How Much Do We Gain From Greater Personalisation?

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**Background**

Stress-hyperglycaemia is a common complication in the ICU. Glycaemic control (GC) can improve outcomes, but has been difficult to achieve safely, increasing hypoglycaemic risk.

STAR is model-based GC with proven safety and performance. It uses a cohort-based 2D stochastic model of patient-specific insulin sensitivity (SI) to predict future SI distributions to dose insulin and nutrition based on specified risk of hypoglycaemia (Figure 1).

**Objectives**

- Metabolic (SI) variability is makes GC hard to achieve safely.
  - A new 3D stochastic model is constructed to improve future SI forecasting based on current and previous SI values.

- What is the impact of greater personalisation?
  - Virtual trial on validated patients assesses performance, safety and workload.

**Methods**

Metabolic data from 3 clinical ICU cohorts (819 episodes and 68629 hours of treatment) are used in this study (Table 1).

**Results**

**Model comparison:**

- The 2D model is over-conservative for 74% of hours mainly where SI is within an absolute 25% change (Figure 3).
- Indicates patients are stable more than 74% of the time.
- Stable patients tend to remain stable.
- The 90% CI width in this region is reduced by 22% (Figure 2).
- More aggressive dosing allowed for these patients.

**Virtual trial simulation results:** Table 2 and Figure 4

- Median BG is lower using the 3D model (6.0 vs. 6.3 mmol/L) for similar high performance (90% in target band). However, tighter for the 3D model (65% vs. 58% in 4.4-6.5 mmol/L).
- Slightly higher incidence of moderate hypoglycaemia for the 3D model (3% vs. 2% < 4.4 mmol/L). No severe hypoglycaemia.
- Higher nutrition rates achieved with the 3D model (99 vs. 92 %GF).

**Conclusions**

- The new, more personalised 3D stochastic model provides moderately improved performance and similar safety for similar workload.
- The 3D model better characterises patient-specific response to insulin, allowing more optimal dosing while ensuring safety.
- These results justify potential clinical implementation to assess its impact on clinical outcomes.

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**Table 1:** Summary of patient demographics for three cohorts. Results are given as median [IQR] where relevant.

<table>
<thead>
<tr>
<th># episodes</th>
<th># hours</th>
<th>% male</th>
<th>APACHE II</th>
<th>LOD-ICU (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPRINT Chirstchurch</td>
<td>462</td>
<td>100</td>
<td>19</td>
<td>8.2 [7.7,13.0]</td>
</tr>
<tr>
<td>STAR Chirstchurch</td>
<td>330</td>
<td>13</td>
<td>15</td>
<td>5.7 [5.3,13.4]</td>
</tr>
<tr>
<td>STAR Gyde</td>
<td>65</td>
<td>4</td>
<td>16</td>
<td>14.0 [8.0,20.3]</td>
</tr>
</tbody>
</table>

**Table 2:** Simulation results of STAR using the 2D and 3D stochastic model. Results reported as median [IQR] where appropriate.

<table>
<thead>
<tr>
<th># patients</th>
<th>Total hours of control</th>
<th>Workload (mean/days)</th>
<th>Median BG (mmol/L)</th>
<th>Insulin rate (U/L)</th>
<th>Nutrition (dextrose) rate (mg/kg/h)</th>
<th>%BG &lt; 4.4 mmol/L (80 mg/dL)</th>
<th>%BG &gt; 10.0 mmol/L (180 mg/dL)</th>
<th>%BG &lt; 2.2 mmol/L (72 mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>518</td>
<td>60246</td>
<td>11.6</td>
<td>6.3 [5.7,6.9]</td>
<td>2.5 [1.5,4.0]</td>
<td>92 [70,100]</td>
<td>50</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>538</td>
<td>60267</td>
<td>11.6</td>
<td>6.0 [5.5,6.7]</td>
<td>3.0 [1.5,5.0]</td>
<td>99 [70,100]</td>
<td>65</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

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**Figure 1:** From insulin sensitivity (SI) is forecast for current SI. The distribution of future SIs is used to predict likely BG outcomes for a given insulin nutrition treatment intervention.

**Figure 2:** Comparison between the 3D model (green) and the original 2D model (green) for the 25th and 95th percentiles.

**Figure 3:** Ratio of the 25th-95th percentile range between 2D and 3D models. Prediction range is reduced mainly when the absolute hours to hour SI variation is within 25%.

**Figure 4:** BG level, insulin rate, and glucose rate charts comparison.