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Carbohydrate intake contribution to HbA1c

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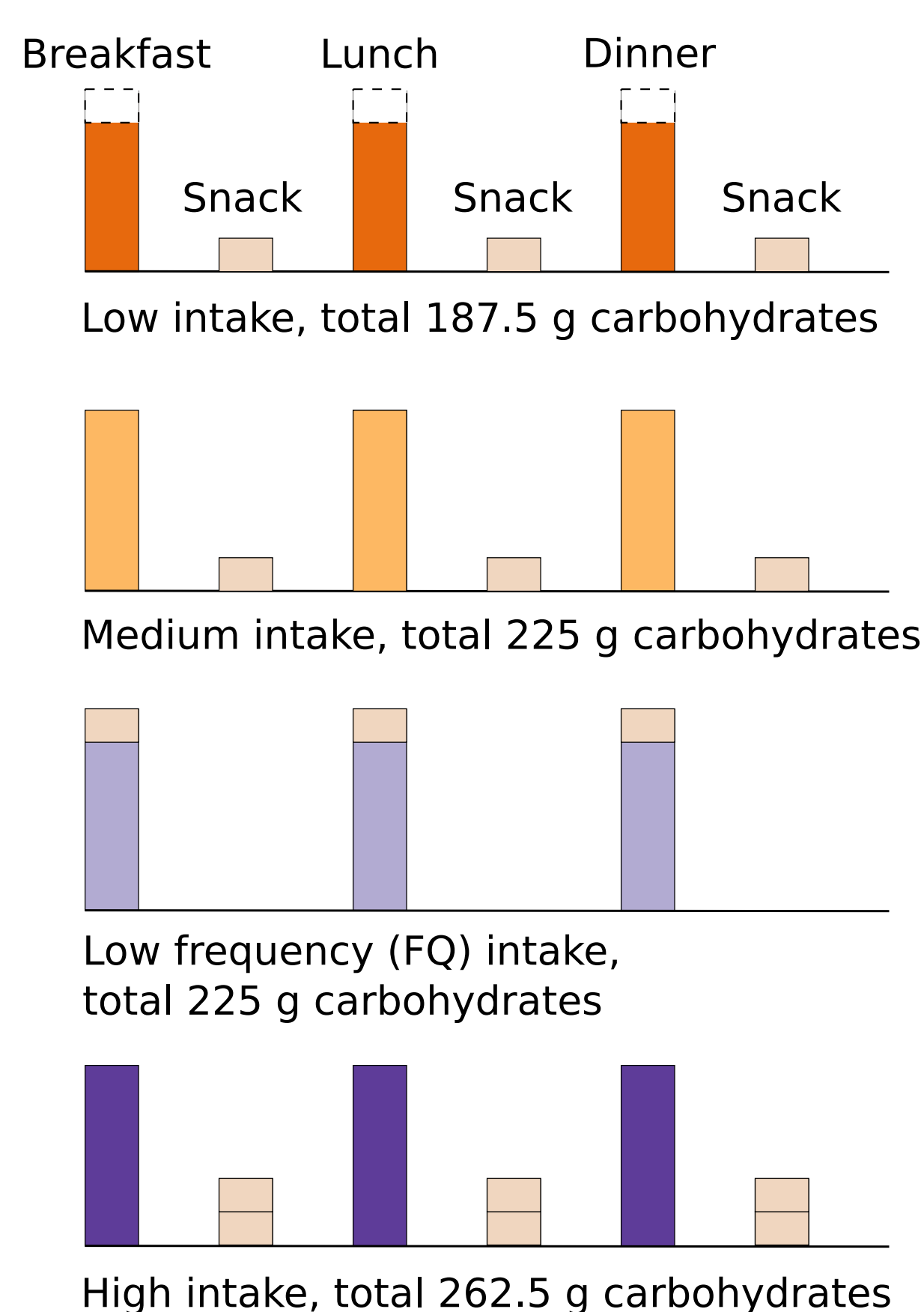
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1 Introduction

Diet control has been suggested as an effective treatment for type 2 diabetes (T2D). We investigate the effect of carbohydrate intake, meal frequency and model-specific decisions to model-predicted HbA1c. This illustrates when diet control will be most effective and when other strategies should be considered.



Well-controlled T2D
FPG=90 mg/dl
n=1000



Uncontrolled T2D
FPG=169 mg/dl
n=1000



1. Four different meal schedules were tested on two populations.

Take home messages

- Diet control as treatment will most likely be more effective for subjects with well-controlled T2D, since post-prandial glucose contributes more to HbA1c for this population, but the overall impact of changing meal regimen is small ($\pm 0.05\%$ HbA1c) within the studied meal range.
- The IGI model is sensitive to assumptions made affecting incretin, e.g. increasing ISS, linear or non-linear equation for the incretin effect and using or not using correlations.
- A diet driven weight change component affecting the insulin sensitivity would make the model predictions more realistic.

2 Methods

- Data was simulated with the IGI model (1) mimicking different populations, well- or uncontrolled T2D, by varying fasting plasma glucose (FPG). Well-controlled subjects were assumed to have suppressed endogenous glucose production (fasting serum insulin, FSI=8.7 mU/l) but an increased insulin secretion (FSI=25.1 mU/l) was also tested.
- Glucose and insulin time-profiles were simulated with four different meal regimens. The amount of glucose concentration-time profiles with a lower MPG than FPG was calculated as a measure of the impact of model-specific assumptions, such as adding correlations between parameters related to the incretin effect in the IGI model.
- Mean plasma glucose (MPG) was calculated from the simulated profiles and used as input to the IGRH model (2) for simulation of HbA1c. The same individuals were tested with all dietary regimens and the difference in HbA1c was calculated relative to the medium intake regimen.

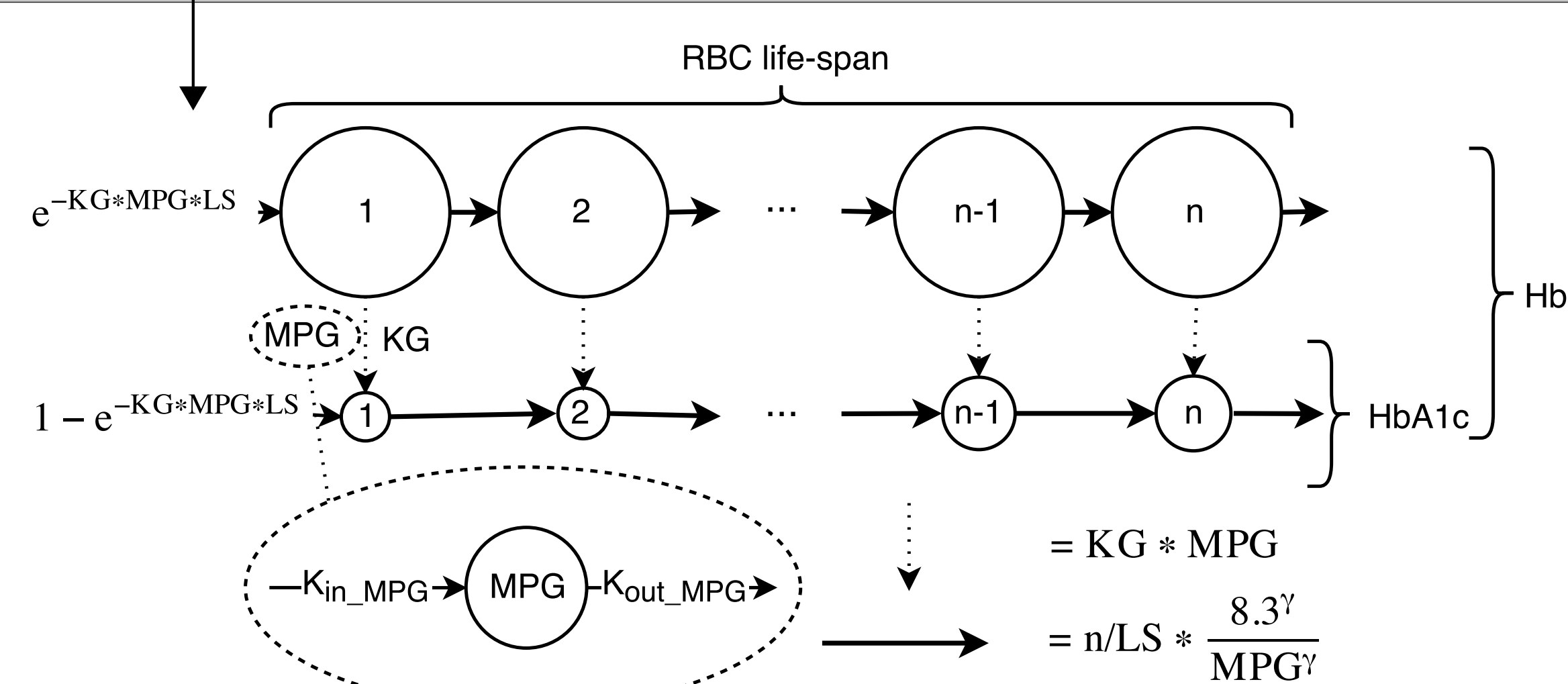
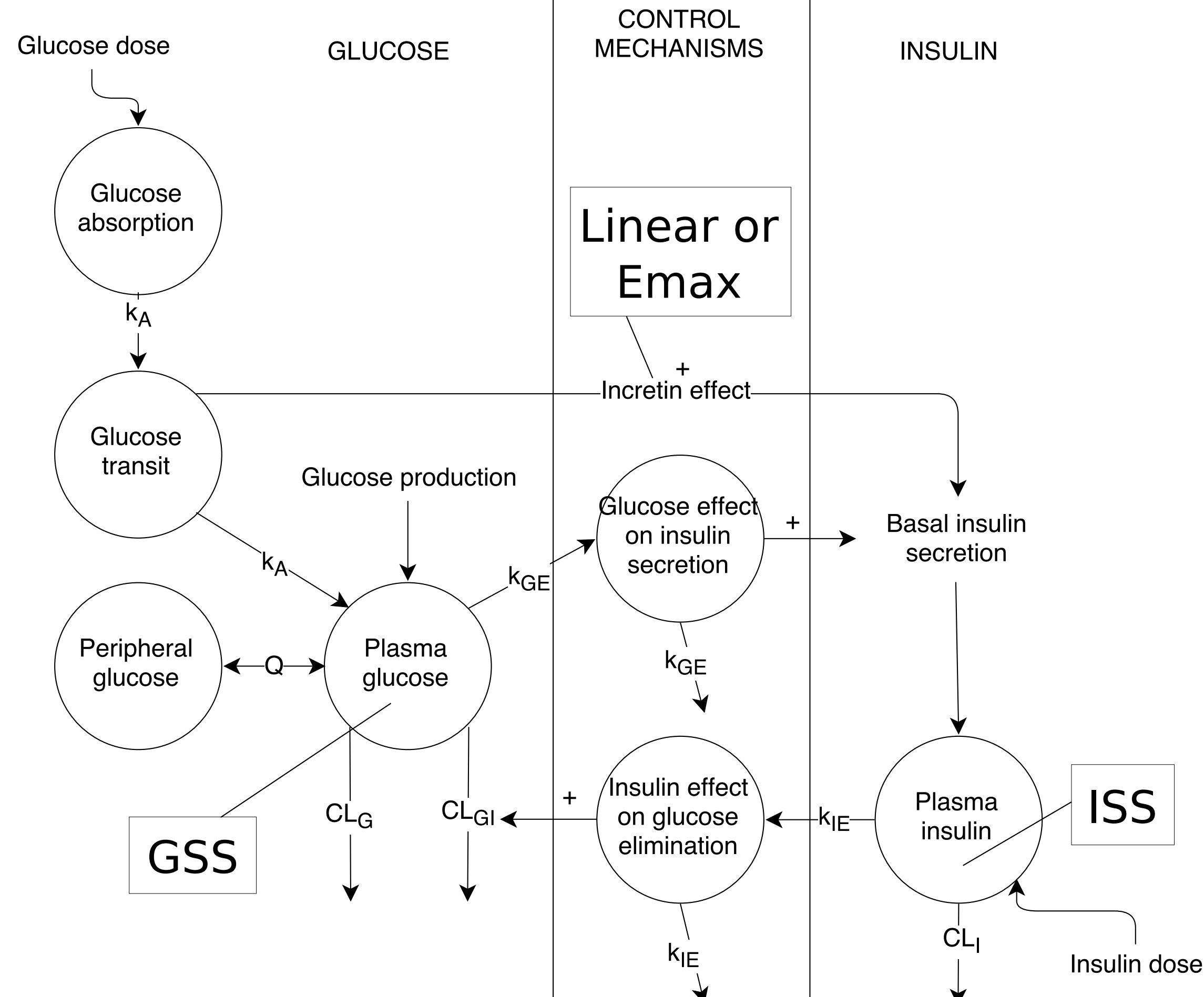
2. Glucose and insulin profiles were simulated with the IGI model.

3. The amount of profiles with MPG<FPG was calculated.

4. HbA1c was simulated with the IGRH model.

Amount of profiles with MPG<FPG for different model assumptions

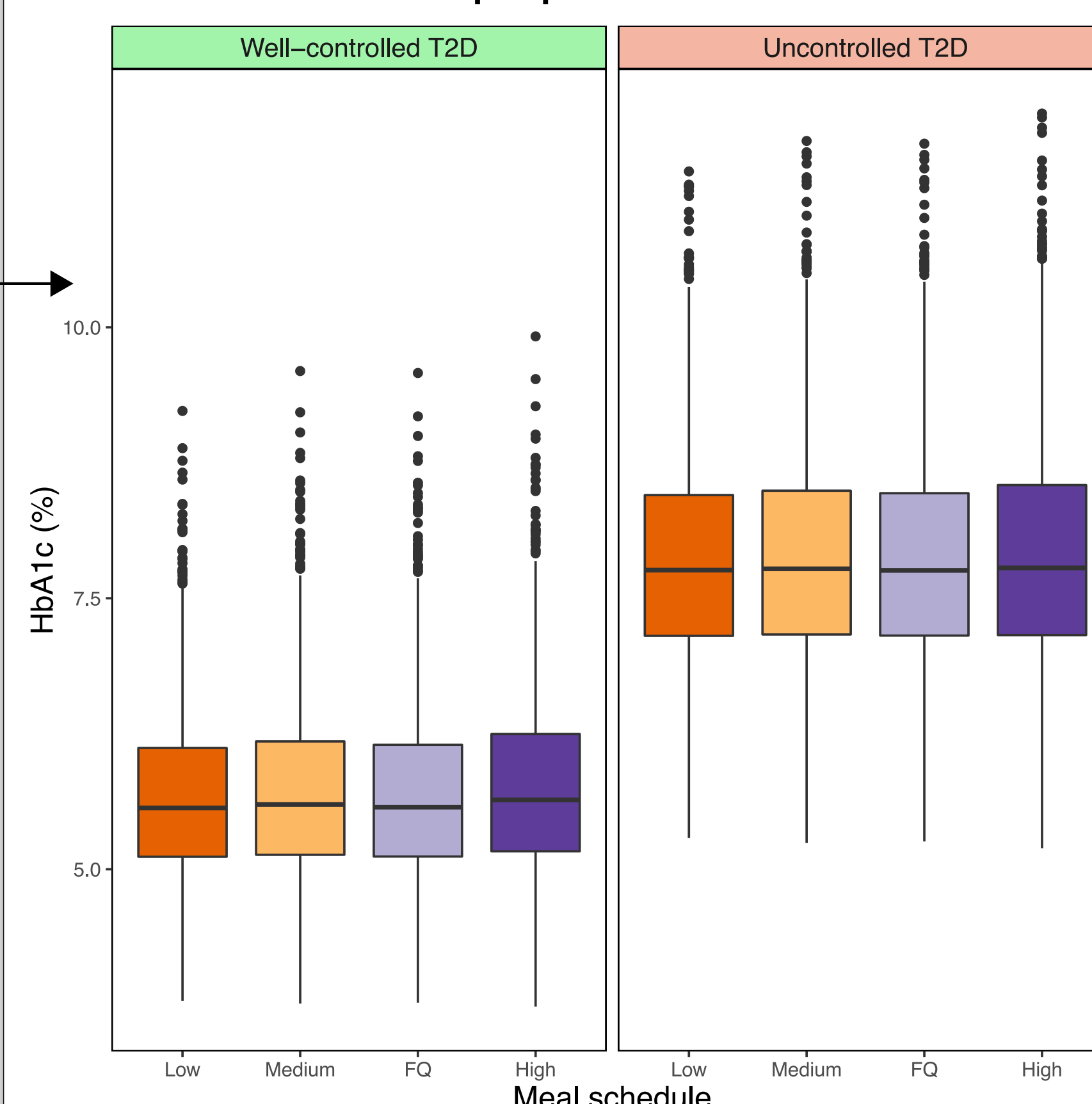
Uncontrolled T2D	
No correlations	35.0%
No correlations, Emax on incretin effect	13.8%
Correlations between ISS, incretin effect and CLGI	30.2%
Correlations between ISS, incretin effect and CLGI without IIV	60.8%
Well-controlled T2D	
Suppressed endogenous glucose production	13.7%
Increased insulin production	56.6%



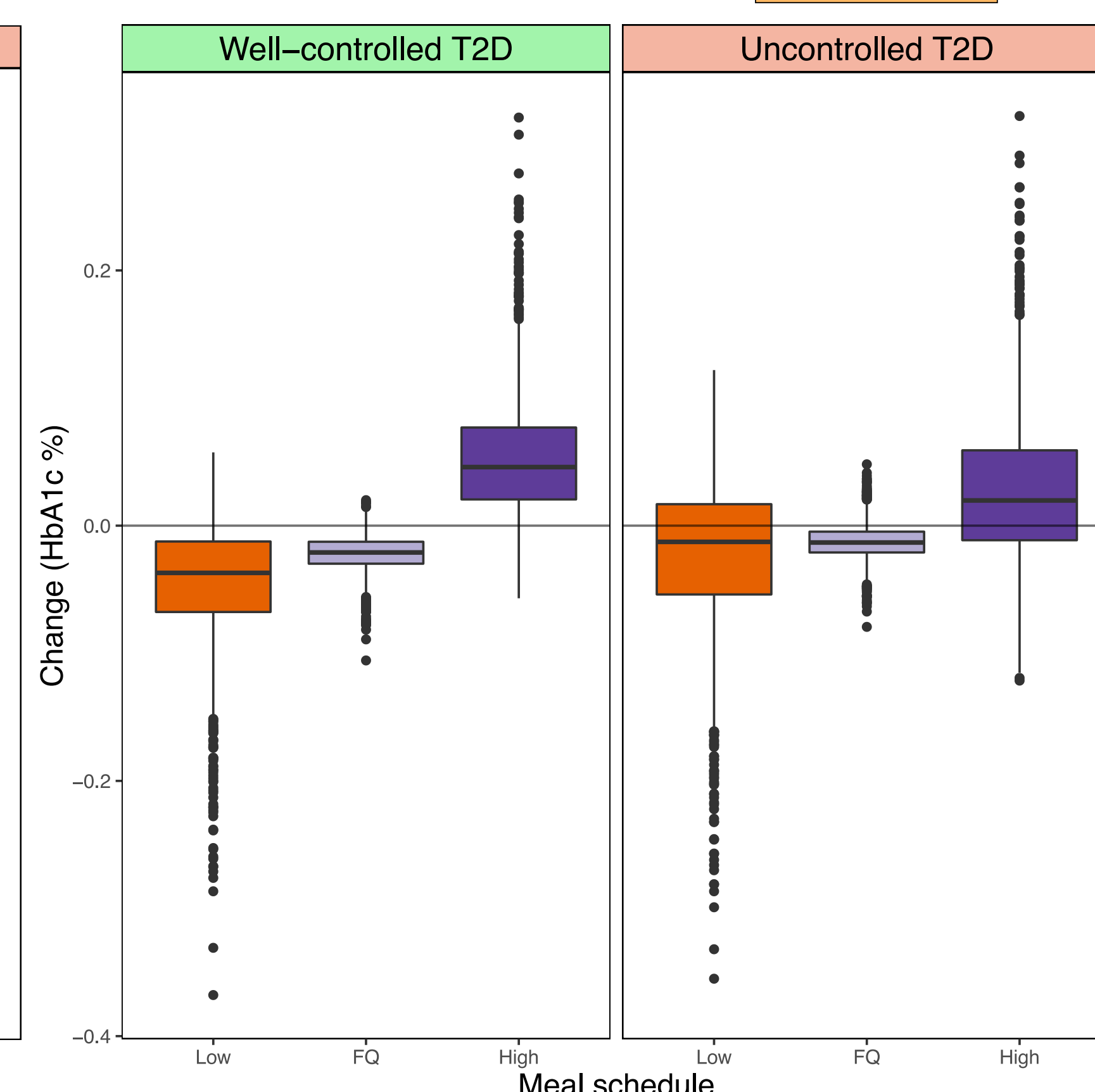
3 Results

Predicted average HbA1c was 5.6% and 7.8% for well-controlled and uncontrolled patients following the Medium carbohydrate intake. For well-controlled patients, the mean difference relative to Medium was -0.04% (HbA1c units) for Low, -0.02% for FQ and +0.05% for High. For uncontrolled patients it was -0.01% for Low, -0.01% for FQ and +0.02% for High. Suppressed glucose production for well-controlled T2D makes simulations realistic. The amount of profiles with MPG<FPG following the medium meal regimen is shown in a separate table.

Predicted HbA1c by carbohydrate intake and population



HbA1c relative to medium



References



Jauslin PM et al. J Clin Pharmacol. 2007.
Lledó-García R et al. J Pharmacokinet Pharmacodyn. 2013.

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