“Is another validation of a clinical prediction rule necessary?”

A demonstration of research wastes using recursive cumulative meta-analyses

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Acknowledgement

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• Dr. Rafael Perera
• Dr. Richard Stevens
Background: Clinical prediction rule development

1. Derivation
2. Validation
3. Impact study

- Of 363 cardiovascular disease risk prediction models, 231 (64%) never had an external validation.

- A few clinical prediction rules have been validated many times.
  
  Framingham Wilson model: 89
  Framingham Anderson model: 73
  SCORE risk chart: 63

How many is enough?

• Problem: most clinical prediction rules never get externally validated but a few prediction rules get validated repeatedly.

• Aim: to demonstrate repeating many validations may be unnecessary and potentially wasteful.

More is not always better!
Methods: Recursive cumulative meta-analysis (Ioannidis et al., 1999)

• Recalculates the results of a cumulative meta-analysis every time a new or updated piece of information becomes available.

• Each step represents the results of a cumulative meta-analysis of the most complete data available up to this specific step.

• Can show whether the trajectory of the treatment effect is converging to a stable estimate over information steps.

Example: Recursive cumulative meta-analysis (Ioannidis et al., 1999)

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Method: Recursive cumulative meta-analysis

- Material: validation studies of PSI (Pneumonia Severity Index) and Alvarado score.

- Performance measure: Predicted/Observed outcome ratio.

- Stability was defined as a sustained less than 5% fluctuation of current to previous cumulative predictive performance ratio.
• 30 validation studies of PSI (26563 participants) were analyzed (Chalmers et al., 2010).

• When the 11\textsuperscript{th} validation study was added to the recursive cumulative meta-analysis, the trajectory of predictive performance became stable.

• 19 (63.3\%) validation studies and the data from 17443 (65.7\%) participants added little value.
• 34 studies validating Alvarado Score (9778 participants) were included.

• The trajectory of predictive performance became stable when the data from the 7th validation study was added to the recursive cumulative meta-analysis.

• 27 (79%) validation studies and data from 8066 (82.5%) participants included in these validation had little value.
Conclusion: “Is another validation of a clinical prediction rule necessary?”

- Substantial degree of research wastes were demonstrated in the validation of PSI and Alvarado Score.

- Before a validation of a clinical prediction rule is carried out, researchers should carefully consider whether it is truly necessary.

- Limitation: used 5% fluctuation of trajectory as threshold for stability.
Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD): The TRIPOD Statement
Gary S. Collins, PhD; Johannes B. Reitsma, MD, PhD; Douglas G. Altman, DSc; and Karel G.M. Moons, PhD

Table. Checklist of Items to Include When Reporting a Study Developing or Validating a Multivariable Prediction Model for Diagnosis or Prognosis*

<table>
<thead>
<tr>
<th>Section/Topic</th>
<th>Item</th>
<th>Development or Validation?</th>
<th>Checklist Item</th>
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</thead>
<tbody>
<tr>
<td>Title and abstract</td>
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<tr>
<td>Title</td>
<td>1</td>
<td>D/V</td>
<td>Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.</td>
</tr>
<tr>
<td>Abstract</td>
<td>2</td>
<td>D/V</td>
<td>Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.</td>
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<tr>
<td>Introduction</td>
<td></td>
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<tr>
<td>Background and objectives</td>
<td>3a</td>
<td>D/V</td>
<td>Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.</td>
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<td></td>
<td>3b</td>
<td>D/V</td>
<td>Specify the objectives, including whether the study describes the development or validation of the model, or both.</td>
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