Safe and Effective Glycaemic Control for Minimal Workload in Critically Ill Patients : Virtual trials analysis on performance and safety

Marie Seret*, V. Uyttendaele*, T. Desaive*, and J. G. Chase**

*GIGA – In silico Medicine, University of Liège, Belgium
**Department of Mechanical Engineering, University of Canterbury, Christchurch, New Zealand

LIÈGE université

UC UNIVERSITY OF CANTERBURY
Te Whare Wānanga o Waitaha

Glycaemic control (GC) in intensive care units (ICU)

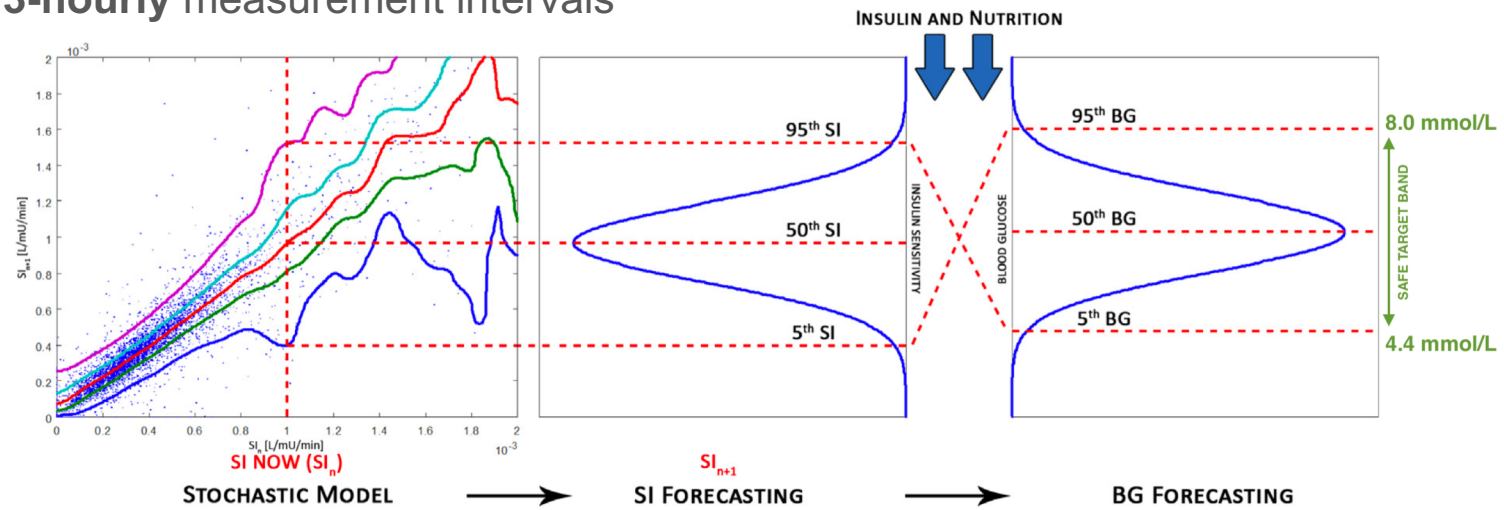
In the ICU (30-50% of patients)

Glycaemic control (GC)

- Decreases mortality and improves outcomes
- Through protocols **modulating insulin**
- **BUT** often fails to account for inter- and intra-patient variability

Stochastic TARgeted (STAR) GC framework

- **Model-based** protocol accounting for inter- and intra-patient variability
- Insulin **AND** nutrition dosing
- **Stochastic and physiological model**
- Key parameter : **insulin sensitivity (SI)**
- **1 to 3-hourly** measurement intervals



[Uyttendaele, V., et al., IFAC. PapersOnLine (2021)]

Stochastic TARgeted (STAR) GC framework

STAR performances and strengths

- Safe and effective clinical control
  - High time in the target band (>80%)
  - High nutrition delivery (>90%GF)
  - Low risk of hyper- and hypoglycaemia (<15% and <5% respectively)
- Accounts for inter- **AND** intra-patient variability

	STAR	***STAR-IO***	***SP***
# Patients	10	12	20
Total hours	455	674	5006
Workload (meas/day)	12	16	7
Median BG (mg/dL)	6.5 [6.1, 7.2]	6.7 [5.9, 7.6]	7.7 [6.5, 8.9]
Median ΔBG (mg/dL)	0.3 [0.1, 0.5]	0.4 [0.2, 0.8]	N/A
Per-patient median insulin (U/h)	3.0 [2.0, 4.0]	3.5 [2.0, 4.5]	2.5 [2.0, 3.0]
Per-patient median dextrose (g/h)	7.3 [5.0, 8.4]	7.8 [6.5, 8.8]	9.8 [8.6, 11.5]
Per-patient median dextrose (%GF)	90 [61, 100]	90 [55, 130]	N/A
% BG in 4.4-6.5 mmol/L	47	42	N/A
% BG in 4.4-8.0 mmol/L	88	78	55
% BG in 5.6-8.3 mmol/L	84	67	54
% BG in 8.0-10.0 mmol/L	9	11	31
% BG > 10.0 mmol/L	2	10	12
% BG < 4.4 mmol/L	1	1	1
% BG < 4.0 mmol/L	1	0.5	0.5
% BG < 2.2 mmol/L	0	0	0
# Patients < 2.2 mmol/L	0	0	0
% intervention unchanged	98	90	79

[Uyttendaele, V., et al., IFAC. PapersOnLine (2020)]

Workload burden impairing STAR clinical adoption

- Excessive workload pointed out in a clinical trial (low nurse per patient ratio)
- Frequent measurements (every 2 hours)
- Low compliance to protocol impacting clinical outcomes

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Extension of the measurement interval from 1 to 3-hourly to 1 to 6-hourly

Virtual trials on STAR Extension

- Prior to implementation → Save clinical time and costs
- Prevent avoidable risks on real patients
- Virtual patient = unique insulin sensitivity profile
- Blood glucose outcome simulation based on longest measurement interval

	STAR Extension
Number of virtual patients	681
Control hours (h)	59439

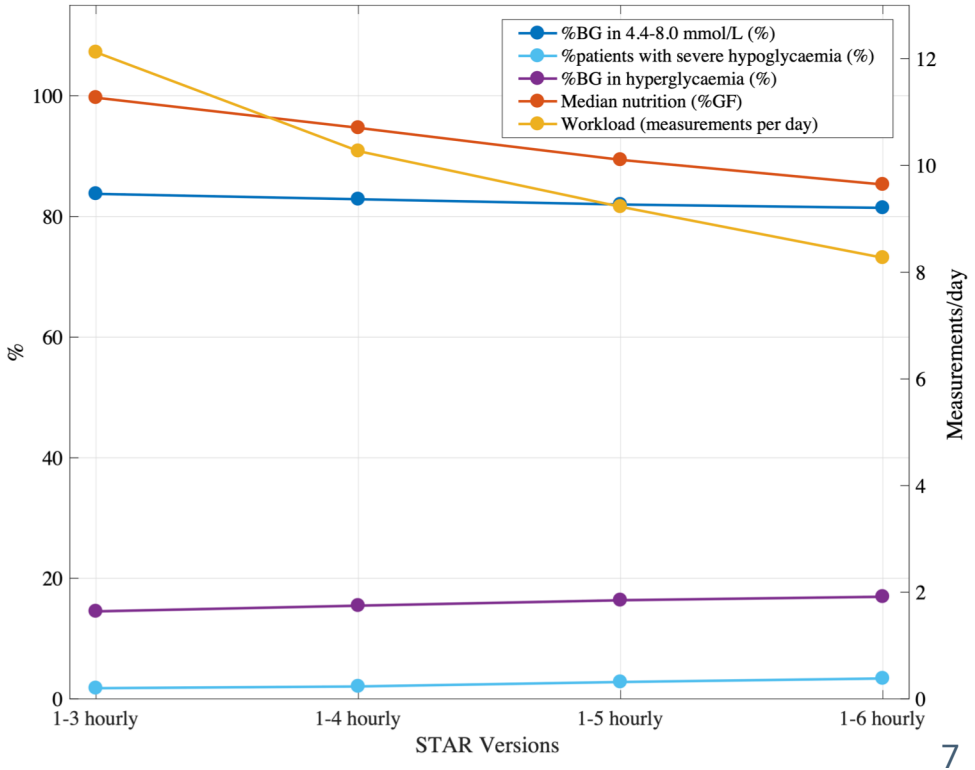
Virtual trials on STAR Extension : Results

Workload

- Reduced workload (from 12 to 8 measurements per day)

Performance and safety

- High percentage of BG in target band (>80%)
- Low incidence of hyper- and hypoglycaemia (<20% and <5%)
- High nutrition (> 85%GF)

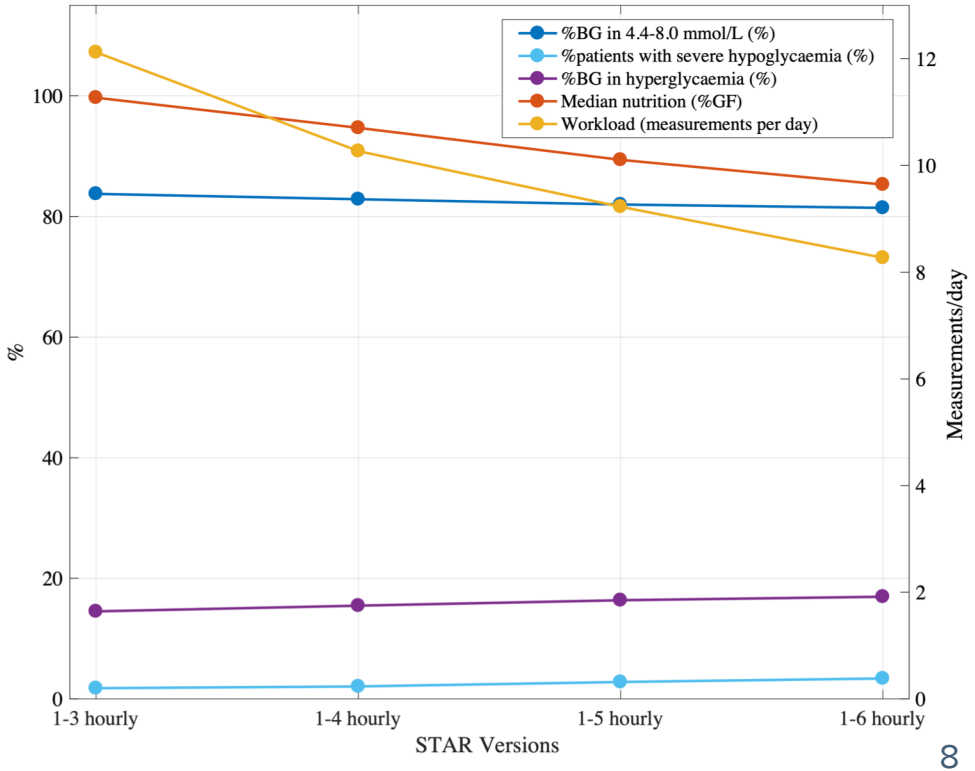


Virtual trials on STAR Extension : Results

Risks

- Reduced nutrition (from 100 [85 - 100] to 85 [70 - 95] % GF)
- Increased risk of severe hypoglycaemia (from 12 to 23 patients)

Trade-off between reduced workload and risks



Virtual trials on STAR Extension : Discussions

Reduced workload does not come without trade-offs…

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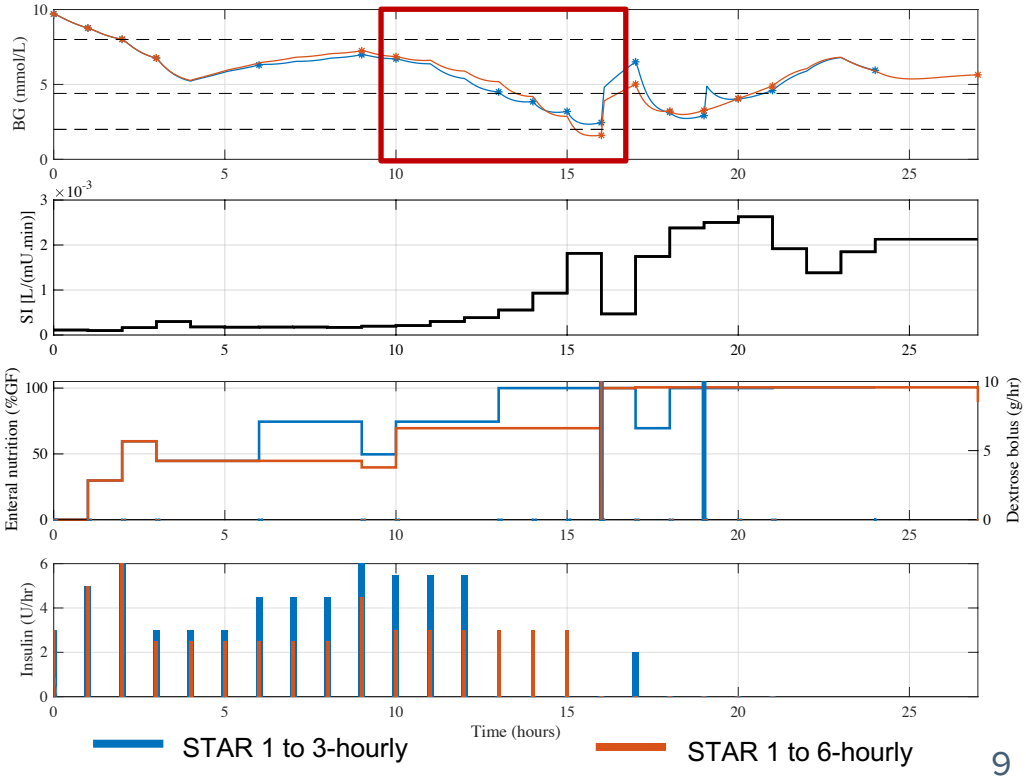

Virtual trials on STAR Extension : Discussions

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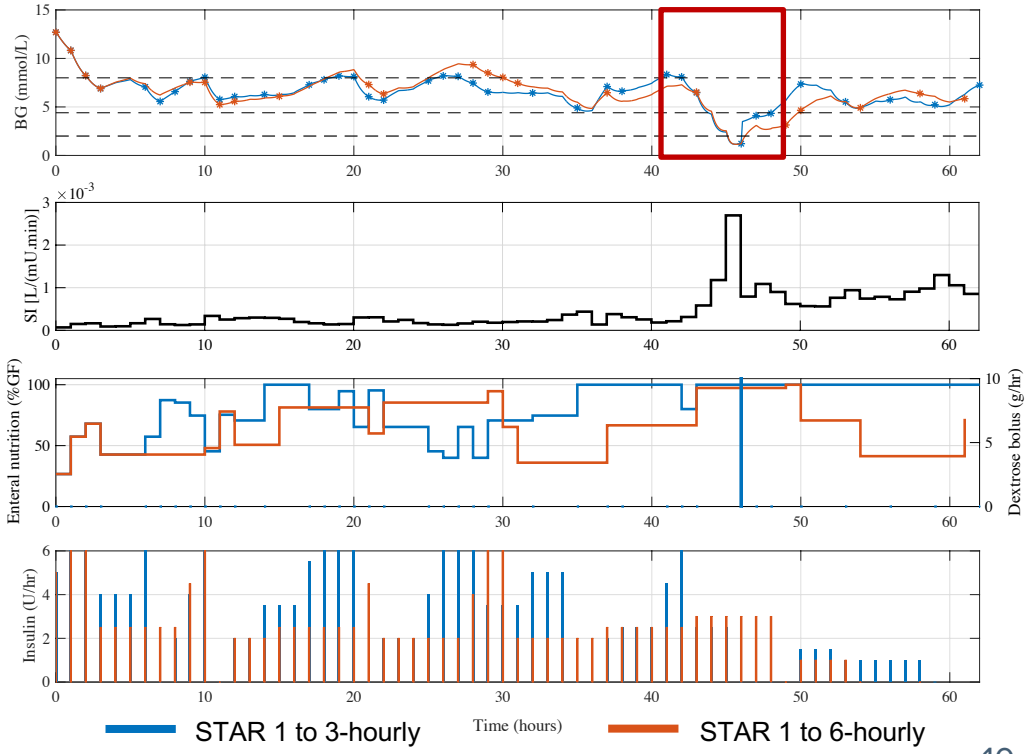
- Longer intervals vs. Reduced nutrition delivery rates
- Longer intervals vs. Higher incidence of hypoglycaemia
- Longer intervals vs. Unseen hypoglycaemic events



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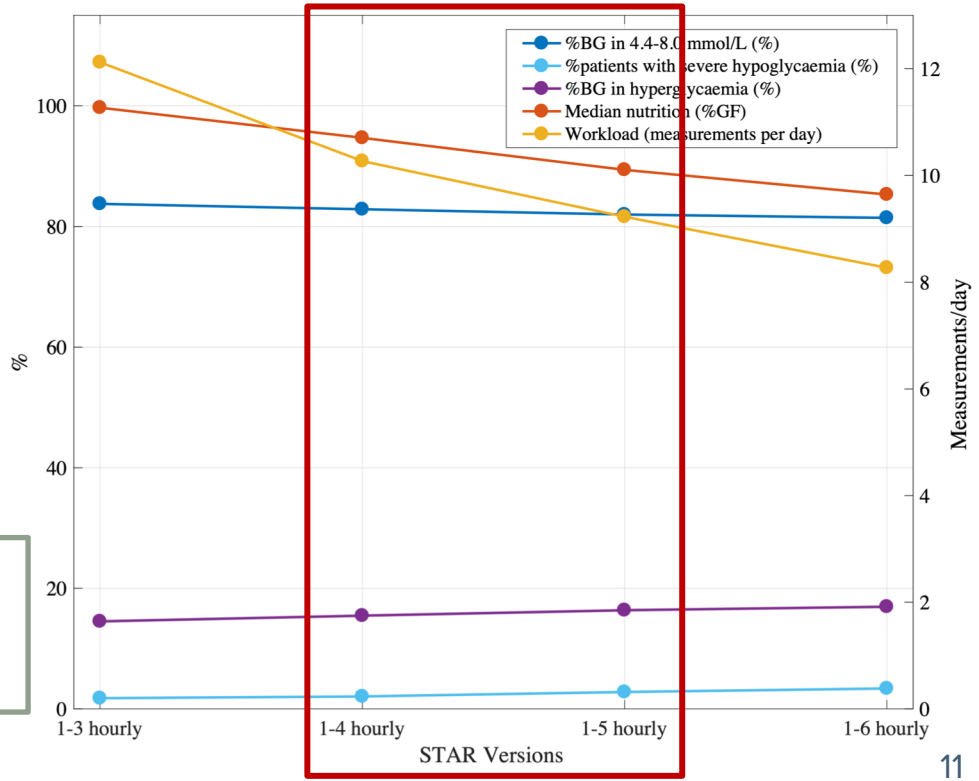
→ Limit the measurement interval **to 1 to 4- or 1 to 5-hourly**, better matching current treatment standards



Limitations

- Virtual trials in **ideal conditions** considering full compliance
- **No external factors** affecting nurse judgement

→ **Results reflecting ideal conditions** compared to real clinical implementation

Conclusions

STAR extension to 1 to 6-hourly measurement intervals allowed :

- Robust control with high safety and performance
- Reduced workload
- Higher risk on safety and reduced nutrition delivery
- Intermediate measurement intervals to mitigate the risks

→ **Clinical trial** to validate the extension on STAR

Acknowledgments and Questions

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