Critical Review Form
Clinical Prediction or Decision Rule

PGY-1

Thiruganasambandamoorthy V, Kwong K, Wells GA, et al. Development of the Canadian Syncope Risk Score to predict serious adverse events after emergency department assessment of syncope. CMAJ. 2016 Sep 6;188(12):E289-E298.

Objectives: **"to develop a clinical decision tool to identify adult patients with syncope who are at risk of a serious adverse event within 30 days after disposition from the emergency department [ED]." (p. E290)**

Methods: **This prospective cohort study was conducted at 6 large EDs in 4 Canadian cities between September 29, 2010 and February 27, 2014. Patients aged 16 or older presenting within 24 hours of a syncopal event were eligible. Exclusion criteria were prolonged loss of consciousness (> 5 minutes), change in mental status from baseline following the syncope, obvious witnessed seizure, trauma requiring hospitalization, intoxication, language barrier, head trauma leading to loss of consciousness, and any serious adverse event identified during the index ED visit. Both admitted and discharged patients were included. Emergency physicians and residents working in the ED screened and enrolled eligible patients.**

The composite outcome was any serious condition related to syncope within 30 days of disposition from the ED, which included "death, arrhythmia, myocardial infarction, serious structural heart disease, aortic dissection, pulmonary embolism, severe pulmonary hypertension, severe hemorrhage, subarachnoid hemorrhage, any other serious condition causing syncope, and procedural interventions for the treatment of syncope." Outcomes were assessed by review of the medical record, records from local adult hospitals or provincial database, and records from the coroner's office, and by 30-day telephone follow-up.
Predictor variables were screened for inclusion in multivariable logistic regression, excluding factors with missing values for >25%o of patients and those with poor interobserver agreement (Kappa value < 0.4). Internal validation was performed by use of 500 bootstrap samples.

Out of nearly 12,000 patients screened, 4322 were enrolled in the study. Of these, 292 were excluded due to loss to follow-up, leaving 4030 in the final analysis. The mean age was 53.6 years and 44.5% were male. 147 patients (3.6%) experienced a serious adverse event within 30 days of disposition from the ED. Of these, 61 (1.5%) had an event outside of the hospital. Out of 43 candidate predictors, 23 were selected for multivariable modeling. The final model included 9 predictors, with a score ranging from -3 to 11.

Guide	Comments

I.	***Is this a newly derived instrument* (Level IV)?**	
A.	Was validation restricted to the retrospective use of statistical techniques on the original database? (If so, this is a Level IV rule & is not ready for clinical application).	Yes. In this study, the authors performed internal validation using bootstrap sampling of the original database.
II.	**Has the instrument been validated? (Level II or III). If so, consider the following:**	
1a	Were all important predictors included in the derivation process?	The authors included 43 predictor variables. These included a wide array of clinical, laboratory, and diagnostic predictors. Clinical gestalt was included in this list. There were no obvious deficiencies in the list of predictor variables being evaluated.
1b	Were all important predictors present in significant proportion of the study population?	Yes. A review of table 3 indicates that among those without a serious adverse event, the predictor variables occurred in 3.4-43.0% of patients; among those with a serious adverse event, the predictor variables occurred in 12.1-60.1% of patients.
1c	Does the rule make clinical sense?	Yes. The rule includes important clinical and laboratory values, electrocardiographic findings, and clinical gestalt as to the potential cause of syncope among the cohort of patients.
2	Did validation include prospective studies on several different populations from that used to derive it (II) or was it restricted to a single population (III)?	No. In this study alone, validation was restricted to bootstrap sampling of the original database (as noted above).
3	*How well did the validation study meet the following criteria?*	
3a	Did the patients represent a wide spectrum of severity of disease?	Yes. As noted, all clinical predictor variables were present in a sufficient proportion of patients. The incidence of adverse outcomes among the entire cohort was fairly low (3.6%) which is typical when considering all patients presenting to the ED with syncope. Among these outcomes, death was fairly rare (n = 21) and cardiac adverse events were most common (n = 147).
3b	Was there a blinded assessment of the gold standard?	Yes. While there was not a specific gold standard test performed, the authors considered a wide array of patient-oriented outcomes in their composite; these were assessed by physicians who were not aware of results of the predictor variables or the final score.

		"All serious adverse events were confirmed by an adjudication committee composed of 2 physicians blinded to the predictors and a third physician who adjudicated in cases of disagreement." (p. E291)
3c	Was there an explicit and accurate interpretation of the predictor variables & the actual rule without knowledge of the outcome?	Yes. Predictor variables were obtained prospectively during the index ED visit by physicians and residents who had undergone a one-hour training session "on how to assess for standardized variables from the history and physical exam..." (p. E290)
3d	Did the results of the assessment of the variables or of the rule influence the decision to perform the gold standard?	No. Again, there was no specific gold standard test performed. Instead, assessment for the composite outcome was performed via review of medical records and records from the coroner's office, and by 30-day telephone follow-up. While follow-up was not obtained in 292 patients, it was intended for all patients, regardless of the outcomes of the rule or presence of predictor variables.
4	How powerful is the rule (in terms of sensitivity & specificity; likelihood ratios; proportions with alternative outcomes; or relative risks or absolute outcome rates)?	● Using a score threshold of -2 or higher, the sensitivity was 99.2% (95% CI 95.9-100%). The estimated risk of a serious event at this level was 0.7%. ● Using a score threshold of -1 or higher, the sensitivity was 97.7% (95% CI 93.5-99.5%). The estimated risk of a serious event at this level was 1.2%.
III.	**Has an impact analysis demonstrated change in clinical behavior or patient outcomes as a result of using the instrument? (Level I). If so, consider the following:**	No impact analysis has been performed.
1	How well did the study guard against bias in terms of differences at the start (concealed randomization, adjustment in analysis) or as the study proceeded (blinding, co-intervention, loss to follow-up)?	N/A
2	What was the impact on clinician behavior and patient-important outcomes?	N/A

Limitations:

1. **Although the authors refer to this as a consecutive sample, over 1200 patients eligible but not enrolled (convenience sample). Additionally, 7% of enrolled patients were excluded due to incomplete follow-up.**

2. **Troponin levels, which were included in the final CDR, were not measured in over half of patients. It was assumed that all missing values were normal.**

3. **This study did not include validation in a separate cohort of patients (though validation has been reported by this group in other studies).**

4. **No impact analysis has yet been conducted to evaluate outcomes or potential monetary savings using this clinical prediction rule. One study utilizing propensity score analysis has suggested that hospital admission may not impact 30-day outcomes among older adults admitted for syncope (Probst 2019).**

Bottom Line:

This prospective derivation of a novel clinical decision rule for adults presenting to the ED with syncope found that use of the Canadian Syncope Risk Score at a threshold score of -2 was 99.2% sensitive for predicting the risk of 3-day serious adverse events. At a score threshold of -1, the score was 97.7% sensitive for predicting 30-day serious adverse events. Further studies will be needed to validate these findings, help determine the most appropriate score threshold for admission or discharge, and evaluate the potential impact of this rule on patient outcomes.