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Björk, Jonas; Green, Michael; Ekelund, Ulf

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LETTER TO THE EDITOR

Comments on ‘Practical experiences on the necessity of external validation’


From: Jonas Björk*,†,1, Michael Green2 and Ulf Ekelund3
1Competence Center for Clinical Research, Lund University Hospital, Lund, Sweden
2Department of Theoretical Physics, Lund University, Lund, Sweden
3Department of Clinical Sciences, Section for Emergency Medicine, Lund University Hospital, Lund, Sweden

In a very interesting empirical study, König et al. investigated the ability of two cross validation (CV) methods, tenfold CV and leave-one-center-out CV, to predict the generalizability of prognostic models [1]. Three different prognostic models, based on logistic regression, support vector machines and random forests, were established and validated. The goal of the prognostic models was to predict accurately the functional independence status of patients 100 days after an acute ischemic stroke. Data from the German Stroke Data bank were used.

The CV methods, which operate on training data, generally overestimated the temporal and geographic transportability of the prognostic models. No important differences in the distribution of the prognostic factors between the training set and the temporal and external validation sets were discerned that could explain the overoptimistic results of the CV methods. However, distributional data for the outcome measure were not presented or discussed. The outcome, the functional status of each patient after 100 days, was measured by Barthel index (BI), which is a continuous measure between 0 (total functional dependence) and 100 (total functional independence). In the prediction models, BI≥95 was used as a binary outcome measure. This, however, imposes a sharp cut-off for something that is indeed continuous. The discrimination problem can be expected to be much easier if the underlying continuous outcome for most patients are either far below or far above the chosen cut-off, compared with if many patients have values near the cut-off [2]. It is therefore recommended that detailed distributional data of continuous measures of the severity of disease (here BI) are presented [3], both for the training and validation sets.

When comparing the two CV methods, the authors draw the intuitively appealing conclusion that the leave-one-center-out approach is probably better than the traditional tenfold CV in predicting geographic transportability to centers not included in the training set. However, there does not seem to be a firm support for this conclusion in their data, given that there is a fairly substantial overlap in the confidence intervals for the estimated accuracy of the two CV methods (see the results for logistic regression in Figure 2 in the original article). It should be stressed that the leave-one-center-out approach can be expected to yield uncertain estimates of the geographic transportability when the number of centers in the training set is limited.

*Correspondence to: Jonas Björk, Competence Center for Clinical Research, Lund University Hospital, Barngatan 2, SE-221 85 Lund, Sweden.
†E-mail: jonas.bjork@skane.se

The work by König et al. stresses the importance of external validation. In many applications, prognostic models have to be optimized for each new target population before implementation [4]. After such optimization, there is a need to estimate the temporal transportability of the redefined model within the new target population. The results of König et al. are a bit reassuring in that respect, since they show that CV methods may predict temporal transportability fairly well, at least for their particular application and the investigated time period. It is not obvious, however, that this is generally true for other disease groups as well, where changes in, e.g., treatment practices or diagnostic criteria may have occurred over time.

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