**Accurate Glycaemic Control using a Stochastic TARgeted (STAR) Framework**

L.M. Fisk, A.J. Le Compte, J.G. Chase, G.M. Shaw

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**INTRODUCTION**

Background: Accurate glycaemic control (AGC) has proven difficult without excessive hypoglycemia risk. Stochastic TARgeted (STAR) glycemic control forecasts changes in insulin sensitivity to calculate a range of glycemic outcomes for an insulin intervention, creating a risk framework to increase safety and performance.

Objective: Create a new protocol with improved safety from prior to clinical pilot trials.

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**RESULTS**

Severe hypoglycemia was reduced from 14 patients (clinical SPRINT data) to 6 with a simultaneous 23% workload reduction from 26,646 BG measurements to 20,050. Moderate nutrition was increased overall by 21% in median amount.

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**METHODS**

Clinically validated virtual trials on 371 virtual patients from the SPRINT AGC cohort were used to adapt the framework to Christchurch ICU. Model forecasts target control to a clinically specified glycemic range (80mg/dL to 145mg/dL). Measurement intervals of 2-3 hours were used when predicted 5th and/or 95th percentile BG were within target range.

Robustness to measurement error limit insulin increases to +2U/hour (max 6U/hour bolus and 3U/hr infusion) and nutrition changes to ±30% (between 30-100% of ACCP goal) per intervention.

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**PILOT CLINICAL TRIALS**

Clinical BG results over 10 pilot patients matched simulation results 93.4% of BG within 80-145mg/dL. Safety was maintained with 0.95% of BG < 72mg/dL and no severe hypoglycaemia events (BG < 40mg/dL). Median BG was 109 mg/dL [IQR: 101-121 mg/dL] versus simulated 111 mg/dL [IQR: 102-122 mg/dL], which matches very closely with the location and spread of BG in virtual trials.

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**CONCLUSIONS**

Safe, accurate glycaemic control that also reduces clinical effort is achieved using stochastic forecasting of potential patient variation. Initial pilot clinical trials matched simulation expectations and are ongoing.

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**STAR DEVELOPMENT**

Traditional insulin/nutrition combination approaches to glycemic regulation.

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**METHODS**

1. **Controller forecast schematic for BG**
   - Target glycaemic range (including ± tolerance on the lower bound)
   - BG forecasting capability to possible forecasts possible for treatment intervals enabled by treatment intervals.
   - BG with 0.95% of BG < 72mg/dL and no severe hypoglycaemia events (BG < 40mg/dL).
   - Median BG was 109 mg/dL [IQR: 101-121 mg/dL] versus simulated 111 mg/dL [IQR: 102-122 mg/dL], which matches very closely with the location and spread of BG in virtual trials.

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**TABLE 1**: STAR simulation results indicated significant improvements over SPRINT. Workload reductions result from permitting 3-hourly treatment intervals enabled by BG forecasting capability to manage safety from insulin/nutrition combinations without extra insulin administration rate increases over SPRINT for greater clinical acceptance and insulin usage was balanced to maintain current BG control performance.

<table>
<thead>
<tr>
<th>Workload</th>
<th>STAR</th>
<th>SPRINT</th>
</tr>
</thead>
<tbody>
<tr>
<td># BG measurements</td>
<td>20,050</td>
<td>26,646</td>
</tr>
<tr>
<td>Measures/day</td>
<td>12.0</td>
<td>16.1</td>
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</table>

<table>
<thead>
<tr>
<th>Control performance</th>
<th>STAR</th>
<th>SPRINT</th>
</tr>
</thead>
<tbody>
<tr>
<td>BG median [IQR] (mmol/L)</td>
<td>91.0</td>
<td>88.0</td>
</tr>
<tr>
<td>% BG within 80-145 mg/dL</td>
<td>99.0</td>
<td>100.0</td>
</tr>
<tr>
<td>% BG &gt; 180 mg/dL</td>
<td>1.7</td>
<td>2.0</td>
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</table>

<table>
<thead>
<tr>
<th>Safety</th>
<th>STAR</th>
<th>SPRINT</th>
</tr>
</thead>
<tbody>
<tr>
<td>% BG &gt; 72 mg/dL</td>
<td>0.97</td>
<td>2.89</td>
</tr>
<tr>
<td>% BG &gt; 40 mg/dL</td>
<td>0.02</td>
<td>0.04</td>
</tr>
<tr>
<td># patients &gt; 40 mg/dL</td>
<td>6</td>
<td>14</td>
</tr>
</tbody>
</table>

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