

Clinical Prediction Models for Patients with Acute Coronary Syndromes: Results from Independent External Validations

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Background: It is increasingly recognized that clinical prediction models (CPMs) often do not perform as expected when they are tested on new databases. Independent external validations of CPMs are recommended but often not performed.

Aims: Here we conduct independent external validations of acute coronary syndrome (ACS) CPMs.

Methods: A systematic review identified CPMs predicting outcomes for patients with ACS. Independent external validations were performed by evaluating model performance using individual patient data from 5 large clinical trials. CPM performance with and without various recalibration techniques was evaluated with a focus on CPM discrimination (c-statistic, % relative change in c-statistic) as well as calibration (Harrell's E_{avg} , E_{90} , net benefit).

Results: Of 276 ACS CPMs screened, 23 (8.3%) were compatible with the trials and 28 clinically appropriate external validations were performed. The median c statistic of the CPMs in the derivation cohorts was 0.76 (IQR, 0.74-0.78). The median c-statistic in these external validations was 0.70 (0.66-0.71) reflecting a 24% decrement in discrimination. Most of this decrement was due to narrower case-mix in the validation cohorts compared to derivation cohorts, as the median model based c-statistic was 0.71 (0.67-0.75). The median calibration slope in external validations was 0.82 (0.72- 0.95) and the median E_{avg} (standardized by the outcome rate) was 0.4 (0.3-0.8). Decision curve analysis indicates that most models had a high risk of causing net harm when not recalibrated, particularly if the decision threshold is not near the overall outcome rate.

Conclusion: For ACS CPMs, independent external validations generally demonstrate that discrimination is relatively preserved once case mix is taken into account. Since calibration is often poor, applying 'off-the-shelf' CPMs often risks net harm unless models are recalibrated.

Validation	Threshold	N	Compared to default strategy		
			% Above	% Neutral*	% Below
Original model	Prev./2	28	14.3	67.9	17.9
	Prevalence	28	92.9	7.1	0.0
	Prev.*2	28	42.9	35.7	21.4
Updated intercept	Prev./2	28	21.4	75.0	3.6
	Prevalence	28	100.0	0.0	0.0
	Prev.*2	28	57.1	35.7	7.1
Updated intercept and slope	Prev./2	28	25.0	75.0	0.0
	Prevalence	28	100.0	0.0	0.0
	Prev.*2	28	64.3	32.1	3.6
Re-estimated	Prev./2	28	64.3	35.7	0.0
	Prevalence	28	100.0	0.0	0.0
	Prev.*2	28	89.3	10.7	0.0

Table: Effects of updating on net benefit. Threshold is the decision threshold and is represented in relation to the outcome prevalence. N is number of independent external validations. % Above refers to net benefit above the default strategy, % neutral refers to net benefit not different from the default strategy and % Below refers to net benefit less than the default strategy (net harm).

Keywords

Acute Coronary Syndrome, Clinical Prediction Models, External Validation