

# Derivation of the San Francisco Syncope Rule to Predict Patients With Short-Term Serious Outcomes

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**Study objective:** The causes of syncope are usually benign but are occasionally associated with significant morbidity and mortality. We derive a decision rule that would predict patients at risk for short-term serious outcomes and help guide admission decisions.

**Methods:** This prospective cohort study was conducted at a university teaching hospital and used emergency department (ED) patients presenting with syncope or near syncope. Physicians prospectively completed a structured data form when evaluating patients with syncope. Serious outcomes (death, myocardial infarction, arrhythmia, pulmonary embolism, stroke, subarachnoid hemorrhage, significant hemorrhage, or any condition causing a return ED visit and hospitalization for a related event) were defined at the start of the study. All patients were followed up to determine whether they had experienced a serious outcome within 7 days of their ED visit. Univariate analysis was performed with  $\chi^2$  and nonparametric techniques on all predictor variables.  $\kappa$  Analysis was performed on variables requiring interpretation. Variables with  $\kappa$  more than 0.5 and a *P* value less than .1 were analyzed with recursive partitioning techniques to develop a rule that would maximize the determination of serious outcomes.

**Results:** There were 684 visits for syncope, and 79 of these visits resulted in patients' experiencing serious outcomes. Of the 50 predictor variables considered, 26 were associated with a serious outcome on univariate analysis. A rule that considers patients with an abnormal ECG, a complaint of shortness of breath, hematocrit less than 30%, systolic blood pressure less than 90 mm Hg, or a history of congestive heart failure has 96% (95% confidence interval [CI] 92% to 100%) sensitivity and 62% (95% CI 58% to 66%) specificity. If applied to this cohort, the rule has the potential to decrease the admission rate by 10%.

**Conclusion:** The San Francisco Syncope Rule derived in this cohort of patients appears to be sensitive for identifying patients at risk for short-term serious outcomes. If prospectively validated, it may offer a tool to aid physician decisionmaking.

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### Capsule Summary

#### *What is already known on this topic*

Many patients are admitted to the hospital because of concerns about potential life-threatening causes of syncope even though the etiology in most patients is benign. Previously, some studies have shown that characteristics such as an abnormal ECG may predict higher complication rates.

#### *What question this study addressed*

This study of 684 patients prospectively derived a decision rule that attempts to predict patients at greater risk for short-term (7 days) serious outcome.

#### *What this study adds to our knowledge*

The 5 risk factors identified in this study (ie, abnormal ECG, anemia, dyspnea, systolic hypotension, history of congestive heart failure) were 96% sensitive in identifying patients who developed short-term serious outcomes and might have reduced admissions by 10%.

#### *How this might change clinical practice*

This clinical decision rule requires validation before emergency physicians should use it. If validated, such a rule could be useful in reducing inpatient admission and allowing safe outpatient evaluation of syncope.

## INTRODUCTION

Syncope is a transient loss of consciousness with a return to pre-existing neurologic function. The lifetime risk of fainting is 1 in 4, and 1% to 2% of all emergency department (ED) visits and hospital admissions are related to a transient loss of consciousness.<sup>1-6</sup> More than a million people are evaluated for syncope each year in the United States, with costs running in the billions of dollars.<sup>7-9</sup>

Patients with syncope create a difficult diagnostic dilemma. Some patients will require emergency hospitalization for workup and treatment of life-threatening or potentially life-threatening causes, some should receive outpatient evaluation, and others need no further evaluation.<sup>10,11</sup> The approach to the evaluation and disposition of these patients is considered one of the most difficult management issues facing physicians.<sup>12</sup>

Extensive work has focused primarily on the diagnostic workup and treatment of patients presenting with syncope.<sup>13-15</sup> Despite intensive diagnostic strategies, 20% to 50% of patients will still have unclear reasons for their syncope, with high-risk patients having death rates as high as 30% within the first year.<sup>2,4,16,17</sup> Diagnostic yield can be improved with standardized clinical evaluation,<sup>18</sup> and research has become more focused on risk stratification of patients.<sup>19,20</sup> Current risk stratification has been based on serious outcomes at 1 year; however, this stratifi-

cation has limited value in determining which patients need aggressive diagnostic workup and warrant acute hospitalization.<sup>21</sup> Recommendations for hospital admission should be based on the potential for adverse outcomes if further evaluation and workup is delayed. Several guidelines and recommendations are available, but no prospective study has focused on this issue.<sup>11,13-15</sup>

In recent work, we have determined that emergency physicians can accurately identify patients at risk for serious outcomes within 7 days of their initial visit; however, we found that they still admitted many patients with benign causes,<sup>22</sup> which led us to believe that there was great potential for clinical decision rules to help guide the decision to admit patients presenting with syncope. In this study, we describe the derivation of the San Francisco Syncope Rule to help predict short-term serious outcomes.

## MATERIALS AND METHODS

### Study Setting and Participants

This prospective cohort study was conducted at a large university teaching hospital and included patients presenting with acute syncope or near syncope as a reason for their ED visit. Research assistants prospectively screened patients with complaints of syncope, loss of consciousness, fall, collapse, seizure, light-headedness, tachycardia, bradycardia, shortness of breath, and chest pain. Exclusion criteria were altered mental status, alcohol- or illicit drug-related loss of consciousness, a definite seizure, or transient loss of consciousness caused by head trauma. A research nurse reviewed daily patient logs and ensured enrollment of all possible patients. Prospective patients were identified and brought to the attention of the attending physician, who made the final decision to enroll the patient. A study nurse completed follow-up on all patients to determine whether they had suffered a serious outcome by day 7. The Committee on Human Research at the University of California–San Francisco approved the study protocol without the need for informed consent.

### Standardized Patient Assessment

After assessing the patients, physicians completed a structured data form. The data form contained 50 predictor variables, which included 34 historical variables, 11 variables related to the physical examination, and 5 variables involving laboratory, radiograph, and findings on the ECG. These variables were determined to be the

most important from a review of the literature and a consensus of experts. Where possible, 2 physicians (attending physician and house staff) independently evaluated patients to measure agreement on subjective variables requiring interpretation. Only attending physician assessments were used in the analysis and derivation of the model. After completing the data form, the physicians treated and admitted patients in their usual manner without any specific study intervention.

### Outcome Measures and Assessment

We defined serious outcomes as death, myocardial infarction, arrhythmia, pulmonary embolism, stroke, subarachnoid hemorrhage, significant hemorrhage, or any condition causing or likely to cause a return ED visit and hospitalization for a related event. This definition was purposely broad and inclusive and was established before the start of the study.

Outcomes were determined by using the following definitions. Death was confirmed with findings in the medical record and death registry. The definition of myocardial infarction used in the study was any elevation of troponin or ECG change with an accompanying diagnosis of myocardial infarction on the discharge diagnosis and confirmed by the cardiology service involved in the care. For an arrhythmia to be considered a serious outcome, it had to be captured on monitoring and thought to have had a temporal relationship to the syncopal or near syncopal event. Pulmonary embolism was determined by ventilation perfusion scanning, computed tomography (CT) of the chest, or angiography. It also had to be confirmed on discharge diagnosis, and the patient needed to have received treatment for the pulmonary embolism or to have had it confirmed on autopsy. The diagnosis of stroke and subarachnoid hemorrhage was determined by discharge diagnosis, chart review to see whether the symptoms were temporally related to the admission, and confirmation that the admitting attending physician believed that the findings were thought to have been related or to have been a cause of the syncopal event. Significant hemorrhage was defined as any episode of syncope or near syncope associated with a source of bleeding that required transfusion. Any patients discharged from the ED or hospital after a syncopal event and then readmitted for the same or similar symptoms related to the initial syncopal event were considered to have had a serious outcome. Patients with related return visits who were not admitted were not considered to have had a serious outcome. Patients admitted who required an acute intervention during their stay that would have caused them to return

if they were discharged were also considered to have had a serious outcome. An acute intervention was any procedure required to treat a condition related to the patient's symptom of syncope, which included pacemaker insertion, surgery for valvular heart disease, balloon pump insertion, use of vasopressors, surgery to treat an abdominal aortic aneurysm, surgery for ruptured spleen, surgery for ruptured ectopic pregnancy, and endoscopic treatment of esophageal varices. Monitoring of patients, medication changes, and intravenous therapy for medications or rehydration were not considered acute interventions.

A trained research nurse and the principal investigator independently reviewed outcomes by using explicit criteria. Disagreements were discussed, and consensus was obtained. Both reviewers were blinded to the predictor variables when making their determination of a serious outcome. Day 7 outcomes were uniformly determined and reported, with patients having follow-up at different points according to their availability for follow-up and completion of investigations. Follow-up was completed by review of inpatient records, discussion with their primary physicians, or discussion with the patients or family members. In circumstances in which patients could not be found or located on follow-up, death records and admissions to local hospitals were checked.

### Statistical Analysis

All predictor variables were analyzed with univariate analysis with the  $\chi^2$  test for categorical variables and the Mann-Whitney rank sum test for continuous variables. Variables subject to interpretation were analyzed with  $\kappa$  or weighted  $\kappa$  statistics to measure physician agreement.<sup>23</sup> Variables with *P* value less than .1 and  $\kappa$  greater than 0.5 were analyzed with recursive partitioning techniques to develop a model that would maximize the prediction of serious outcomes. The objective was to find the best combination of predictor variables (ie, those highly sensitive for detecting the outcome while achieving the maximal specificity). Recursive partitioning was performed with KnowledgeSEEKER software (KnowledgeStudio, version 3.1; Angoss Software International, Toronto, Ontario, Canada) by using variables with the strongest association with serious outcomes (highest  $\chi^2$  values), with 0.05 as the basis of partitioning, and by using significant manual override to allow for the selection of clinically appropriate variables.<sup>24</sup> Our experience suggested that recursive partitioning was more suitable and efficient than automated models such as logistic

regression when the objective is to correctly classify one outcome group at the expense of the other (ie, when high sensitivity is more important than overall accuracy); it was thus used as the primary multivariate method of analysis. By using a simple normal approximation method and assuming our serious outcome rate would be 10%, we determined that 62 patients would be required to have a 95% confidence interval (CI) with a total width of 15%.

## RESULTS

Syncope visits represented 1.4% of the 58,884 ED visits during the study period from July 1, 2000, until February 28, 2002. Fifty-five percent of all patients were admitted, 59% were women, and the average age was 62 years. All patients had some form of follow-up: 48% by medical record review, 37% with direct telephone follow-up, and 11% through telephone calls to the patient's physician; less than 4% required indirect follow-up through checks to local hospitals and the death registry. Of the 684 patients evaluated by attending physicians, 79 (11.5%) patients developed serious outcomes by day 7 (Table 1). Of the 50 predictor variables analyzed, 26 were significantly associated with a serious outcome by using a significance level of 0.1 (Tables 2 and 3).

Variables associated with organic heart disease were all significant predictors of a serious outcome. These variables included increased age, a complaint of chest pain, and a history of coronary artery disease, arrhythmia, diabetes, or congestive heart failure. Physical findings such as rales, abnormal heart sounds, and either a systolic or diastolic murmur were also significantly associated with serious outcomes, as were the findings of a non-sinus rhythm or abnormal ECG (an ECG with new changes).

The use of anti-arrhythmic medications and diuretics was significantly associated with serious outcomes. No other cardiac medications were significantly associated with a serious outcome, except for nitrates. In this case, the use of nitrates was found in a greater proportion of patients who had a nonserious outcome, which was also the case for vagal symptoms, also more common in patients without serious outcomes.

Two physicians evaluated 265 patients independently, and agreement was calculated on variables subject to interpretation. Variables with significant agreement ( $\kappa > 0.5$ ) were the presence of new changes on ECG (0.69; 95% CI 0.61 to 0.77) and ECG rhythm interpretation (0.56; 95% CI 0.45 to 0.67). The presence of a mur-

mur (0.50; 95% CI 0.37 to 0.63) and the presence of facial trauma (0.67; 95% CI 0.50 to 0.74) were the only physical findings with good agreement. The presence of rales had reasonable agreement (0.48; 95% CI 0.30 to 0.66), but new neurologic findings, abnormal CT findings, the presence of abnormal heart sounds, and the presence of vagal symptoms (0.33; 95% CI 0.20 to 0.46) had only fair agreement. The physical finding of carotid bruits was rare, and its presence had poor agreement (0.01; 95% CI 0 to 0.2).

Significant variables with good agreement were analyzed with multivariate models. Recursive partitioning techniques produced a clinically acceptable model that maximized the prediction of serious outcomes. The prediction variables in this model were combined into a simple algorithm, the San Francisco syncope rule. This clinical decision rule includes an abnormal ECG (not sinus rhythm or new changes compared with previous ECG), complaint of shortness of breath, hematocrit less than 30%, a triage systolic blood pressure less than 90 mm Hg, and a history of congestive heart failure (Table 4; Figure).

**Table 1.**  
*Characteristics of patients presenting with syncope (N=684).\**

| Characteristic                                       | No. (%)            |
|--|--------------------|
| Age, y, mean (SD) [range]                            | 62.1 (23) [10–102] |
| Female, No. (%)                                      | 403 (58.9)         |
| Admitted   | 376 (54.9)         |
| Admission length, days, median (IQR) [range]         | 2 (1–3) [1–19]     |
| 1-Day admissions                                     | 161 (23.5)         |
| 2-Day admissions                                     | 74 (10.8)          |
| Syncope as primary complaint                         | 500 (73.1)         |
| Patients with serious outcomes by Day 7 <sup>†</sup> | 79 (11.5)          |
| Death  | 5 (0.7)            |
| Cardiac causes                                       | 56 (8.2)           |
| Myocardial infarction                                | 21 (3.1)           |
| Non-Q wave myocardial infarction                     | 12 (1.8)           |
| Arrhythmia   | 30 (4.4)           |
| Structural   | 5 (0.7)            |
| Pulmonary embolism                                   | 5 (0.7)            |
| Significant hemorrhage                               | 12 (1.8)           |
| Gastrointestinal tract bleed                         | 10 (1.5)           |
| Spontaneous ruptured spleen                          | 1 (0.2)            |
| Ruptured ectopic pregnancy                           | 1 (0.2)            |
| Subarachnoid hemorrhage                              | 3 (0.4)            |
| Stroke syndromes                                     | 3 (0.4)            |
| Other  | 5 (0.7)            |
| Sepsis   | 1 (0.2)            |
| Anemia   | 2 (0.3)            |
| Readmit  | 2 (0.3)            |

IQR, Interquartile range.

\*All values are number (%) unless otherwise noted.

<sup>†</sup>Some patients had >1 diagnosis as a cause for a serious outcome.

Applying the rule to this derivation set of patients would result in a sensitivity (for identifying 79 cases with serious outcomes) of 96.2% (95% CI 92% to 100%) and a specificity of 61.9% (95% CI 58% to 66%). We estimated that the rule would place 45% of patients at high risk, suggesting the need for admission, a potential 10% absolute reduction in the admission rate of 55% found in this cohort.

**LIMITATIONS**

Clinical decision rules have generally been derived and validated to achieve 100% sensitivity.<sup>25-31</sup> They can be hard and fast rules that in some instances can even

**Table 2.**  
*Historical predictor variables: univariate analysis.\**

| Variable                                 | Serious Outcome (N=79) | Nonserious Outcome (N=605) |
|--|------------------------|----------------------------|
| <b>Presenting features</b>               |                        |                            |
| Age, y, mean*                            | 75                     | 61                         |
| Female sex, %                            | 53.2                   | 59.7                       |
| Loss of consciousness, mean, s           | 86                     | 84                         |
| Witnessed, %                             | 58.2                   | 57.4                       |
| Postural change, %                       | 15.2                   | 14.5                       |
| Standing position, %                     | 59.5                   | 53.9                       |
| Prodrome, %                              | 31.6                   | 38.8                       |
| Exertional, %                            | 7.6                    | 7.8                        |
| Palpitations, %                          | 5.1                    | 3.8                        |
| Diaphoresis, %                           | 15.2                   | 15.0                       |
| Incontinence, %                          | 2.5                    | 3.5                        |
| Vomiting, %                              | 20.3                   | 21.5                       |
| Vagal symptoms, %                        | 12.7                   | 22.8                       |
| Abdominal pain, %                        | 3.8                    | 2.8                        |
| Back pain, %                             | 2.5                    | 1.8                        |
| Headache, %                              | 3.8                    | 6.4                        |
| Chest pain,* %                           | 15.2                   | 7.6                        |
| Shortness of breath,* %                  | 22.8                   | 5.5                        |
| <b>Medical history, %</b>                |                        |                            |
| Coronary artery disease*                 | 24.1                   | 16.0                       |
| Hypertension*                            | 39.2                   | 28.9                       |
| Congestive heart failure*                | 17.7                   | 4.5                        |
| Arrhythmia*                              | 19.0                   | 7.1                        |
| Diabetes*                                | 16.5                   | 8.3                        |
| Syncope                                  | 16.5                   | 18.3                       |
| Stroke                                   | 1.3                    | 3.8                        |
| Seizure                                  | 1.3                    | 2.1                        |
| <b>Medication use, %</b>                 |                        |                            |
| Diuretics*                               | 19.0                   | 10.6                       |
| Nitrates*                                | 1.3                    | 6.0                        |
| Anti-arrhythmic*                         | 11.4                   | 4.0                        |
| Calcium channel blockers                 | 8.9                    | 9.6                        |
| β-Blockers                               | 25.3                   | 18.0                       |
| α-Blockers                               | 6.3                    | 3.3                        |
| Angiotensin-converting enzyme inhibitors | 16.5                   | 12.4                       |
| Viagra                                   | 0.3                    | 0.3                        |

\*Variables that were considered for entry into the multivariate model.

replace physician judgment.<sup>32</sup> Such a rule for syncope, although desirable, would be an unrealistic goal for a symptom with diverse causes that is only occasionally diagnosed. However, we do think that this highly sensitive and specific derived rule may play an important role in physician decisionmaking and has benefits over unstructured physician judgment.<sup>33</sup> Without 100% sensitivity, this rule should be viewed by physicians as a risk stratification tool to help with decisionmaking as opposed to a rule to replace judgment. Because of the limitations outlined here, physicians should wait for

**Table 3.**  
*Physical examination, tests, and laboratory findings: univariate analysis.\**

| Variables                                      | Serious Outcome (N=79) | Nonserious Outcome (N=605) | κ    |
|--|------------------------|----------------------------|------|
| <b>Vital signs at triage</b>                   |                        |                            |      |
| Systolic blood pressure <90 mm Hg <sup>†</sup> | 15.2                   | 4.0                        |      |
| Pulse rate <50 or >110 beats/min <sup>†</sup>  | 25.3                   | 5.8                        |      |
| Respiratory rate >24 breaths/min <sup>†</sup>  | 11.5                   | 2.3                        |      |
| SaO <sub>2</sub> <95% <sup>†</sup>             | 18.8                   | 10.8                       |      |
| <b>Physical findings</b>                       |                        |                            |      |
| Facial or head trauma                          | 7.6                    | 6.6                        |      |
| New neurologic deficits                        | 2.5                    | 1.3                        | 0.43 |
| Rales  | 20.5                   | 7.1                        | 0.26 |
| Abnormal heart sounds                          | 22.8                   | 6.0                        | 0.34 |
| Carotid bruits                                 | 3.8                    | 0.7                        | 0.01 |
| Systolic murmur <sup>†</sup>                   | 26.3                   | 17.0                       | 0.56 |
| Diastolic murmur <sup>†</sup>                  | 3.3                    | 0.6                        | 0.49 |
| <b>Tests and laboratory findings</b>           |                        |                            |      |
| Abnormal rhythm (nonsinus) <sup>†</sup>        | 43.4                   | 18.7                       | 0.55 |
| Abnormal ECG (new changes) <sup>†</sup>        | 55.7                   | 17.5                       | 0.68 |
| Abnormal CT                                    | 8.9                    | 5.0                        | 0.35 |
| Hematocrit <30% <sup>†</sup>                   | 23.3                   | 5.4                        |      |
| Glucose, mean, mg/dL <sup>†</sup>              | 153                    | 122                        |      |

\*All values are percentages unless otherwise indicated.

<sup>†</sup>Variables that were considered for entry into the multivariate model.

**Table 4.**  
*Performance of the San Francisco Syncope Rule to predict patients with short-term serious outcomes.\**

| Decision Rule | Yes | No  |
|---------------|-----|-----|
| Yes           | 76  | 230 |
| No            | 3   | 375 |

\*Sensitivity 96.2% (95% CI 92%–100%); specificity 61.9% (95% CI 58%–66%); negative predictive value 99.2% (95% CI 98%–100%); positive predictive value 24.8% (95% CI 20%–30%); negative likelihood ratio 0.06 (95% CI 0.02–0.19); positive likelihood ratio 2.53 (95% CI 2.3–2.8). Bootstrap estimates for CI.

validation studies before implementing the rule in their clinical practice.

When developing any prediction rule, one could always achieve 100% sensitivity, but often at the expense of specificity and overfitting of the statistical model. For example, in this model we could have achieved 100% sensitivity by adding age older than 75 years to the rule, which would have identified the 3 patients not predicted by the rule. In this scenario, specificity would have dropped to 44% because 108 patients without serious outcomes would have been classified as high risk. We thought that the tradeoff was suboptimal because the absolute admission rate for patients deemed to be high risk would be the same as, if not slightly higher than, baseline. We were also aware

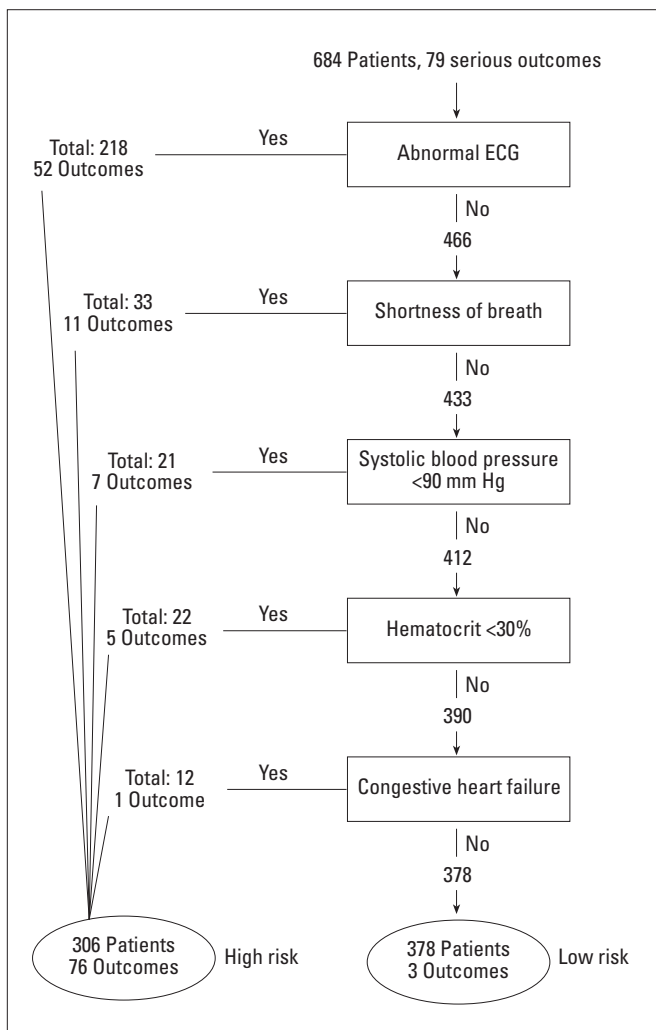
that rare serious outcomes not in our derivation set would make validating any rule with 100% sensitivity and certainty almost impossible. We thus accepted a rule that maximized sensitivity and specificity at the expense of not achieving 100% sensitivity.

In most situations, clinical decision rules have been developed in which the outcome measure is discrete, clearly defined, and easily measured, such as fracture versus no fracture on radiograph. For syncope, determining and defining an outcome for a symptom that is often not diagnosed and whose causes are so diverse was a challenging and important part of this study. This problem was addressed before the start of our study by creating a definition of a serious outcome that would define outcomes that most people would agree were serious and would require acute evaluation or treatment should they have occurred by day 7. The outcome measure in this study was achieved through a consensus of experts, and we purposely made the outcome broad and inclusive to try to include all possible serious outcomes.

The use of this broad inclusive composite outcome does lead to further limitations. Most important, by using a composite outcome the rule may not accurately predict outcomes represented by just a few cases or by potentially rare cases not even present in this cohort. For example, in our study we had only 6 serious neurologic outcomes and 1 ectopic pregnancy that were explained by the rule. Unlike cardiac outcomes, which were the majority in this study, these outcomes will require much larger numbers of patients in validation studies to determine whether the rule really fits these conditions, which may cause our sensitivity to be lower than reported in this study. However, many underrepresented outcomes usually do not present solely as syncope and have other presentations with definitive and alternative means of testing and diagnosis available (eg, subarachnoid hemorrhage). Tests for some of these conditions have been shown to be of limited value in assessing all patients with syncope<sup>17</sup> (eg, CT scanning).

The seriousness of the 3 outcomes not predicted by our rule and predicted only by a nonspecific age criterion can be debated. Of these 3 patients, 2 had small troponin elevations less than 2 µg/L, with normal ECG results, and 1 of these 2 patients had a negative cardiac catheterization result. Although they were considered non-Q wave myocardial infarctions by the physicians caring for the patients, the seriousness of the isolated troponin elevations can be questioned.<sup>34</sup> Our broad definition of myocardial infarction and our focus on

**Figure.**  
Decision tree to derive the San Francisco Syncope Rule.



short-term outcomes also explains the proportionally high rate of acute myocardial infarctions in this cohort compared with studies with long-term follow-up.<sup>18</sup> A third patient was a patient readmitted for syncope within a week of her initial visit, without a cause found. All these patients are alive at 1 year without any related morbidity. Physicians should draw their own conclusions about these patients that the rule did not correctly classify and should be aware of important limitations introduced into the study by using such a broad and all-encompassing outcome definition.

Finally, we purposely did not develop the rule with the physician's decision to admit as the primary outcome. Thus, this rule is not a decision rule to predict admission. The reasons to admit often take other factors (eg, social factors) into consideration that, although important, we believed were not specific to whether patients with syncope are at acute risk for serious outcomes that require acute hospitalization.

## DISCUSSION

Despite the noted limitations, to our knowledge this is one of the largest prospective cohort studies of syncope patients reported and the only attempt to derive a clinical decision rule to identify patients at risk for short-term serious outcomes. We evaluated the accuracy and reliability of 50 predictor variables used in the evaluation of patients with syncope and developed a highly sensitive clinical decision rule that we believe will augment physician judgment and allow physicians to rationally decide which patients with syncope need admission according to their risk for short-term serious outcomes. The rule is not complex and is easily remembered by a simple mnemonic, CHES (history of Congestive heart failure, Hematocrit <30%, abnormal ECG, a patient complaint of Shortness of breath, and a triage Systolic blood pressure <90 mm Hg). The San Francisco Syncope Rule was derived according to strict methodologic standards and provides tight CIs around the estimated sensitivities and specificities for determining patients at risk.<sup>35,36</sup> Further work will evaluate the rule for accuracy and reliability, acceptability to clinicians, actual effect on patient care, and cost-effectiveness.

Others agree with us that the current use of hospitalization for patients with syncope is inefficient and highly variable and that there is a need for a more cost-effective approach.<sup>21,37-44</sup> Many things can cause syncope, and the potential diseases that cause it span multiple specialties, making it sometimes difficult to

develop an optimal evaluation and management plan. Other investigators have also done excellent work to determine the best diagnostic and treatment strategies for patients with syncope<sup>13-15</sup>; however, even the most rigorous strategies still result in the majority of patients having unclear causes for their loss of consciousness.<sup>13,15,45</sup> Multiple studies have shown that the 1-year mortality rates for patients with unknown cause of syncope are 4% to 6%, and rates for high-risk patients are as high as 30%.<sup>16,17,19,45</sup> Kapoor and Hanusa<sup>46</sup> also showed that syncope itself is not an independent risk factor for increased overall mortality, cardiac mortality, or cardiovascular events. What is clear is that underlying heart disease is a risk factor for mortality, regardless of whether the patient had a syncopal episode. It could be argued that all patients with syncope and cardiac risk factors need further evaluation beyond the ED and that admission should be recommended for patients whose syncope is believed to be a symptom of active cardiac disease.<sup>11,13-15</sup> This is often unclear, and it is also evident that there are other noncardiac causes of syncope that require immediate attention.<sup>47</sup> Leading experts have concurred that recommendations for hospital admission should be based on the potential for adverse outcomes if the evaluation is delayed, but they concluded that no studies have directly addressed this question.<sup>11,14</sup>

To answer this question, instead of focusing on long-term outcomes and diagnoses, we focused on 7-day outcomes to achieve our goals, our rationale being that if a serious outcome happened 7 days after an initial ED visit, it would be hard to justify that an emergency admission 7 days earlier was the only way to diagnose and treat that patient. Although some may argue that an acute admission could be warranted for diagnosing a serious condition that could present as a serious outcome in 14 days, 1 month, or even a year, that rationale assumes that important diagnoses can be made only for inpatients and that outpatient follow-up is inefficient or unavailable. Furthermore, researchers choosing to validate our rule should be careful to choose their outcome measures, should they attempt to validate the rule for other than short-term outcomes. Outcomes in our study were picked as important outcomes by day 7 because we believed that they would justify an admission. Using the same outcomes at 1 year or even a month would not be appropriate. For example, in this study 3 patients had pacemakers placed after outpatient evaluation between days 14 and 30 and by our day 7 study definition had serious outcomes. Two of these patients had uneventful 1-day admissions after their ini-

tial ED evaluation, and subsequently all 3 patients did well and had no other hospitalizations or further ED visits. Reporting day 30 outcomes with our defined outcome measures would have been inappropriate for these cases for the purposes of helping with acute admission decisions because it could be argued that not admitting these patients would have been the right decision and the rule correctly classified these patients. Investigators interested in the performance of the rule in predicting long-term outcomes should pick more appropriate well-defined long-term outcomes such as mortality.

This large prospective cohort study has shown that many variables are associated with serious outcomes in patients with syncope. In this derivation set, our decision rule was 96% sensitive and 62% specific for predicting acute day 7 serious outcomes. The rule emphasizes the importance of the ECG and a history of congestive heart failure that have also been important predictors of 1-year mortality and surrogates for organic heart disease on other multivariate analysis.<sup>19,20,48</sup> Our derived decision rule now needs to be prospectively validated on a large cohort of patients before physicians consider introducing it into clinical practice.

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Author contributions: JVQ, IGS, and GAW conceived and designed the trial. JVQ, DAM, KLS, and MAK supervised the conduct of the trial and data collection and provided database management and quality control. JVQ, IGS, MAK, and GAW contributed to the statistical analysis with advice, with JVQ and IGS doing the primary analysis. JVQ drafted the manuscript, with all authors contributing significantly to its revisions. JVQ takes responsibility for the paper as a whole.

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