WHAT PREDICTS INDEPENDENT EXTERNAL VALIDATION OF CARDIOVASCULAR RISK PREDICTION RULES?

COX PROPORTIONAL HAZARDS REGRESSION ANALYSES

Introduction

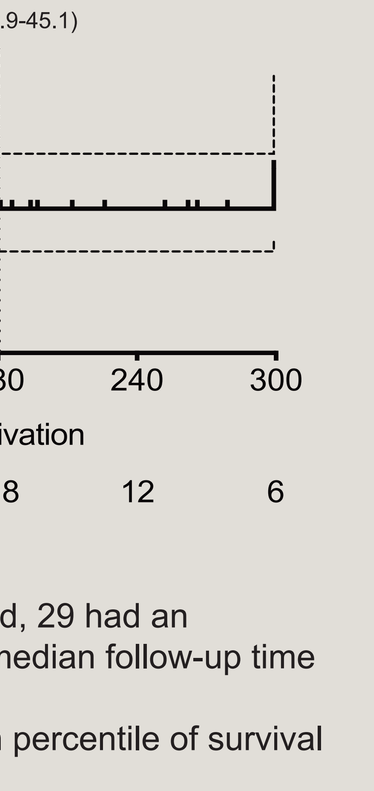
Clinical prediction rules (CPRs) should be externally validated by independent researchers unrelated to their derivations. Although there are many cardiovascular risk CPRs, most have not been externally validated. It is not known why some CPRs are externally validated by independent researchers and others are not.

Methods

We analyzed cardiovascular risk CPRs included in a systematic review. Independent external validations were identified by forward citation searches of derivation studies. Time between the publication of a cardiovascular CPR and the first independent external validation was calculated. We assessed Kaplan-Meier estimates of the probability to have an independent external validation. Using Cox regression, we explored whether 12 characteristics of derivation, reporting, and publication of cardiovascular risk CPRs are associated with time to the first independent external validation.

Independent External Validation

1. No author overlapped with the authors of the derivation study.
2. No author had prior co-authorship with the authors of the derivation study.
3. No other potential conflict of interest was identified after reviewing the author affiliation, funding source, acknowledgement, and conflict of interest statement.



Results

Figure 1. Kaplan-Meier event curve

- Of 125 cardiovascular risk CPRs analyzed, 29 had an independent external validation and the median follow-up time was 118 months (95% CI, 99-130).
- The 25th percentile of event time (or 75th percentile of survival time) was 122 months (95% CI, 91-299).

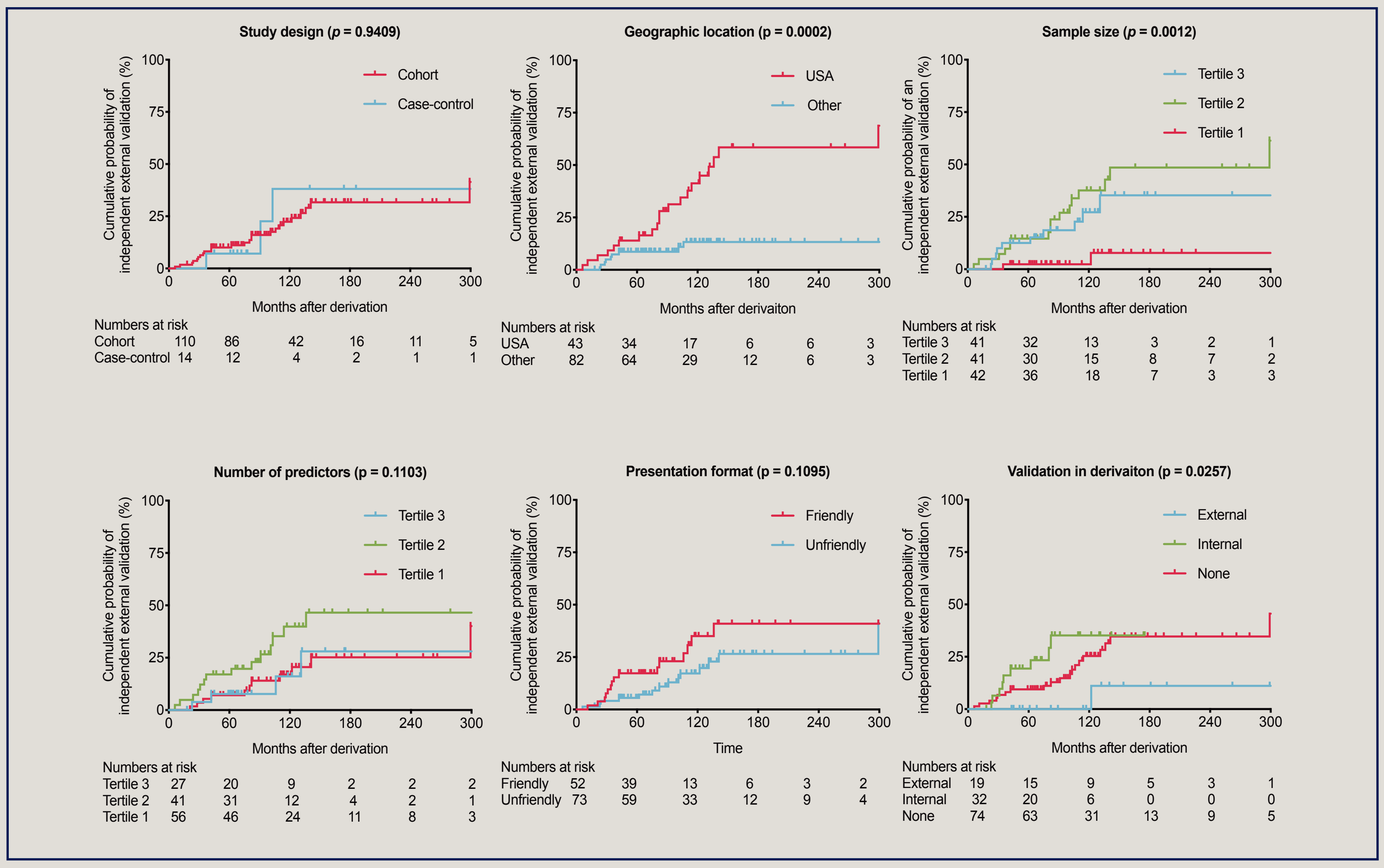


Figure 2. Probability of an independent external validation for derivation related predictor variables.

- Cardiovascular risk CPRs from the US were 4.15 times (95% CI, 1.89-9.13) more likely to have an independent external validation.
- Raising the sample size of derivation by ten times was associated with a 2.32-fold (95% CI, 1.37-3.91) increase in the probability of having an independent external validation.

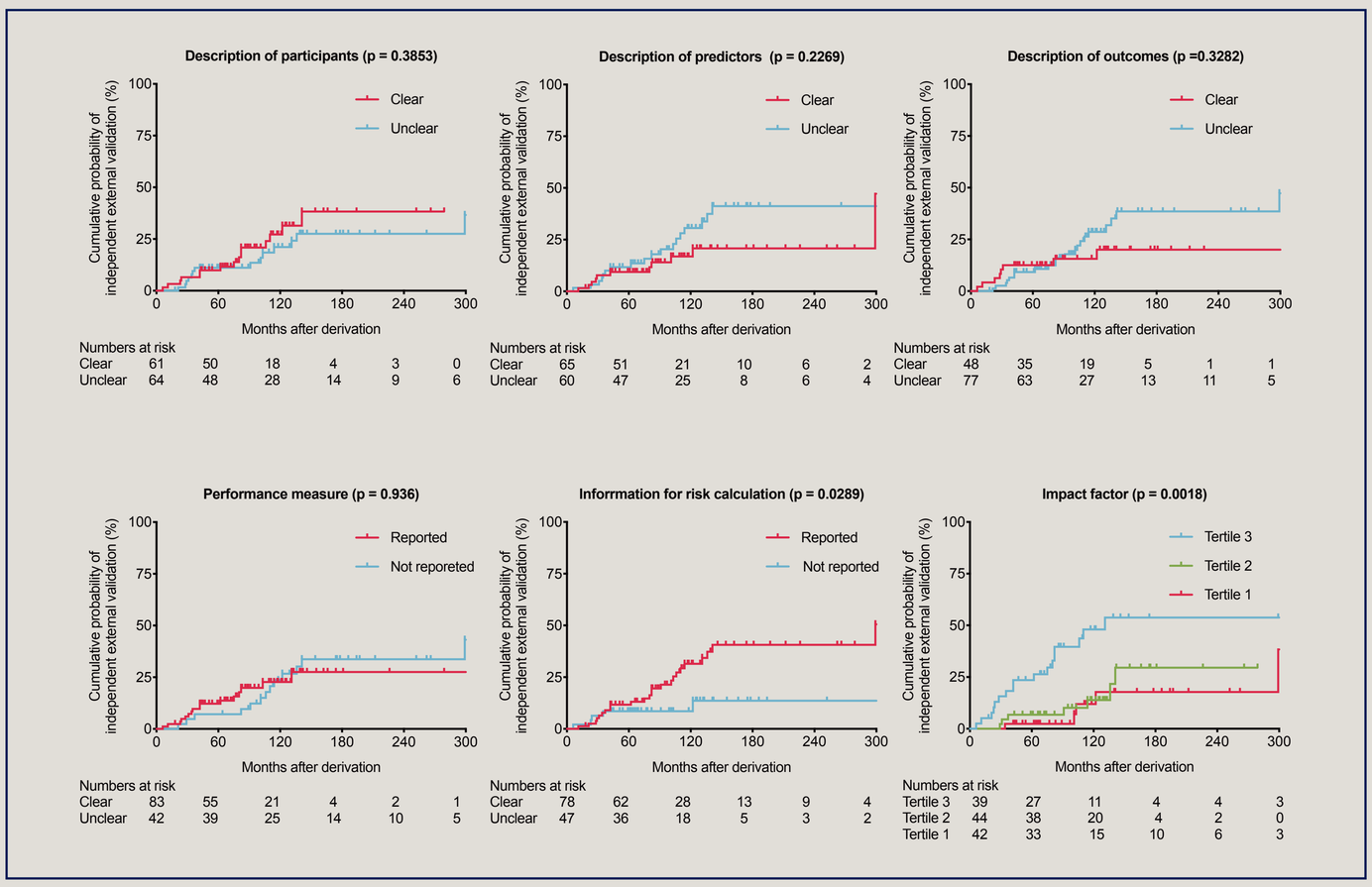


Figure 3. Probability of an independent external validation for reporting and publication related predictor variables.

- Cardiovascular risk CPRs presented with an internal validation tend to get an independent external validation sooner (HR = 1.73, 95% CI, 0.77-3.93).
- Cardiovascular risk CPRs reporting all the information necessary for calculating individual risk were 2.65 (95% CI, 1.01-6.96) times more likely to have an independent external validation.
- Publishing a cardiovascular risk CPR in a journal that has one unit higher impact factor was associated with a 6% (95% CI, 3-9) higher incidence of an independent external validation.

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Conclusions

1. The probability for cardiovascular risk CPRs to get an independent external validation was low even many years after their derivations.
2. Authors of new cardiovascular risk CPRs should consider using adequate sample size, conducting an internal validation, and reporting all the information needed for risk calculation as these features were associated with an independent external validation.