Prediction Validation of Two Glycaemic Control Models in Critical Care

Ulrike Pielmeier, J. Geoffrey Chase, Steen Andreassen, Birgitte Steenfeldt Nielsen, Pernille Haure, Geoffrey M. Shaw
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)

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

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 errors "ordered" by hourly prediction interval
Root mean square (RMS) calculated for each interval
RMS % error prediction

As error grows over time, so does the need to intervene. 90 mins matches SPRINT avg on similar cohort.
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

MCBMS 2009
12.08.2009 - 14.08.2009
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**