March 7, 2026

RE: Performance of the CRISP Risk Score for Clinically Meaningful Adverse Events (CMAE)

Key Message

The CRISP risk score remains a valid risk stratification tool for predicting CMAE after the registry transition from SAE to CMAE.

The **CRISP risk score** was originally developed to predict **significant adverse events (SAE)** in congenital cardiac catheterization. With the recent transition of the CRISP registry primary safety outcome from **SAE to clinically meaningful adverse events (CMAE)**, it was important to evaluate whether the existing risk prediction model remains applicable under the updated outcome definition.

To address this question, the CRISP registry organizers conducted a preliminary analysis using registry data from December 2023 through November 2025. The study cohort included 8,138 pediatric catheterization cases after exclusion of adult cases from 20 participating U.S. centers.

The incidence of SAE was 4.5% (365/8,138), while the incidence of CMAE was 2.8% (229/8,138). The CRISP risk score demonstrated good discrimination for predicting both SAE and CMAE. Model discrimination for predicting CMAE was comparable to that for SAE, with c-statistics of 0.703 for CMAE and 0.684 for SAE. Similarly, CRISP risk categories effectively stratified risk across increasing risk groups, with c-statistics of 0.682 for CMAE and 0.663 for SAE.

These findings demonstrate that the **CRISP risk score continues to provide effective risk stratification under the updated CMAE outcome definition**. Accordingly, the CRISP registry will **continue to utilize the CRISP risk score and risk categories for risk stratification and benchmarking across participating sites.**

A brief summary of the analysis and supporting tables/figures are provided on the Pages 2-4 for your reference.

Thank you for your continued participation and support of the CRISP registry.

Sincerely,

CRISP Registry Organizers

Brief Summary of the Analysis and Supporting Tables/Figures

Title: Performance of the CRISP Risk Score for Predicting Clinically Meaningful Adverse Events (CMAE)

Background:
The CRISP Registry recently transitioned its primary safety outcome measure from Significant Adverse Events (SAE) to Clinically Meaningful Adverse Events (CMAE). The original CRISP risk score was developed to predict the occurrence of SAE. However, the predictive performance of the CRISP risk score for CMAE has not been evaluated. Therefore, we conducted an analysis to assess the performance of the CRISP score and CRISP risk categories in predicting CMAE within the CRISP Registry.

Objectives:
To evaluate the predictive performance of the CRISP risk score and CRISP risk categories for clinically meaningful adverse events (CMAE).

Methods:
This was a retrospective analysis of prospectively collected data from the U.S. CRISP Registry. Patients aged <18 years who underwent cardiac catheterization between December 2023 and November 2025 were included. The primary outcomes were the occurrence of Significant Adverse Events (SAE) and Clinically Meaningful Adverse Events (CMAE). Univariable logistic regression analysis was performed to evaluate the predictive performance of the CRISP score and CRISP risk categories for both SAE and CMAE. Model discrimination was assessed using receiver operating characteristic (ROC) analysis, with performance quantified by the c-statistic.

Results:
The study cohort included 8,138 cases after exclusion of 1,562 adult cases from 20 participating U.S. centers. The incidence of SAE was 4.5% (365/8,138), while the incidence of CMAE was 2.8% (229/8,138). The CRISP score demonstrated good predictive performance for both SAE and CMAE. The model discrimination for predicting CMAE was comparable to that for SAE, with c-statistics of 0.703 for CMAE and 0.684 for SAE. Similarly, the CRISP risk category effectively stratified the risk of both SAE and CMAE across increasing risk groups. Model discrimination for CRISP risk category was 0.682 for CMAE and 0.663 for SAE. There was no significant difference in event rates between CRISP categories 1 and 2, suggesting that further refinement of the lower risk strata may improve risk discrimination.

Conclusions:
The CRISP risk score remains a useful risk stratification tool for predicting clinically meaningful adverse events. These results support the continued use of the CRISP risk model after the registry's transition from SAE to CMAE as the primary safety outcome.

Table 1: Frequency of Adverse Events by Severity Grade for SAE and CMA

Severity Grade	3a	3b	3c	4	5	Rate (%)
SAE	135	75	77	66	11	4.5% (365/8,138)
CMAE		75	77	66	11	2.8% (229/8,138)

Table 2. Univariable Logistic Regression Evaluating the Predictive Performance of the CRISP Score

	Odds ratio (95% CI)	P value	C-statistics
SAE	1.15 (1.11 – 1.18)	<0.001	0.684
CMAE	1.22 (1.18 – 1.26)	<0.001	0.703

Table 3. Predictive Performance of CRISP Risk Categories for SAE and CMAE

	SAE rate (%)	Odds ratio	P value	C-statistics
CRISP category				
Category 1 (score 0-2)	2.2% (21/950)	Reference	NA	
Category 2 (score 3-5)	2.5% (85/3,445)	1.12 (0.69 – 1.81)	0.648	0.663
Category 3 (score 6-9)	5.3% (143/2,698)	2.48 (1.56 – 3.94)	<0.001	
Category 4 (score 10-14)	9.9% (91/916)	4.88 (3.01 – 7.92)	<0.001	
Category 5 (score 15-21)	19.4% (25/129)	10.63 (5.75 – 19.67)	<0.001	
	CMAE rate (%)			
CRISP category				
Category 1 (score 0-2)	1.5% (14/950)	Reference	NA	
Category 2 (score 3-5)	1.3% (46/3,445)	0.91 (0.50 – 1.65)	0.745	0.682
Category 3 (score 6-9)	3.2% (86/2,698)	2.20 (1.25 – 3.89)	0.007	
Category 4 (score 10-14)	6.7% (61/916)	4.77 (2.65 – 8.59)	<0.001	
Category 5 (score 15-21)	17.1% (22/129)	13.75 (6.83 – 27.66)	<0.001	

Figure 1. Rates of SAE and CMAE according to CRISP score, with ROC curve analysis demonstrating the predictive performance of the CRISP score for SAE and CMAE.

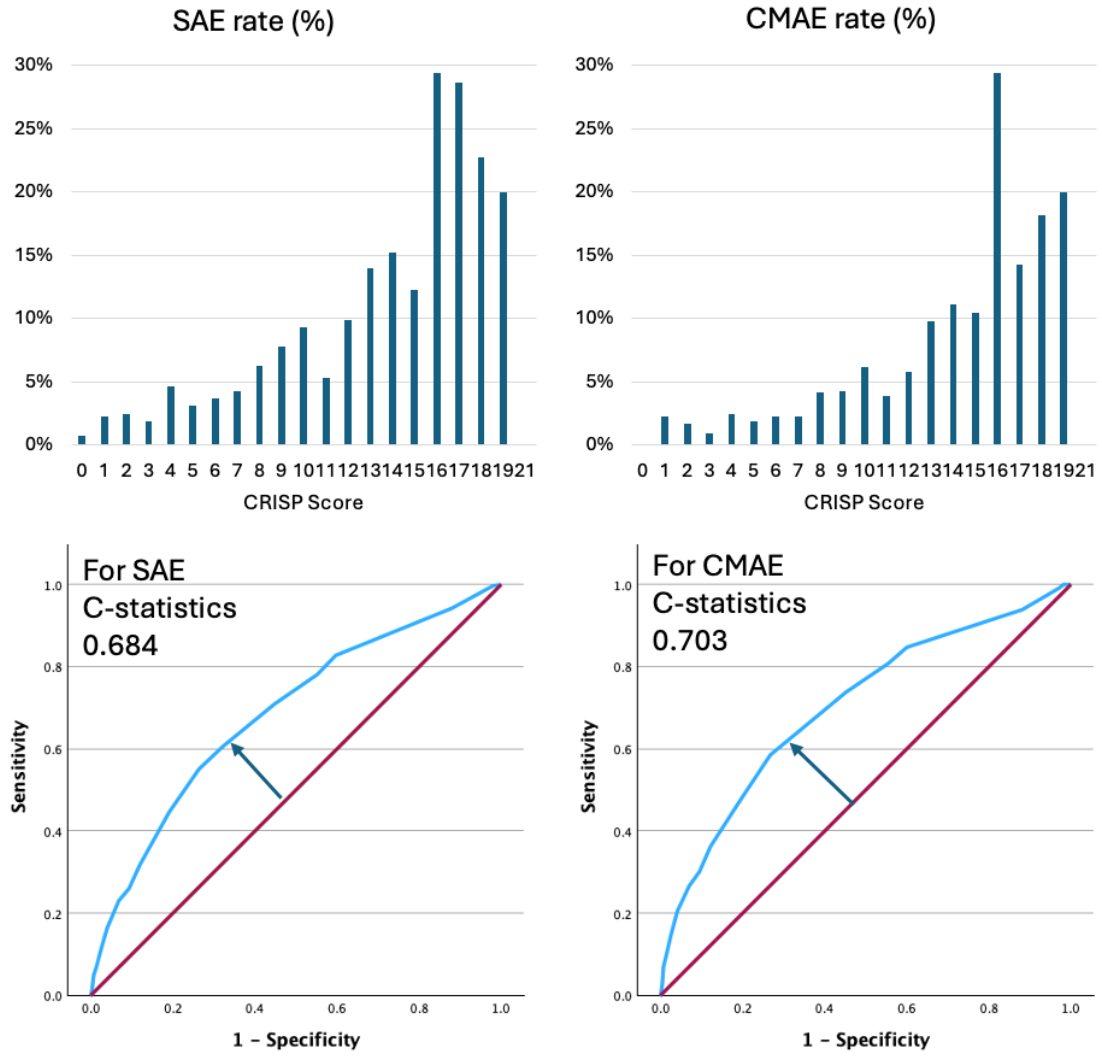

Figure 2. Rates of SAE and CMAE according to CRISP risk category.