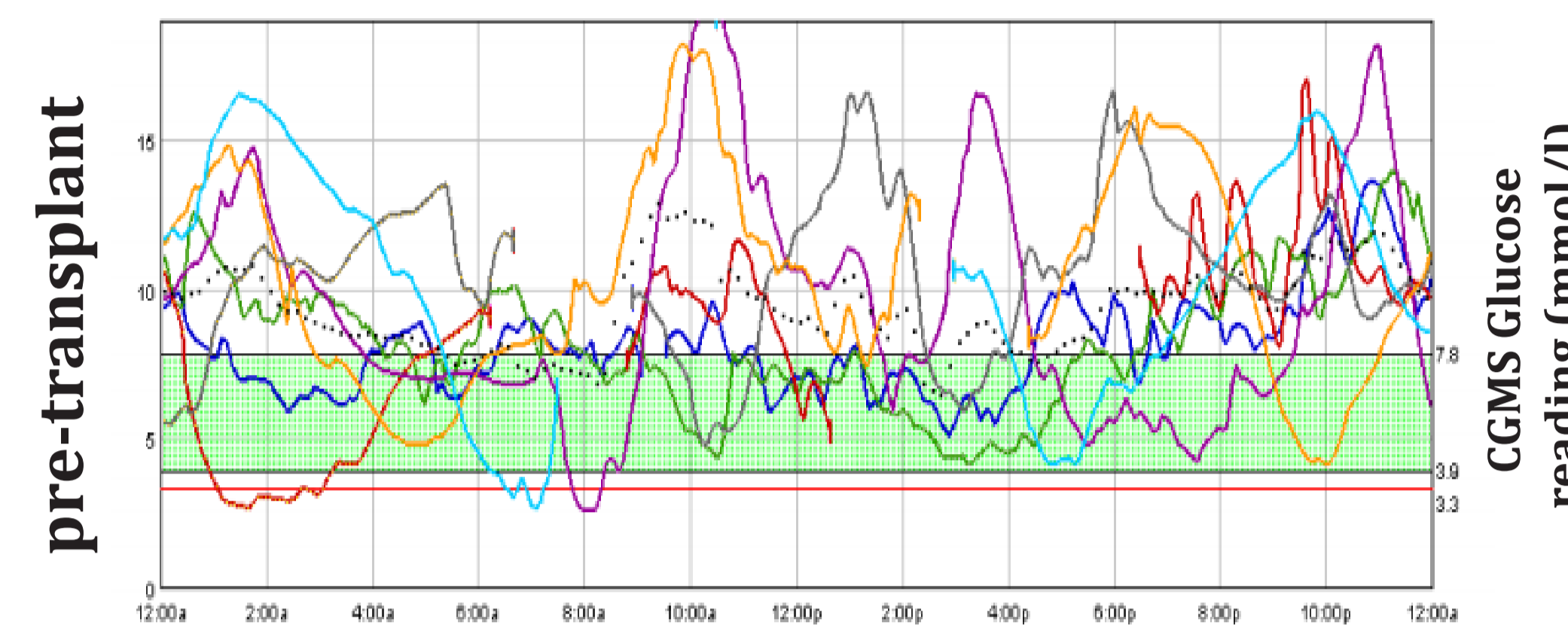

Figure 1 – Typical patient CGMS reading pre-transplant

2. Measure Impaired Awareness of Hypoglycemia (IAH) using Gold & Clarke scores

Figure 2 – Questionnaire to obtain Gold[6] & Clarke[7] scores

RESULTS

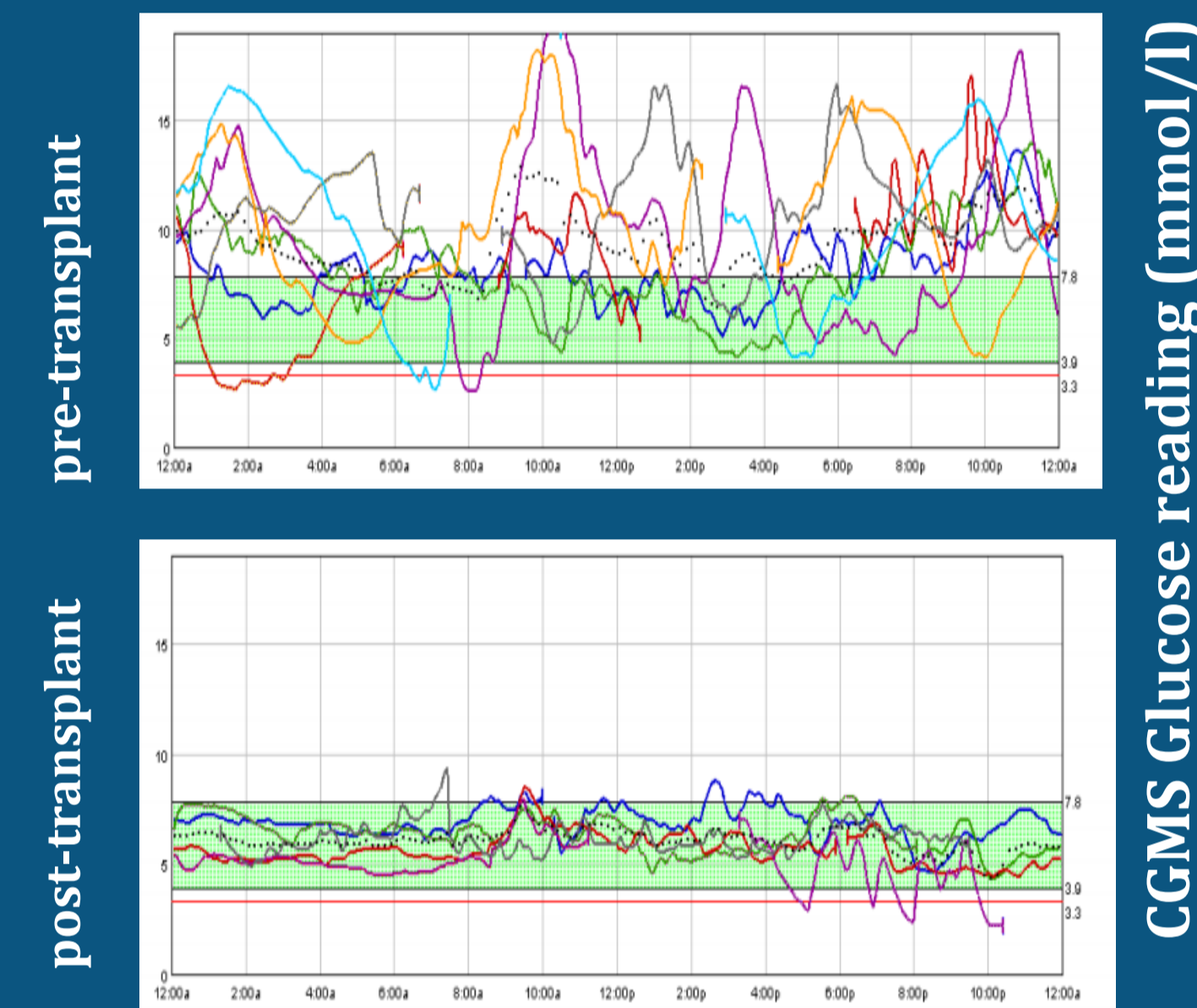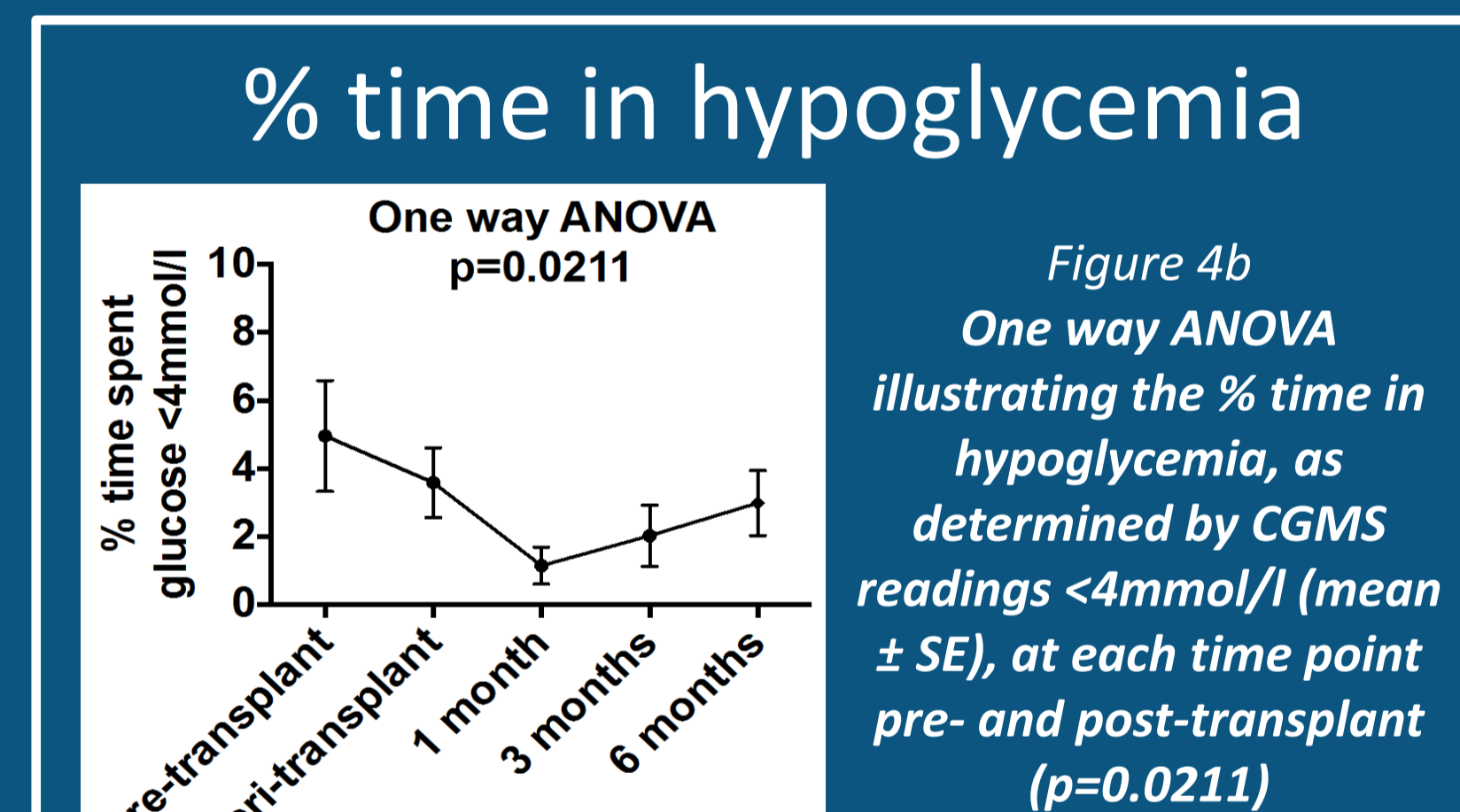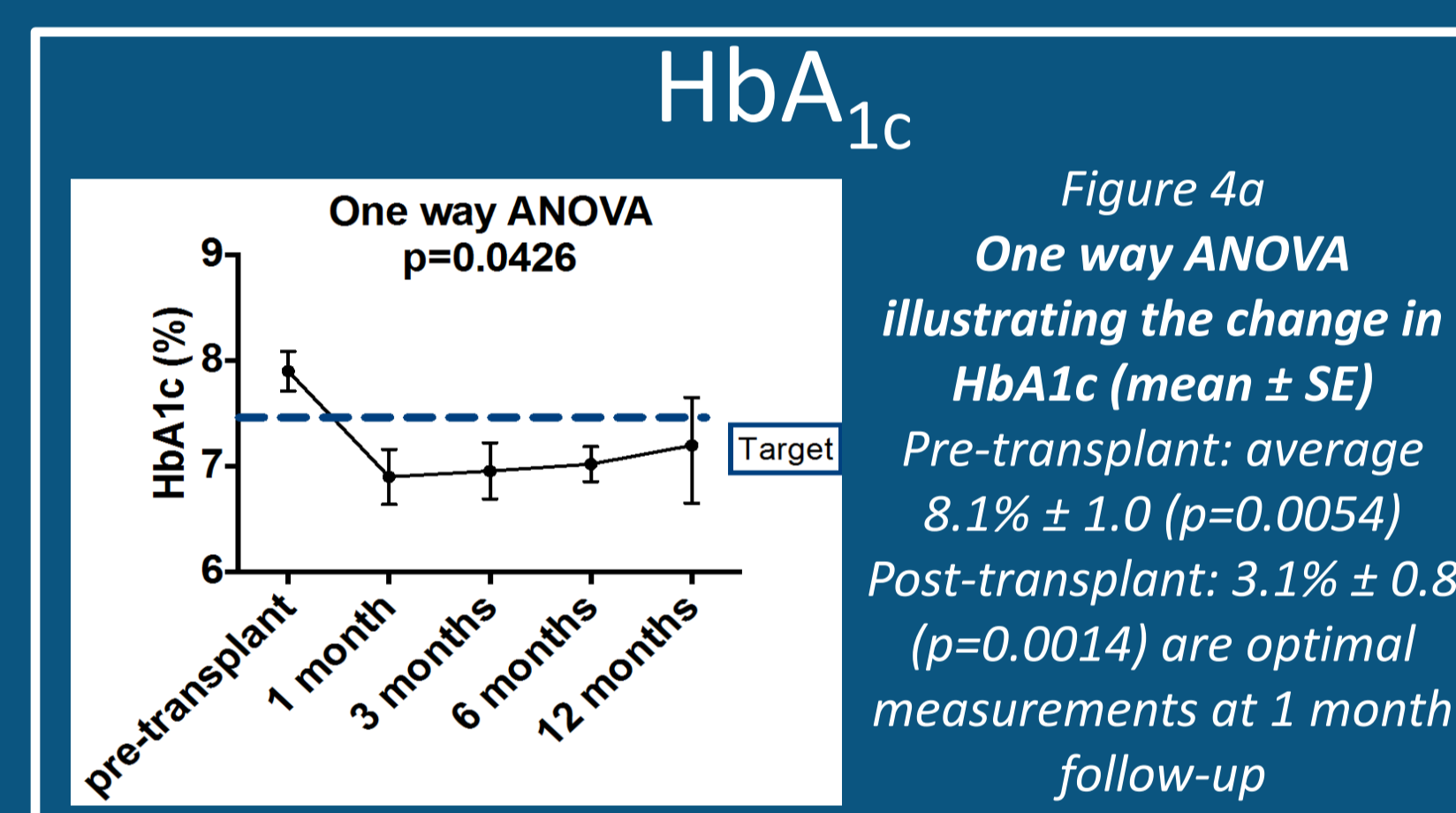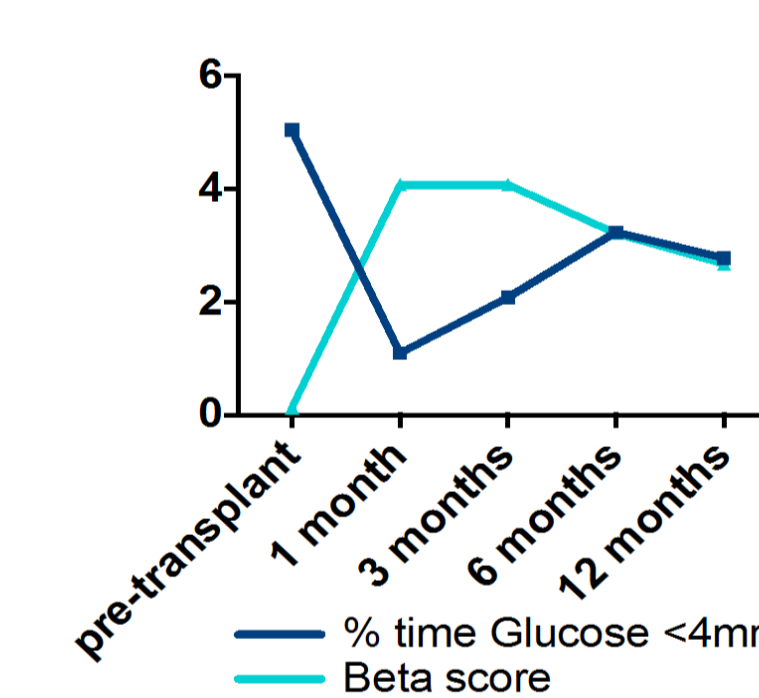### 1. Analyse CGMS data to determine changes in glycemic variability post-transplant

Figure 3– Typical patient CGMS pre- and post-transplant (1 month follow-up)

HbA1c

Figure 4a
One way ANOVA illustrating the change in HbA1c (mean ± SE)
Pre-transplant: average 8.1% ± 1.0 (p=0.0054)
Post-transplant: 3.1% ± 0.8 (p=0.0014) are optimal measurements at 1 month follow-up

% time in hypoglycemia

Figure 4b
One way ANOVA illustrating the % time in hypoglycemia, as determined by CGMS readings <4mmol/l (mean ± SE), at each time point pre- and post-transplant (p=0.0211)

Correlation statistics

Figure 5 – Percentage time in hypoglycemia vs beta score (measure of graft function) p=0.033 correlation coefficient = -0.872

2. Analyse Gold & Clarke score data to determine changes in impaired awareness of hypoglycemia

Clarke score

CLARKE SCORE
Figure 6a – Improvement from pre-transplant to most recent consultation. (p=0.018)
Figure 6b – One way ANOVA (p=0.0034)

Gold score

GOLD SCORE
Figure 6c – Improvement from pre-transplant to most recent consultation. (p=0.002)
Figure 6d – One way ANOVA (p=0.0001)

Correlation statistics

Figure 7a – Change in % time in hypoglycemia vs Gold & Clarke scores.
Clarke vs hypoglycemia p=0.68, correlation coefficient = 0.30
Gold vs hypoglycemia p=0.95, correlation coefficient = 0.10
Figure 7b – Beta score versus Gold & Clarke scores.
Clarke vs beta score p=0.60, correlation coefficient = -0.21
Gold vs beta score p=0.90, correlation coefficient = -0.05

STATISTICAL ANALYSIS

- Determine distribution
- Parametric: student's t-tests to compare two groups (pre-transplant vs each time point post-transplant)
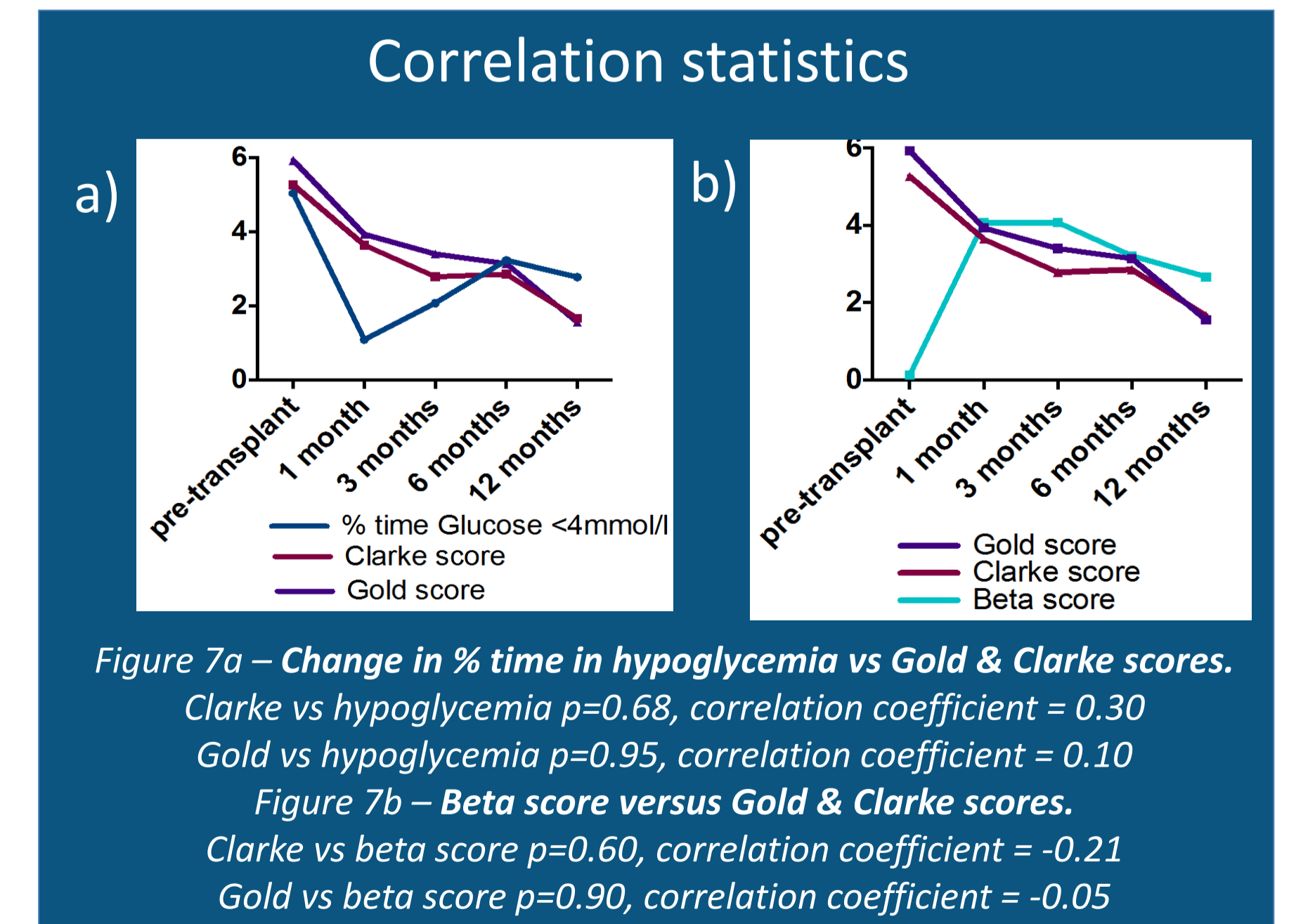- Non-parametric: Wilcoxon matched-pairs signed rank test
- ANOVA to establish significance over multiple time-points
- Spearman correlation statistics to compare parameters

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LIMITATIONS

- Lack of data
- Small sample size
- Lack of control group

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