PERSONALIZING THE INTENSITY OF BLOOD PRESSURE CONTROL: Modeling the Heterogeneity of Risks and Benefits from the SPRINT Trial

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ABSTRACT

• In SPRINT (Systolic blood Pressure Intervention Trial), patients with hypertension and high cardiovascular risk treated with intensive blood pressure (BP) control (<120 mmHg) had fewer major adverse cardiovascular events (MACE) and deaths, but higher rates of treatment-related serious adverse events (SAE), than those randomized to standard BP control (<140 mmHg).
• However, the degree of benefit or harm for an individual patient likely varies due to heterogeneity in treatment effect.

BACKGROUND

• Using patient-level data from 9361 randomized patients in SPRINT, with median follow-up of 3.3 years, we developed models to predict risk for:
  - MACE or death (MI, non-MI ACS, stroke, all-cause death)
  - Treatment-related SAE (hypertension, syncope, injurious falls, AKI, electrolyte abnormalities, others)
• Models developed using logistic regression
  - Candidate variables selected a priori
  - Interaction terms between treatment and all candidate variables were added to assess heterogeneity
  - Model reduction with Harrell’s backward selection strategy
• Distribution of predicted absolute risks of both outcomes between the 2 treatment strategies (difference in predicted absolute risks of MACE or death and treatment-related SAE, respectively, for each SPRINT patient if treated with intensive and standard BP control) were plotted with histograms
• Validation
  - Internal with Bootstrap resampling
  - External in ACCORD trial (4741 Diabetics with hypertension—mean follow-up of 4.7 years)

RESULTS

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<tr>
<th>Table 1: Patient Table Characteristics</th>
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<tr>
<td>Mean (SD)</td>
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<td>Min-Max</td>
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<td>Median</td>
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<th>Table 2: Treatment-related SAE Model Characteristics</th>
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<tr>
<td>Mean predicted SAE rate: 2.2% ± 1.2%</td>
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<td>Slope = 0.93, R² = 88%</td>
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<td>Model c-statistic = 0.73, Optimism corrected c-statistic = 0.72</td>
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<td>Figure 1: MACE or Death Model</td>
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<td>Figure 3: Validation in ACCORD</td>
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<td>Figure 5: Potential Model Output at Point of Care</td>
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DISCUSSIONS

• Inability to consider potentially related but unmeasured/unavailable factors.
• Patients enrolled in clinical trials are generally healthier, more compliant with treatments, and better monitored for safety than patients in the real world.
• While we did find evidence of some treatment interactions suggesting heterogeneity in treatment effect, there might be other interactions which we did not have the power to detect.

LIMITATIONS

• These models enable the results of a landmark clinical trial to be used in routine patient care to tailor the treatment approach.
• Comparable performance of our models in a cohort of patients with vastly different baseline characteristics strongly supports their external generalizability.
• Further studies are needed to understand the clinical impact of using these models in care and to define performance in other populations including low-risk, younger patients with HTN.

CONCLUSION

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Using these Risk Prediction Models

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