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## Risk-stratification of Older Adults who Present to the Emergency Department with Syncope: The FAINT Score

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BCS and MAP designed the study. BCS obtained funding for this study. ANY and SEM were responsible for data collection and management. TG and REW provided statistical advice on study design and analyzed the data. MAP and BCS drafted the manuscript. All authors contributed substantially to manuscript revisions. BCS takes responsibility for the paper as a whole. BCS, TG, REW, ANY, and SEM had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors approved the final report for submission.

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**Abstract**

**Background:** Older adults with syncope are commonly seen in the emergency department (ED). We sought to derive a novel risk-stratification tool to predict 30-day serious cardiac outcomes.

**Methods:** We performed a prospective, observational study of older adults ( ≥ 60 years) with unexplained syncope/near-syncope who presented to 11 EDs in the United States. Patients with a serious diagnosis identified in the ED were excluded. We collected clinical and laboratory data on all patients. Our primary outcome was 30-day all-cause mortality or serious cardiac outcome.

**Results:** We enrolled 3,177 older adults with unexplained syncope/near-syncope between April 2013 and September 2016. Mean age was 73 years (SD: 9.0 years). The incidence of the primary outcome was 5.7% (95% CI: 4.91-6.52%). Using Bayesian logistic regression, we derived the FAIN T score: 1) history of heart Failure, 2) history of cardiac Arrhythmia, 3) Initial abnormal electrocardiogram, 4) elevated pro B-type Natriuretic peptide, and 5) elevated high-sensitivity Troponin T. A FAIN T score of 0 vs. ≥ 1 had sensitivity of 96.7% (95% CI: 92.9, 98.8%) and specificity 22.2% (95% CI: 20.7, 23.8%), respectively. The FAIN T score tended to be more accurate than unstructured physician judgment: area under the curve 0.704 (95% CI 0.669-0.739) vs 0.630, (95% CI 0.589-0.670).

**Conclusions:** Among older adults with syncope/near-syncope of potential cardiac etiology, a FAIN T score of zero had a reasonably high sensitivity for excluding death and serious cardiac outcomes at 30 days. If externally validated, this tool could improve resource utilization for this common condition.

**Introduction**

**Background**

Emergency department (ED) visits for syncope (transient loss of consciousness) in the United States (US) are common<sup>1</sup> and increasing yearly<sup>2</sup>, resulting in over \$2.4 billion in annual hospital costs.<sup>3</sup> Due to the wide range of potential serious causes, particularly in older adults, the clinical management and disposition of these patients is often challenging.<sup>4</sup>

**Importance**

The quest for an accurate risk-stratification tool has been the “holy grail” of syncope research for the last two decades.<sup>5–14</sup> Despite these efforts, significant uncertainty remains

regarding which patients with syncope can be safely discharged from the ED.<sup>7,15,16</sup> None of the published risk-stratification rules have gained widespread adoption largely due to small sample sizes, failure of external validation, or lack of face validity.<sup>7,17–22</sup> Moreover, these tools have not been compared with unstructured physician judgment<sup>16</sup>, a necessary comparison prior to investment in implementation efforts.<sup>23</sup>

Roughly 30% of patients presenting to the ED with syncope are hospitalized;<sup>1,2</sup> for older adults (>60 years), it is over 50%.<sup>24</sup> If a serious diagnosis is found in the ED, these patients may be hospitalized for specific therapeutic reasons (e.g., pacemaker insertion, blood transfusion). However, many older adults with syncope, despite having an unremarkable ED evaluation, are still admitted to inpatient or observation units solely for observation or further testing.<sup>2,25,26</sup> These diagnostic admissions are costly<sup>3</sup> and may be of little to no clinical benefit.<sup>27–30</sup> An accurate, easy-to-use syncope risk-stratification tool focused on older adults could help decrease low-yield hospitalizations and diagnostic testing while maintaining patient safety.

### Goals of This Investigation

Using a large sample size and Bayesian methodology, we sought to derive a novel clinical risk-stratification tool to predict 30-day all-cause mortality and serious cardiac outcomes in older adults with unexplained syncope/near-syncope of potential cardiac etiology. If externally validated in a new data set, such a tool could guide the ED clinical management and disposition of these patients to optimize resource use and improve clinical outcomes.

## Methods

### Study design and setting

We conducted a multicenter, prospective, observational study of older adults who presented to an ED with syncope or near-syncope ([ClinicalTrials.gov](https://clinicaltrials.gov) identifier: ). The study was conducted at 11 academic EDs, all located in not-for-profit hospitals, across the US (eTable 1), recruiting a diverse patient population, from April 28, 2013 to September 21, 2016. Ten out of 11 of the EDs were teaching hospitals with a trauma center; ED volume ranged from 47,000 to 120,000 visits per year. The institutional review boards at each site approved the study and study staff obtained written, informed consent from all participating subjects or their legally authorized representatives.

### Selection of Participants

Our inclusion criteria were age ≥ 60 years with an ED complaint of syncope or near-syncope. Syncope was defined as transient loss of consciousness, associated with postural loss of tone, with immediate, spontaneous, and complete recovery. Near-syncope was defined as the sensation of impending loss of consciousness, without actual loss of consciousness. We excluded patients if their symptoms were thought to be due to intoxication, seizure, stroke, transient ischemic attack, head trauma, or hypoglycemia. Additional exclusion criteria were the need for medical intervention to restore consciousness (e.g., defibrillation), new or worsening confusion, and inability to obtain informed consent from the patient or a legally authorized representative.

For this analysis, we also excluded all patients who had a new serious diagnosis identified in the ED: death, significant cardiac arrhythmia, myocardial infarction, significant structural heart disease, stroke, pulmonary embolism, aortic dissection, hemorrhage or anemia requiring blood transfusion, subarachnoid hemorrhage, cardiopulmonary resuscitation, or major traumatic injury (eTable 2). We identified serious diagnoses via ED chart review performed by trained research assistants (RAs) and confirmed by the local physician site investigator.

## Measurements

All patients underwent standardized history, physical examination, cardiac biomarker testing, and 12-lead electrocardiogram (ECG) testing. Any additional diagnostic testing was performed at the discretion of the treating providers, and availability of diagnostic testing was similar across sites. Trained RAs screened for eligible patients using standard definitions, approached potential subjects, collected data variables consistent with reporting guidelines for ED-based syncope research,<sup>31</sup> and directly questioned patients about symptoms associated with the syncopal or near-syncopal episode. RAs prospectively collected data on the patient's past medical history, medications, and physical examination by querying treating ED providers. A sub-sample of data was collected a second time by another provider who blinded to the first evaluation to allow for assessment of inter-rater agreement using a kappa statistic.

Research staff obtained blood samples for testing at a core laboratory (University of Rochester, Rochester, NY). Two assays were performed using the Roche Elecsys platform: N-terminal pro B-type natriuretic peptide (NT-proBNP) and the 5<sup>th</sup> generation high-sensitivity cardiac troponin T, hs-cTnT. NT-proBNP was classified as abnormal above a cutoff of 125 pg/ml and hs-cTnT was classified as abnormal above the 99<sup>th</sup> percentile for a reference population i.e. 19 ng/L. Core laboratory results for NT-proBNP and hs-cTnT were not available at the time of the ED evaluation; however, the ED providers were free to order local BNP and troponin testing. We abstracted objective quantitative data, such as age, vital signs, and laboratory test results, from the electronic medical record. The first obtained ECG was abstracted by one of five research study physicians blinded to all clinical data. Research study physicians demonstrated high interrater reliability (kappa >0.80) in distinguishing normal from abnormal ECGs in a training set of 50 ECGs. Abnormal ECG interpretations included non-sinus rhythms (including paced rhythms), multiple premature ventricular complexes, sinus bradycardias (< 40 bpm), ventricular hypertrophies, short PR segment intervals (<100 ms), axis deviations, first degree blocks (>200 ms), complete bundle branch blocks, Brugada patterns, Wolff-Parkinson-White patterns, abnormal QRS duration (>120 ms) or abnormal QTc prolongations (>450 ms), and Q/ST/T segment abnormalities suggestive of acute or chronic ischemia. The disposition of the patients (admission vs. observation vs discharge) was decided by the treating providers per usual care.

In order to compare our final risk score to unaided physician gestalt,<sup>32</sup> we also prospectively collected unstructured physician risk assessment by asking the treating ED attending to estimate the probability that the patient would experience cardiac death or serious cardiac event at 30 days (0-100%).

## Outcomes

Our primary outcome was 30-day all-cause death or serious cardiac outcome. Serious cardiac outcomes included significant cardiac arrhythmia, myocardial infarction, new diagnosis of significant structural heart disease, or cardiac intervention. Significant cardiac arrhythmias included ventricular fibrillation, ventricular tachycardia, sick sinus disease, Mobitz II atrioventricular heart block, complete heart block, symptomatic supraventricular tachycardia, symptomatic bradycardia and pacemaker malfunction. Structural heart disease included aortic stenosis with valve area  $\leq 1 \text{ cm}^2$ , hypertrophic cardiomyopathy with outflow tract obstruction, severe pulmonary artery hypertension (mean arterial pressure  $>30 \text{ mm Hg}$ ), left atrial myxoma or thrombus with protrusion and outflow tract obstruction. Cardiac interventions were defined as placement of a pacemaker or automated internal cardiac defibrillator, coronary artery bypass graft, percutaneous transluminal coronary angioplasty, or other invasive cardiac surgery. These outcomes are consistent with standardized research reporting and clinical management guidelines.<sup>15,31</sup>

We determined occurrence of the primary outcome using data collected via a review of the electronic medical records conducted by local research staff, as well as telephone calls to enrolled patients at 30 days to identify out-of-hospital deaths, ED visits, and hospitalizations that occurred outside the study sites. To minimize outcome bias, RAs performing chart review were blinded to the clinical outcomes determined by telephone follow-up at 30 day. Multiple strategies were employed to maximize follow-up rates including patient incentives, electronic follow-up tracking, real-time confirmation of phone numbers, and continuing performance monitoring, as previously described.<sup>33</sup> If a patient or his or her authorized representative reported an ED or hospital visit that occurred outside of the study site, then we obtained and reviewed the medical charts associated with those visits. If research staff were unable to contact a patient at 30 days, we queried the Social Security Death Index Master File 16 months after enrollment completion.

To assess inter-rater reliability of chart review, records for the first five sequentially enrolled patients at each of the 10 external sites (excluding the coordinating center) were independently reviewed by local research staff and the coordinating center. The number of charts chosen (50) for this training set was limited by availability of research staff resources. All ten serious ED diagnoses and 30-days serious outcomes in the training set were identified by local site reviewers.

## Predictors

We identified candidate predictors using a previously published systematic review and meta-analysis of the existing syncope risk-stratification literature.<sup>34</sup> We then performed a Bayesian meta-analysis allowing for the possibility of exact zero effects. We excluded variables that the Bayesian meta-analysis found to have little chance of being predictive of a serious cardiac outcome (e.g., co-occurring palpitations, history of stroke, syncope occurred while supine) and variables deemed irrelevant by expert physician judgment (e.g., Hispanic ethnicity). This left 13 variables: age, gender, hypotension, dyspnea, abnormal ECG, history of heart disease, history of arrhythmia, history of heart failure, low hematocrit ( $<30\%$ ), elevated hs-cTnT, elevated NT-proBNP, elevated blood urea nitrogen, and elevated

creatinine. Further detail describing the selection of candidate predictors can be found in the statistical appendix.

### Statistical Analysis

Using the 13 candidate variables as predictors, we fit a Bayesian logistic regression to the primary outcome variable. We choose to use a Bayesian approach over a conventional frequentist analysis since the former allows for the incorporation of previously reported empirical data pertaining to syncope risk-stratification.<sup>35,36</sup> In particular, the Bayesian approach allowed us to incorporate both shrinkage and variable selection through choice of prior and also incorporated a component that performed multiple imputation of missing predictors. This model was fit to the entire data set. Complete details of the model are given in the statistical appendix. Inter-rater agreement was assessed using a kappa statistic with 95% confidence intervals (CIs) using normal approximation methods.

Five variables were identified as having a high probability of being predictive of a serious cardiac outcome. We fit the same Bayesian logistic model with selection/shrinkage priors and multiple imputation using just these five variables to ensure all five remained important in the absence of the excluded variables. With this final subset of five important variables, we performed Bayesian logistic regression with shrinkage but without model selection to obtain our final model.

We created the final syncope risk score by dividing posterior means of all regression coefficients by the smallest posterior mean and rounding to the nearest integer, as has been done for other health-related risk scores.<sup>37</sup> For each score cutoff we calculated sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), with 95% CI using the exact binomial method. To account for overoptimism of the internal results we performed cross validation on the entire model selection and score creation procedure to get cross-validated estimates for sensitivity, specificity, PPV and NPV. A C-statistic, as well as positive and negative likelihood ratios were calculated for a risk score cutoff of zero. We assessed the calibration of the model by comparing the observed versus expected risk at each level of the score, as well as the Hosmer-Lemeshow goodness-of-fit statistic. We compared the predictive accuracy of the risk score with unstructured physician judgment using area under the receiving operator characteristic (ROC) curve with 95% CIs, as done in previous studies.<sup>38,39</sup> Finally, we assessed the net reclassification improvement (NRI) statistic by comparing the performance of the final risk score to the disposition decision made by the treating physician. This was calculated by taking the percentage of correctly reclassified patients and subtracting the percentage of incorrectly reclassified patients. Correctly reclassified patients were defined as i) those who were risk score positive, had a serious outcome, and yet were discharged by the treating physician (i.e., inappropriate discharge), and ii) those who were risk score negative, had no serious outcome, and yet were admitted by the treating physician (i.e., unnecessary admit/observation unit stay). Incorrectly reclassified patients were defined as i) those who were risk score positive, had no serious outcome, and were discharged by the treating physician, and ii) those who were risk score negative, had a serious outcome, and were admitted by the treating physician.

## Results

### Characteristics of study subjects

Between April 2013 to September 2016, there were 6,930 eligible patients screened, of which 3,686 (53.2%) consented to participation in the study (See Figure 1). Of those consented, 396 were excluded from this analysis for a serious diagnosis found during the ED visit (10.7%), 103 (2.8%) were lost to follow-up and 10 (0.3%) were withdrawn leaving 3,177 with complete follow-up data at 30 days. The mean age of the study sample was 72.7 years (Standard Deviation [SD]: 8.97), 50.6% were male, and 82.9% reported white race. The majority of patients experienced syncope (n=1,965, 61.9%), while the remainder (38.1%) had near-syncope. Just over half (53.3%) had an abnormal initial ECG, and 29.3% had an elevated hs-cTnT. See Table 1 for further baseline characteristics.

At 30 days post-index ED visit, 180 (5.7%) patients experienced the primary outcome; 65 of these patients experienced an event after discharge. The most common outcome was a serious cardiac arrhythmia (n=94/180, 52.2%), of which symptomatic supraventricular tachycardia was the most common (n=35/180, 19.4%). Overall mortality at 30 days was 0.82% (26/3,177). Further data on 30-day serious outcomes are presented in Table 2. Missing data for predictor variables ranged from 0% to 7.6% for predictor variable (hs-cTnT 7.6%, NT-proBNP 4.9%, Dyspnea 2.2%). After multiple imputation, all 3,177 subjects were included in the analysis.

### Main results

Our model selection process, using Bayesian logistic regression, resulted in five variables being significantly associated with the primary outcome: 1) history of heart failure, 2) history of cardiac arrhythmia, 3) abnormal initial electrocardiogram, 4) elevated NT-pro BNP, and 5) elevated hs-cTnT. The odds ratios (OR) and corresponding confidence intervals (CI) are presented in Table 3. These five variables make up the FAINT score (Failure, Arrhythmia, Initial ECG abnormal, abnormal Natriuretic peptide, abnormal high-sensitivity Troponin). The kappa statistic was good for all three of the non-numerical variables, heart failure: 0.70 (95%CI: 0.55 to 0.85), arrhythmia: 0.77 (95%CI: 0.66 to 0.87), and abnormal ECG: 0.65 (95%CI: 0.55 to 0.74). An older adult with unexplained syncope/near-syncope would be considered low-risk if none of the five FAINT variables are present during the ED evaluation, i.e. a FAINT score of zero. The sensitivity, specificity, positive and negative predictive values of a FAINT score of more than zero were 96.7%, 22.2%, 6.9%, and 99.1%, respectively (Table 4). The risk of death or serious cardiac outcome at 30 days for a patient with a FAINT score of zero was 0.9% (95% CI: 0.3, 1.9%) and 6.9% (95% CI: 6%, 8%) if greater than zero. The positive and negative likelihood ratios (LR) for a FAINT score of 1 or more were 1.24 (95%CI: 1.156, 1.336) and 0.15 (95%CI: 0.068, 0.329), respectively.

We modified the regression coefficients to obtain the point score associated with each variable, which resulted in point value of +2 for elevated NT-proBNP and +1 for all others. Total FAINT scores range from 0 to 6. Our model was well-calibrated demonstrating good agreement between observed and predicted risk at various score levels (See Figure 2a and



Figure 2b). Adequacy of calibration was confirmed by a non-significant Hosmer-Lemeshow goodness-of-fit statistic ( $\chi^2 = 6.21$ , 3 degrees of freedom,  $p = 0.102$ ).

The test characteristics for each level of the FAIN score (0-6) are presented in Table 4. Results of our cross-validation are presented in eTable 3 and discussed in the statistical appendix (Section 5). The FAIN score had significantly better area under the curve (AUC) statistic (AUC = 0.704, 95% CI 0.669-0.739) compared to that of unstructured physician risk assessment (AUC = 0.630 95% CI 0.589-0.670), (DeLong's test for two correlated ROC curves,  $Z=3.13$ ,  $p=0.002$ ). The ROC curves are presented in Figure 3. Accounting for the optimism of internal validation, the cross-validated C-statistic of the FAIN score was 0.653 (95% CI: 0.534, 0.765). The total number of correctly reclassified patients was 466: 11 who were FAIN score positive, with a serious outcome, but discharged and 455 who were FAIN score negative, without a serious outcome, but were hospitalized by the treating physician. The total number of incorrectly reclassified patients was 456, 450 who were FAIN score positive, without a serious outcome and were discharged, and 6 who were FAIN score negative with a serious outcome, and were admitted by the treating physician. The percentage of correctly and incorrectly reclassified patients was 466/3,174 (14.68%) and 456/3,174 (14.37%), respectively, for a net reclassification improvement of 0.31% favoring the FAIN score (not significant  $p=0.33$ ).

The FAIN score failed to predict the serious outcomes of 6 patients; these outcomes were: complete heart block leading to insertion of a pacemaker, structural heart disease, percutaneous transluminal coronary angioplasty, symptomatic bradycardia, sick sinus syndrome leading to the insertion of a pacemaker, and death. Conversely, the FAIN score would have identified 11 patients, which were not admitted to the hospital, as being high-risk; these outcomes were: 2 cases of symptomatic bradycardia, 2 cases of myocardial infarction, a case of ventricular tachycardia and coronary artery bypass graft, a pacemaker insertion, a coronary artery bypass graft, and four deaths (See eTable 4).

## Limitations

Since we did not enroll patients <60 years old, the FAIN score was not designed to be applied to adults under this cut-off, which may limit its clinical utility. In light of the high patient refusal rate and low enrollment rate (53.2%), it is possible that sampling bias occurred. Our score requires the use of two assays that may not be readily available in all EDs (hs-cTnT and NT-proBNP), which may limit its use in such clinical settings. Our score would likely exhibit decreased sensitivity if used with a contemporary troponin assay. Our data apply only to the specific brand of these cardiac biomarkers (Roche Elecsys) and our result may not hold true when using other commercially available high-sensitivity troponin assays, (e.g. Abbott, Beckman, Siemens). These various assays have different limits of detection and imprecisions at the 99<sup>th</sup> percentile.<sup>40</sup> However, we do anticipate that high-sensitivity troponin assay will become increasingly common in the US in the coming years.<sup>41,42</sup> Of note, substituting a conventional BNP assay for the NT-proBNP assay could be considered reasonable in EDs where only the former is available.<sup>43,44</sup> Our composite primary outcome includes diagnoses with a wide range of severity, from atrial fibrillation to death. Clinicians should remember that certain diagnoses may be less serious and time-

sensitive than others when applying this score. While we did perform an internal cross-validation, an external validation was not within the scope of this project. We intend to pursue such a study in the future to validate this score in a distinct population of ED syncope patients. Although the specificity and positive LR of a FAINT score above zero are not markedly high, the purpose of this score is primarily to “rule-out” serious cardiac outcomes and was derived with this objective in mind. Clinicians should focus on the high sensitivity and low negative LR of this score.

## Discussion

Using prospectively collected data from a large, multicenter sample of older adults presenting to the ED with syncope/near-syncope, we were able to derive an objective, 5-variable syncope risk score to predict the occurrence of serious cardiac outcomes at 30 days. This tool, if externally validated, could be used as a “one-way rule”<sup>45</sup> to guide clinical management for these patients by empowering clinicians to discharge low-risk patients (FAINT score =0) and consider further testing or observation for non-low-risk patients (FAINT score = 1).

The FAINT score differs from previous syncope risk-stratification tools in the following five important ways. First, it was developed on the subset of syncope patients in which resource utilization is greatest, patients  $\geq 60$  years, whereas other tools have been developed on samples that include adolescents and adults of all ages.<sup>6,8–11</sup> Adolescents and young adults (age  $<30$  years) with syncope are at much lower risk for serious cardiac outcomes than middle-aged or older adults, and often have different etiologies of their syncope.<sup>15,25</sup> Inclusion of younger adults in such a study sample would reduce the rate of serious outcomes; application of a syncope risk score to an inherently very low-risk cohort could lead to overtesting and false-positive screening. Second, our risk score incorporated novel cardiac biomarkers, i.e. NT-proBNP, hs-cTnT, both processed at a single, central laboratory, eliminating assay-to-assay variability. Although the hs-cTnT assay was not approved by the US Food and Drug Administration (FDA) at the time of study onset, we anticipated it would receive approval and eventually be integrated into clinical care (FDA granted approval in January 2017). Third, the components of our risk score are relatively simple and objective, i.e. does the patient have a history of heart failure or arrhythmia? Are the NT-proBNP or hs-cTnT levels elevated? These straightforward questions are less operator-dependent and more likely to show high inter-rater agreement than questions that require clinical gestalt.<sup>9</sup> Fourth, our sample is one of the largest prospectively collected cohorts of ED syncope patients published, much larger than that used to derive prior risk-stratification tools.<sup>5,6,8,10</sup> Fifth, our study set out to predict death and serious cardiac outcomes, and not *all* serious clinical outcomes, as other authors have done.<sup>6,8,9</sup> We excluded non-cardiac outcomes a priori (e.g. ischemic stroke, subarachnoid hemorrhage, gastro-intestinal hemorrhage, aortic dissection, pulmonary embolism). Although the best definition of the primary outcome for a study of this nature is debatable, we believe that limiting the primary outcome to death and serious cardiac outcomes only is more suitable for the clinical scenario in question, i.e. unexplained syncope/near-syncope. There are already several risk-stratification tools currently available to predict the likelihood of pulmonary embolism,<sup>46,47</sup> subarachnoid hemorrhage,<sup>48,49</sup> aortic dissection,<sup>50,51</sup> upper gastrointestinal hemorrhage,<sup>52,53</sup> and ischemic stroke<sup>54,55</sup>. The FAINT

score should be used only after these other diagnoses have been excluded during the initial ED evaluation, using clinical gestalt, relevant risk-stratification tools, or both, and potential cardiac etiologies remain. Moreover, the factors that predict cardiac arrhythmia, subarachnoid hemorrhage, occult gastrointestinal bleeding, and pulmonary embolism are like to be very different, as has been argued previously.<sup>16</sup> Thus, a syncope risk score should predict serious *cardiac* outcomes and death, analogous to the HEART score for low risk chest pain.<sup>56,57</sup>

As with any clinical decision rule that maximizes sensitivity, our corresponding specificity was less than desired. This creates the potential for application of the rule to paradoxically increase resource utilization if used in a “two-way” fashion, i.e. admitting all patients with a positive FAINT score.<sup>32</sup> Thus, we caution clinicians to not use this rule prior to external validation, and, if validated, use it as a tool to justify the discharge of low-risk patients.

Our results add to the growing body of literature supporting the utility of BNP as a predictor of serious cardiac outcomes after an episode of syncope.<sup>6,58–63</sup> An elevated NT-proBNP had an OR of 2.5, greater than that of any other clinical predictor we collected (Table 3). This suggests that a BNP assay should be strongly considered in the ED evaluation of older adults presenting with syncope or near-syncope. Given the score’s reliance on cardiac biomarkers, implementation could lead to an increase in laboratory testing, with a concomitant increase in costs, but could potentially lead to a decrease in admissions for unexplained syncope. A formal cost analysis would be required to determine the net effect.

Although the AUC for the FAINT score was modest (0.704), it did out-perform unstructured physician judgement (0.63), a statistically significant difference. The FAINT score did not result in a statistically significant improvement in correct reclassifications as compared to the physician’s disposition decision. The FAINT score did fail to predict a small number of serious clinical outcomes and the lower bound of the 95% CI was less than optimal. However, no risk-stratification tool should be used in isolation, but rather should be used to inform clinical decision-making while taking overall clinical gestalt and other non-clinical factors into account, e.g. social support of the patient, ability to obtain expedited follow-up care, values and preferences of the patient, and feasibility of returning to the ED promptly, to name a few. The FAINT score provides an objective, structured approach to risk-stratification that can be used by clinicians at all levels of skill and experience, which could reduce unwanted variation in the clinical management of syncope<sup>27,64,65</sup>. The risk-stratification tool is meant to inform, not replace, clinical judgement, while potentially decreasing cognitive load for clinicians.

In summary, we used a large, multicenter, prospective dataset of older adults with syncope/near-syncope to derive a clinical risk score to identify patients at very low risk for death or serious cardiac outcomes at 30 days. Our score requires external validation prior to clinical implementation. If validated in a separate cohort of patients, the FAINT score has the potential to help guide clinical management by safely reducing low-yield hospitalizations.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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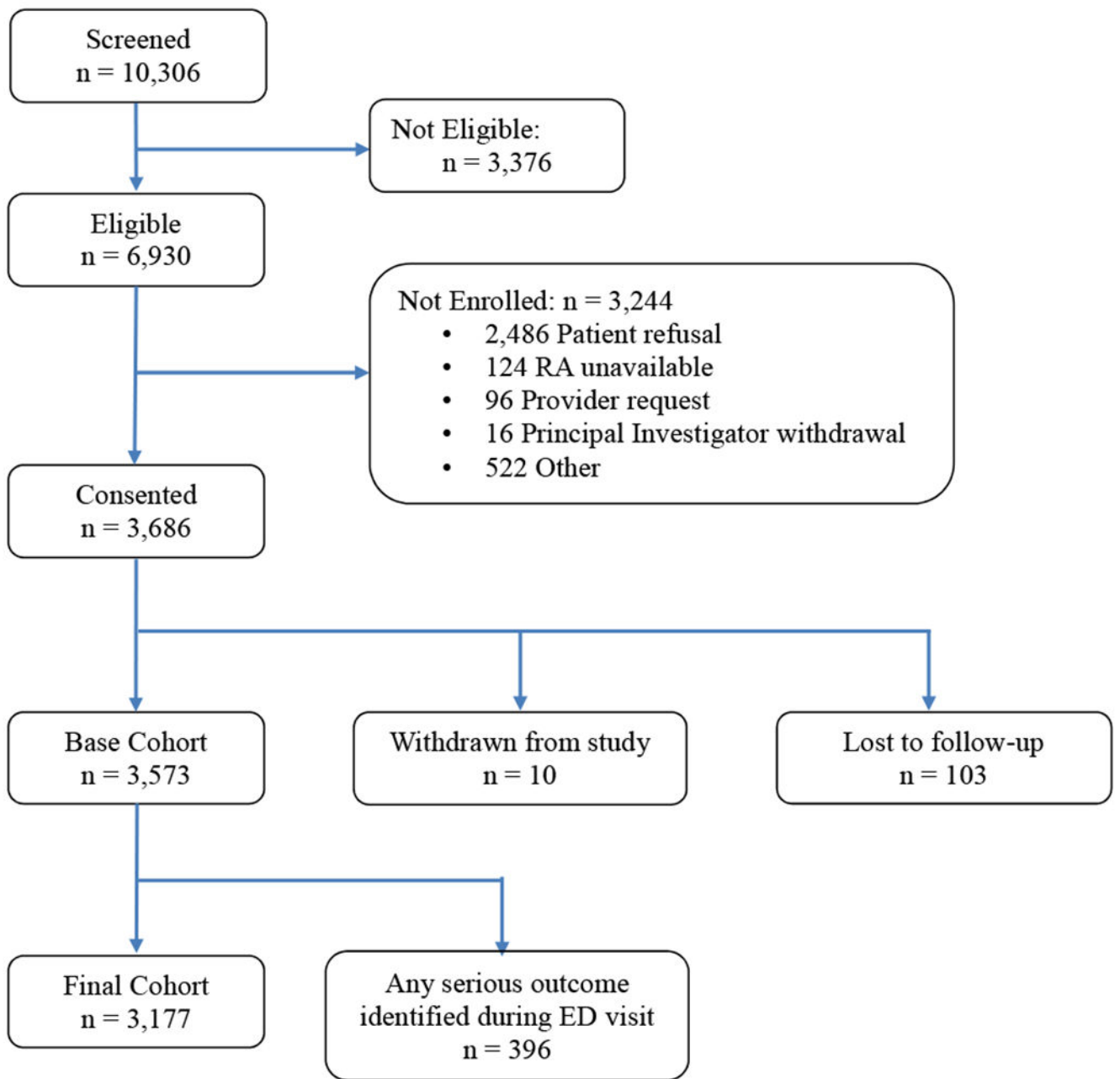
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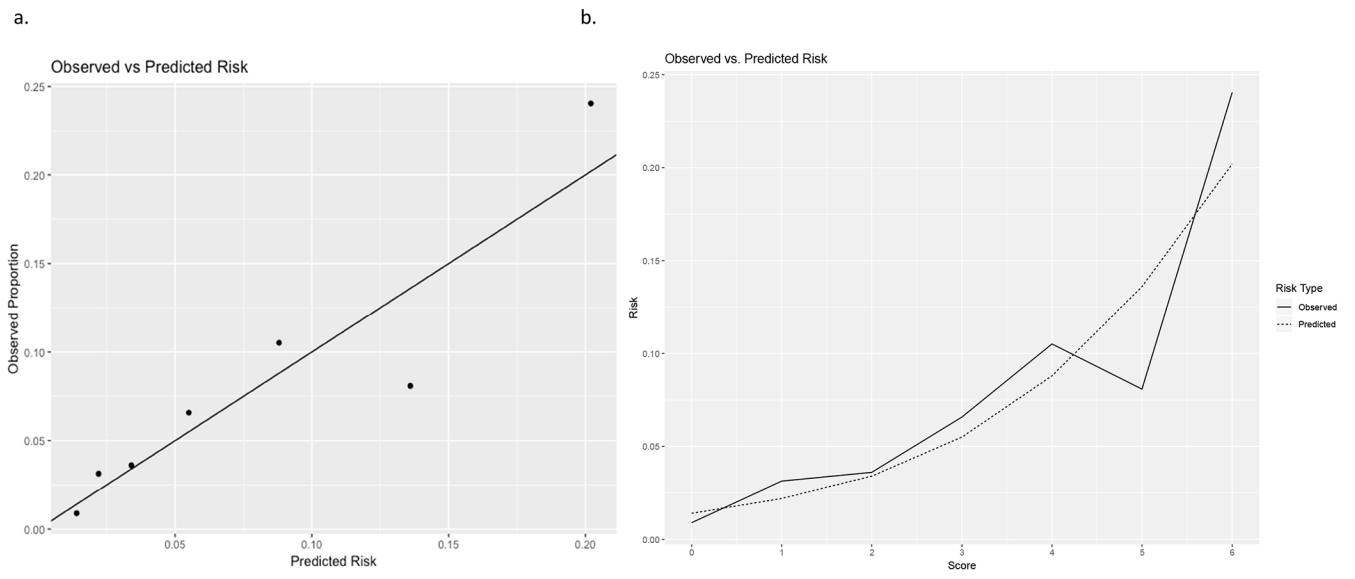
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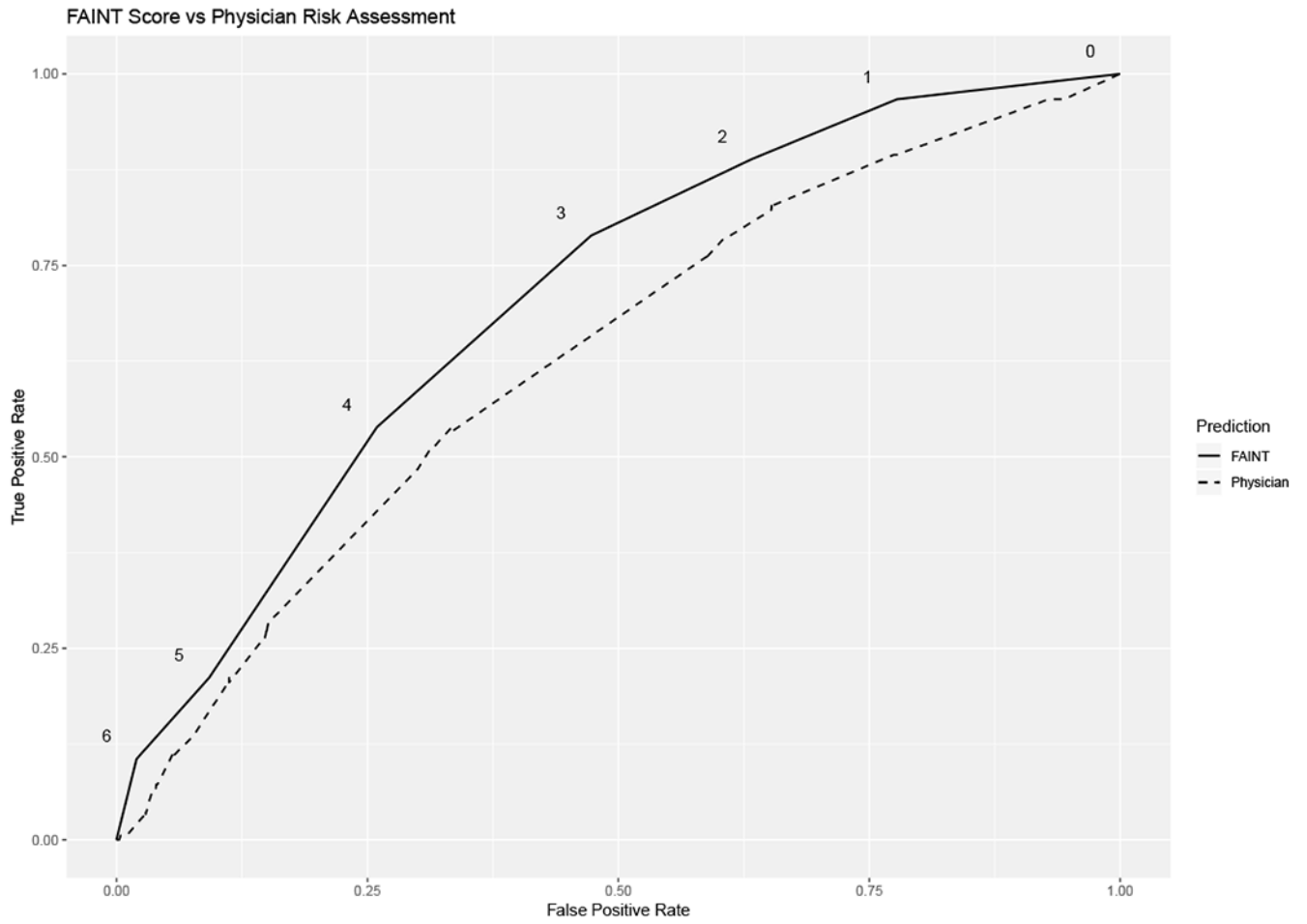


**Figure 1:**  
Patient Flow Diagram





**Figure 2a and 2b:**  
Observed vs Predicted Risk Plot



**Figure 3. Comparison of the ROC Curves for the FAINT score vs. Physician Risk Assessment**  
ROC: Receiver Operating Characteristic.

**Table 1:** Characteristics of Older Adults Presenting to the ED with Syncope or Near-Syncope

Variable	Overall (N=3,177)	With Serious Outcome at 30 days(n=180)	No Serious Outcome at 30 days (n=2,997)	Missing Data
Age				
Mean (SD)	72.74 (8.97)	73.52 (9.14)	72.69 (8.96)	0 (0.0%)
Age Category (n, %)				
60 to <70	1384 (43.6)	70 (38.9)	1314 (43.8)	0 (0.0%)
70 to <80	1013 (31.9)	61 (33.9)	952 (31.8)	
80 to <90	643 (20.2)	39 (21.7)	604 (20.2)	
90+	137 (4.3)	10 (5.6)	127 (4.2)	
Gender				
Male	1608 (50.6)	103 (57.2)	1505 (50.2)	19 (0.6%)
Race				
White or Caucasian	2618 (82.9)	151 (83.9)	2467 (82.8)	
Black or African American	442 (14.0)	25 (13.9)	417 (14.0)	
Other	98 (3.1)	4 (2.2)	94 (3.2)	
Near-syncope	1,212 (38.1)	67 (37.2)	1,145 (38.2)	
Syncope	1,965 (61.9)	113 (62.8)	1,852 (61.8)	
<b>History of:</b>				
Congestive Heart Failure	376 (11.8)	45 (25.0)	331 (11.1)	3 (0.1%)
Coronary Artery Disease	847 (26.7)	68 (37.8)	779 (26.0)	3 (0.1%)
Arrhythmia	630 (19.8)	63 (35.0)	567 (18.9)	3 (0.1%)
Dyspnea	617 (19.9)	44 (25.3)	573 (19.5)	71 (2.2%)
Chest discomfort	268 (8.4)	20 (11.1)	248 (8.3)	0 (0.0%)
Hypotension	313 (9.9)	26 (14.5)	287 (9.6)	20 (0.6%)
Abnormal ECG	1665 (53.3)	128 (72.7)	1537 (52.1)	51 (1.6)
Physician Risk Assessment, mean (SD)	5.00 [2.00, 10.00]	8.00 [5.00, 15.00]	5.00 [2.00, 10.00]	90 (2.8%)
<b>Cardiac Biomarkers</b>				
NT-proBNP > 125 pg/ml	1928 (63.8)	152 (87.4)	1776 (62.4)	156 (4.9%)
NT-proBNP, median [IQR]	213.00 [82.00, 661.00]	874.00 [227.50, 1846.50]	200.00 [80.00, 597.00]	
Hs-Troponin T > 19 ng/L	863 (29.4)	90 (53.3)	773 (27.9)	240 (7.6%)
Hs-Troponin T, median [IQR]	11.00 [6.00, 22.00]	21.00 [11.00, 41.00]	11.00 [6.00, 21.00]	

ECG: Electrocardiogram; SD: Standard Deviation. NT-proBNP: N-terminal pro B-type natriuretic peptide; hs: high-sensitivity; IQR: Interquartile Range.

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All-cause Death and Serious Cardiac Outcomes at 30 days

**Table 2:**

	Overall	Post-discharge	In hospital
Any 30-day serious outcome	180	56	124*
30-day death	26	24	2
<b>Serious Cardiac Arrhythmias:</b>			
Any cardiac arrhythmia	94	24	70
Ventricular fibrillation	3	1	2
Ventricular tachycardia (>30 secs)	10	2	8
Symptomatic ventricular tachycardia (<30 secs)	3	1	2
Sick sinus disease with alternating sinus bradycardia and tachycardia	14	3	11
Sinus Pause >3 seconds	4	0	4
Mobitz II atrioventricular heart block	5	3	2
Complete heart block	8	2	6
Symptomatic supraventricular tachycardia	35	9	26
Symptomatic bradycardia	11	3	8
Pacemaker or AICD malfunction with cardiac pauses	1	0	1
<b>Cardiac Intervention:</b>			
Any cardiac intervention	74	22	52
Pacemaker	36	10	26
AICD	9	2	7
CABG	8	4	4
PTCA	11	4	7
Other	10	2	8
<b>Other Serious Outcomes:</b>			
Myocardial infarction	24	9	15
New diagnosis of structural heart disease	26	3	23

\* Nine patients had events both in hospital and post-discharge; these were counted in the “in hospital” column.

AICD: Automated Implantable Cardioverter-Defibrillator. CABG: Coronary Artery Bypass Graft. PTCA: Percutaneous Transluminal Coronary Angioplasty.

Results of Bayesian Logistic Regression (FAINT score)

Predictor	Point Score	Odds Ratio	95% CI
F: History of Heart Failure	+1	1.585	(1.091, 2.269)
A: History of Arrhythmia	+1	1.549	(1.103, 2.143)
I: Initial ECG Abnormal	+1	1.578	(1.114, 2.263)
N: NT-proBNP	+2	2.535	(1.581, 4.131)
T: Hs-Troponin T	+1	1.853	(1.323, 2.587)

ECG: electrocardiogram; hs: high-sensitivity; NT-proBNP: N-terminal pro B-type natriuretic peptide; CI: Confidence Interval.

Table 3:

**Table 4:** Test Characteristics of the FAINTE Score to Predict Serious Clinical Outcomes at 30 days

Score	No. Patients	No. Bad Outcomes	Estimated Risk	Sensitivity	Specificity	PPV	NPV
0	672	6	0.9%	NA	NA	NA	NA
1	447	14	3.1%	0.967 (0.929, 0.988)	0.222 (0.207, 0.238)	0.069 (0.060, 0.080)	0.991 (0.981, 0.997)
2	499	18	3.6%	0.889 (0.834, 0.931)	0.367 (0.349, 0.384)	0.078 (0.067, 0.090)	0.982 (0.973, 0.989)
3	684	45	6.6%	0.789 (0.722, 0.846)	0.527 (0.509, 0.545)	0.091 (0.077, 0.106)	0.977 (0.968, 0.983)
4	561	59	10.5%	0.539 (0.463, 0.613)	0.740 (0.724, 0.756)	0.111 (0.091, 0.134)	0.964 (0.955, 0.971)
5	235	19	8.1%	0.211 (0.154, 0.278)	0.908 (0.897, 0.918)	0.121 (0.087, 0.162)	0.950 (0.942, 0.958)
6	79	19	24.1%	0.106 (0.065, 0.160)	0.980 (0.974, 0.985)	0.241 (0.151, 0.350)	0.948 (0.940, 0.956)
Total:	3177	180					

PPV: positive predictive value, NPV: negative predictive value.

\* Sensitivity/Specificity/PPV/NPV calculated by defining "at risk" as having that score or above (e.g. score >=1 gives sensitivity=0.967)