Prediction Validation of Two Glycaemic Control Models in Critical Care

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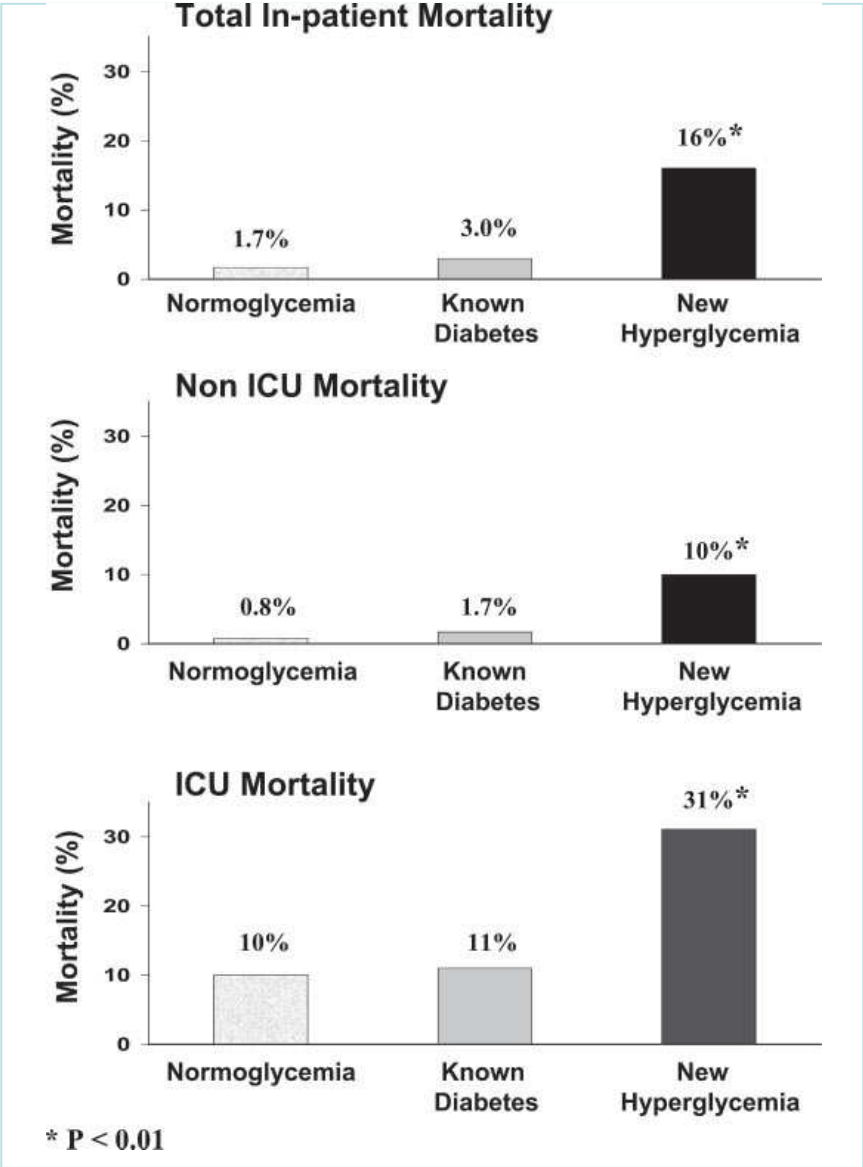
Hyperglycaemia in the ICU

- Dysfunctional glucose regulatory mechanisms, due to stress
- Prevalent in critical care (10-65%) [Krinsley, 2003; Umpierrez 2003]
- A marker of severity of illness
- Associated with increased:
  - **Mortality**
  - Sepsis
  - Myocardial infarction
  - Polyneuropathy
  - Multiple-organ failure

- Treatment recommendations vary

Hyperglycaemia in the ICU



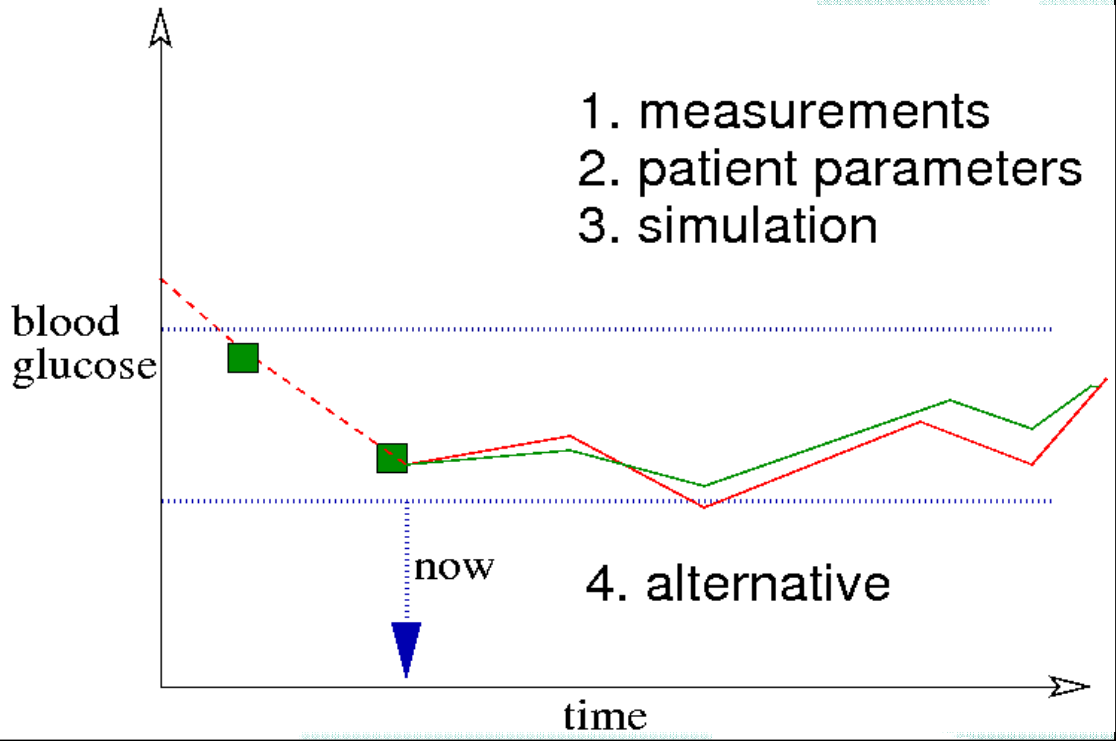
- Treatment:
  - insulin
  - reduction in total glucose uptake [Patino et. al., 1999]
- Treatment recommendations vary

(medical records of
2030 consecutive adult patients)

[Umpierrez, 2002]

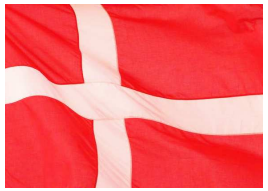
Model-based blood glucose control

- Predictive control to:
  - Simulate outcomes of therapeutic interventions
  - Help on scheduling of blood glucose measurements
  - Give advice on insulin and/or nutrition
- Aim
  - Ensure patient safety
  - Facilitate treatment
  - Reduce clinical burden



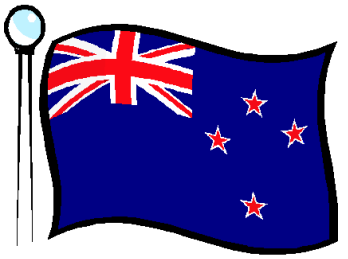
The models

GlucoSafe model



- Aalborg, DK
- Composite physiological model
- Based on work by Van Cauter et.al. (1992), Arleth et.al.(2000), Lotz et. al.(2005)
- Tested with retrospective patient data
- Clinical testing in preparation

CC model

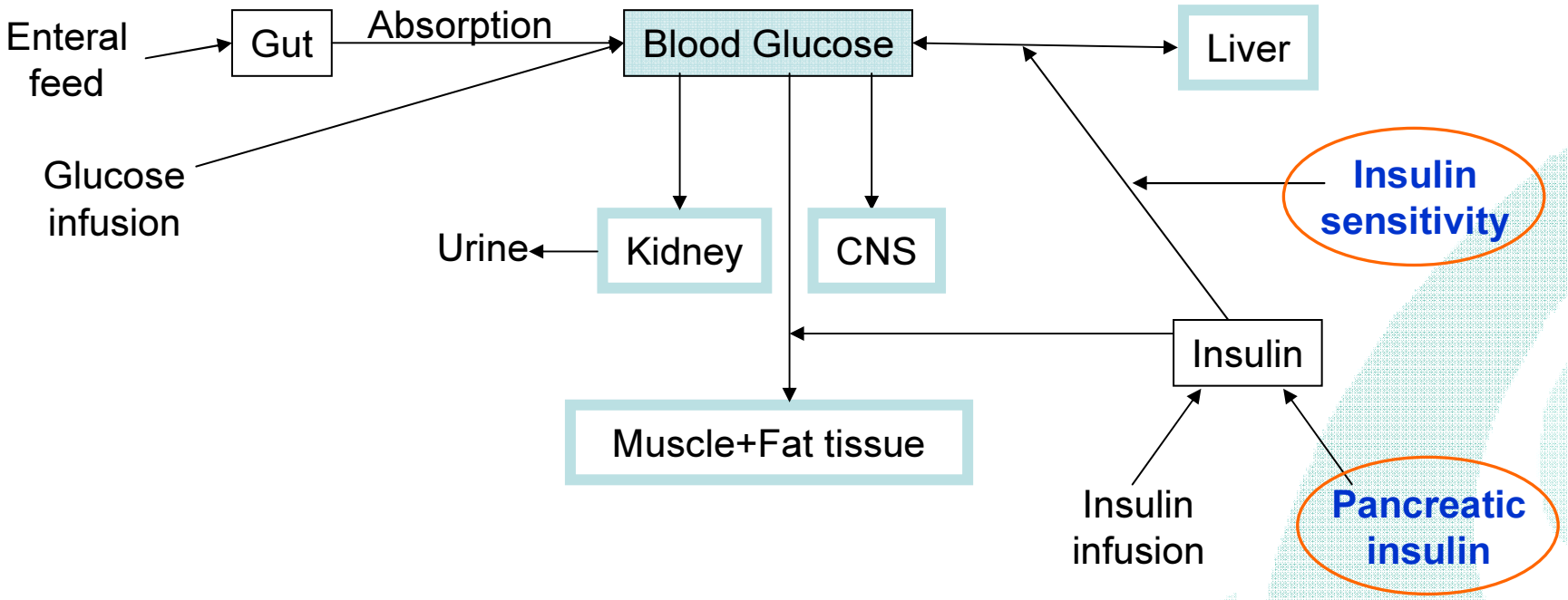


- Christchurch, NZ
- Clinically validated (SPRINT + several trials)
- Good glycaemic control in 400+ general ICU patients:
  - 54% measurements in the range 4.4-6.1 mmol/l
  - 0.02% < 2.2 mmol/l (2% by patient)
  - 35% reduction in hospital mortality (P=0.02)

[Chase, 2008]

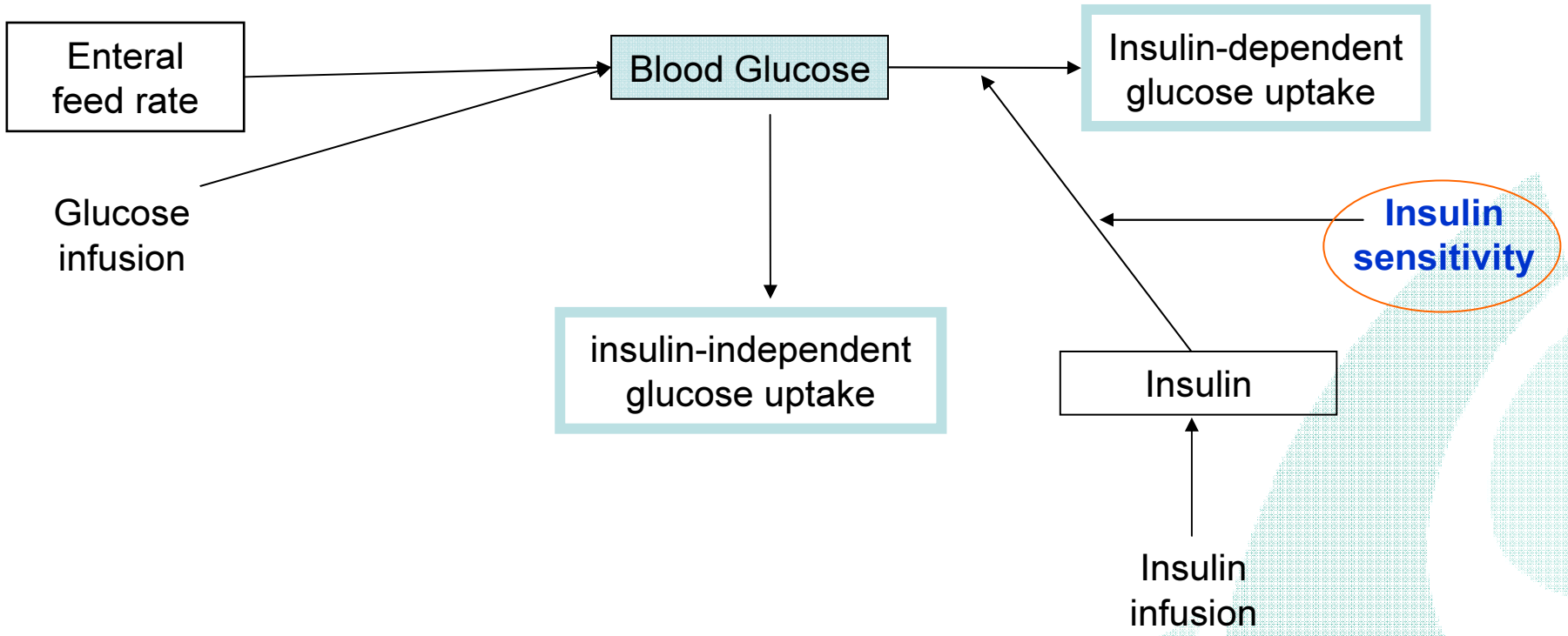
This study validates GlucoSafe using clinical data and in comparison to the CC model

The GlucoSafe model



- Patient specific parameters:
  insulin sensitivity
  +
  pancreatic insulin production

The CC model (SPRINT protocol)

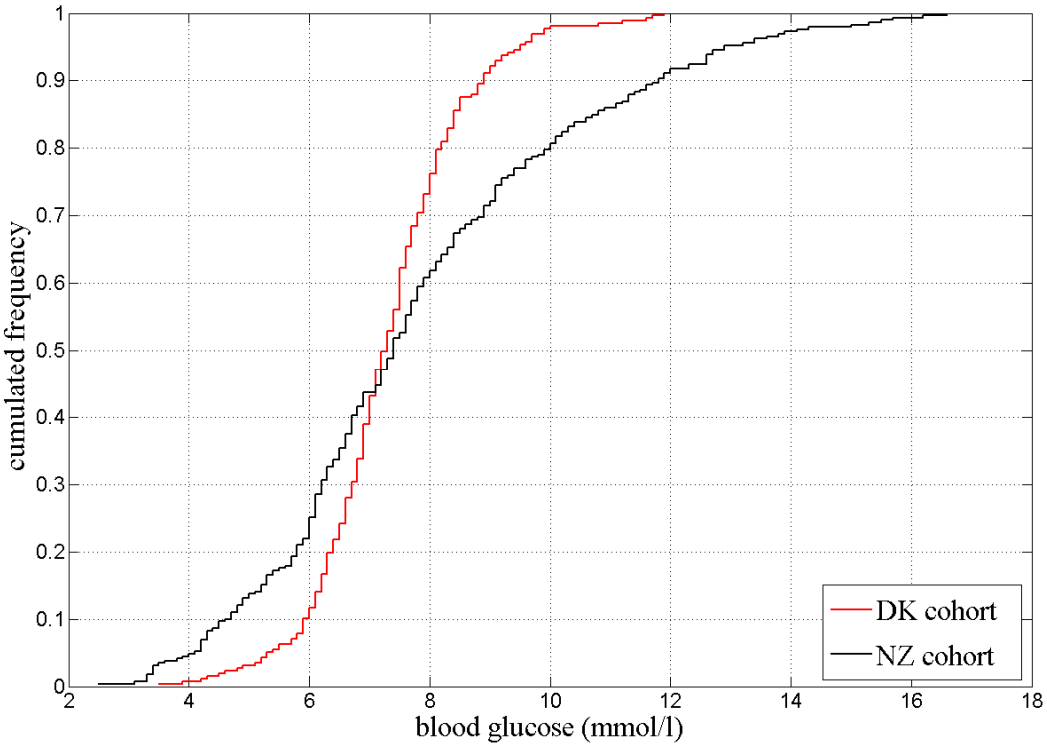


- Patient specific parameter: insulin sensitivity
- pancreatic insulin production assumed largely suppressed

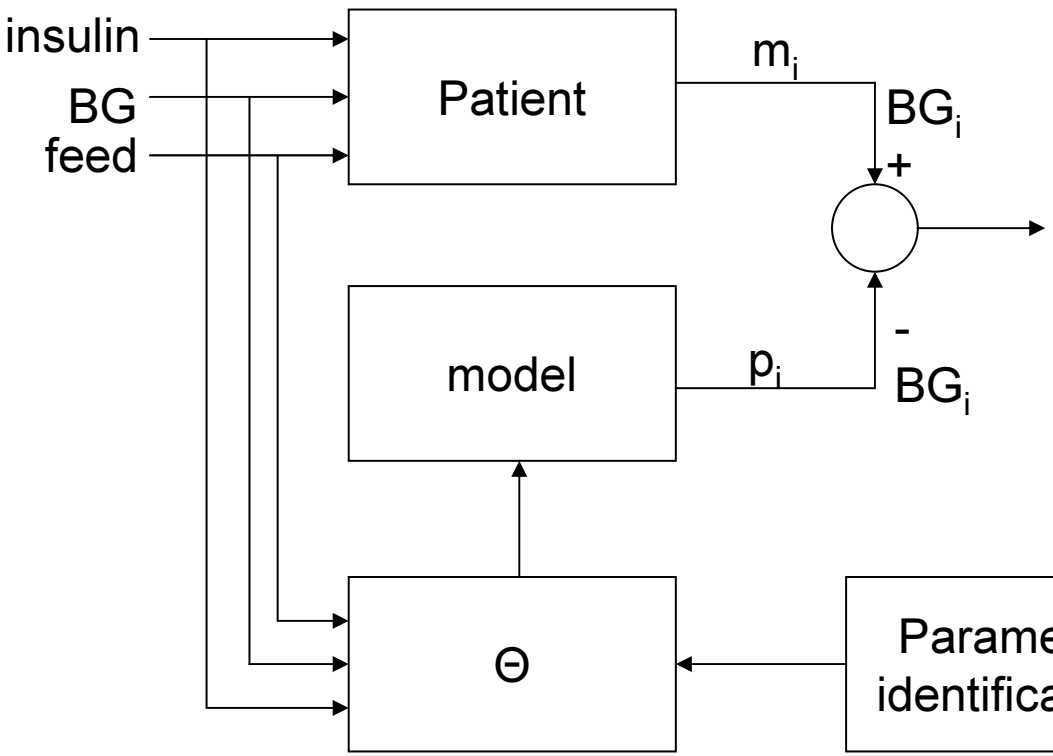
[Wong et al, 2006, Chase et al, 2004, Hann et al, 2005 – a work in progress...]

Patient data

- Retrospective data from 11 hyperglycaemic patients
  - 5 **trauma ICU** patients (Aalborg, ”DK” cohort)
  - 6 **medical ICU** patients (Christchurch, ”NZ” cohort pre-SPRINT)
  - DK less critically ill than NZ
  - Effectively 2 different cohorts
- Mean sampling interval:
  - DK: 221 min
  - NZ: 154 min
- Mean % (4-7 mmol/l):
  - DK: 41 %
  - NZ: 38%
- 4 diabetic patients
  - 2 type 2
  - 2 type 1



Model prediction algorithm



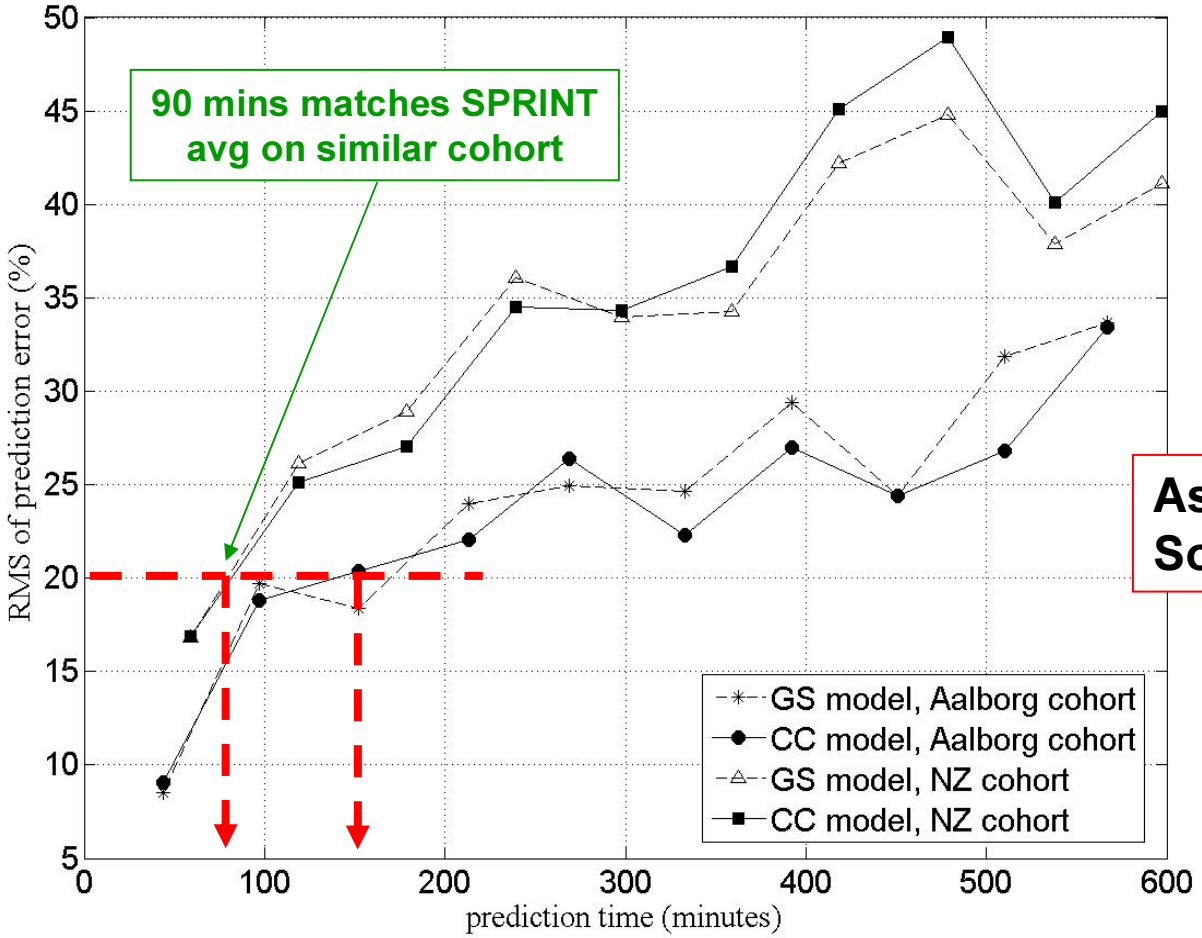
Prediction error

$e_i=(p_i - m_i)/ m_i$

for any measurement within the next 10 hours

- Prediction errors ”ordered” by hourly prediction interval
- Root mean square (RMS) calculated for each interval

RMS % error prediction



As error grows over time
So does need to intervene

RMS Prediction Error Summary

- Median errors over all time periods can vary significantly by patient
  - -5.4% → 12.2% for GS
  - -16.8 → 9.7% for CC
  - GS tends to overpredict with predominantly positive errors
  - CC more even with some larger outliers extending range.

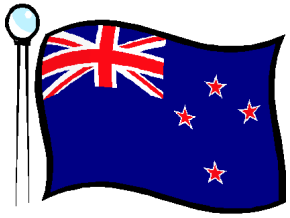
- Prediction errors are felt to be a better predictor of clinical utility than fitting errors as they represent or illustrate the model as it would be used

Conclusions

- **GlucoSafe is expected to be a safe and effective model for glycaemic control in intensive care**
- **Prediction accuracy and time to act depends on patient cohort (level of critical illness)**
- **The Future: advice, customization of models to cohort, influence of enteral glucose absorption, pancreatic secretion under insulin infusion…**

…

Thank you for your attention



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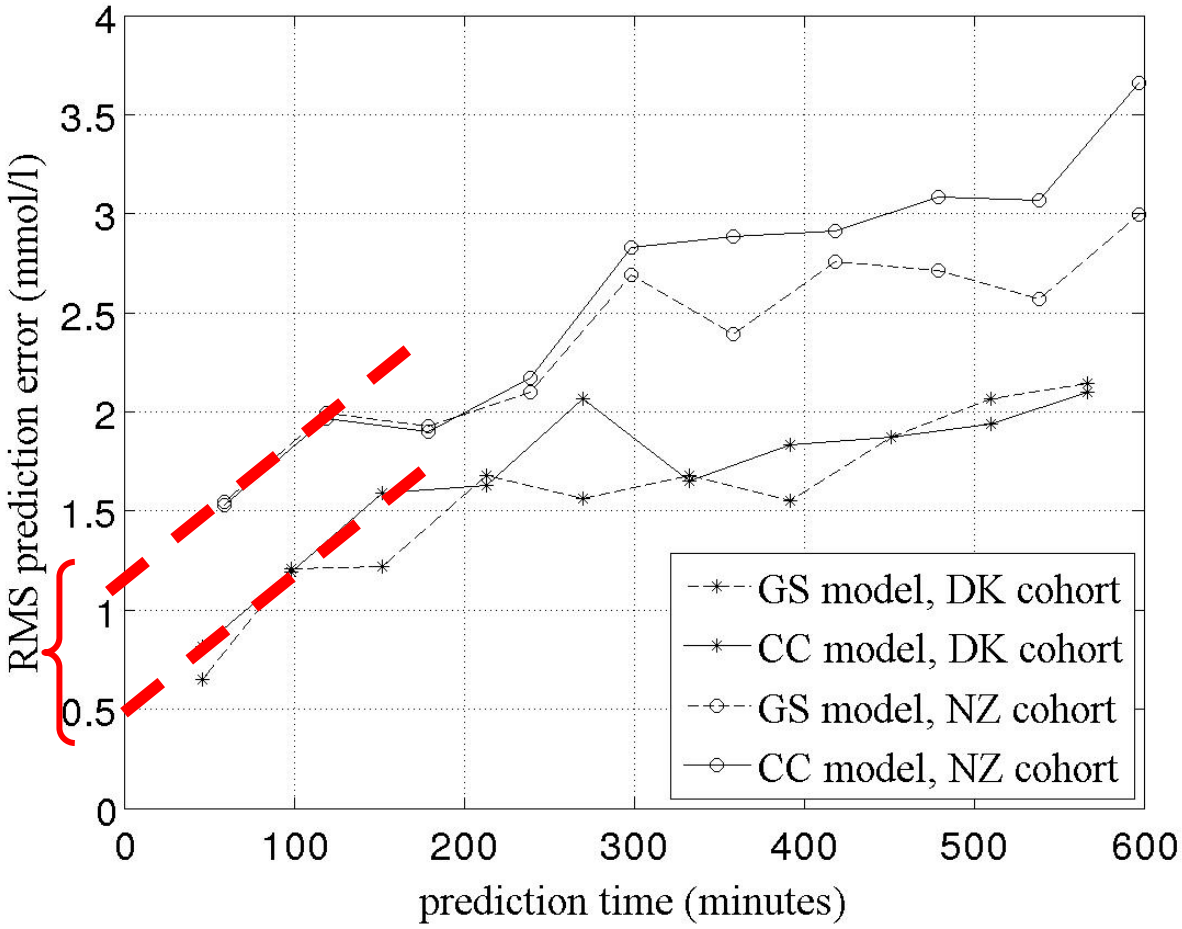
CHRISTCHURCH NEW ZEALAND

MMOS

RMS mmol/L Prediction Error

~1.41*Meas. Error
At intercept



When to measure as a patient or cohort specific metric

- **User interface to support clinical control based on RMS errors**