Annual CCISC Meeting

PICS 2024 | September 6, 2024

[Agenda]

1. Forbes: Opening Remark
2. Kobayashi:
   - ✓ CRISP Registry
   - ✓ PFR Registry
   - ✓ New CRISP Registry Modules
3. Forbes: Closing and Q&A

CCISC
CRISP/CRISA
PFR/PASS/PAST/KA Trials

CCISC Consortium

Thomas Forbes, MD

CRISP Registry

- CRISP Registry is a Clinical Case Registry for Children and Adults undergoing Cardiac Catheterization in CCCL.
- CRISP Registry version 1 was launched in March 2008
- The initial goal of the CRISP Registry was to develop Risk Prediction Model/Score for Significant Adverse Event

2016 CRISP Score

Multicenter Study > Catheter Cardiovasc Interv. 2016 Feb 1;87(2):302-9.

doi: 10.1002/ccd.26300. Epub 2015 Nov 3.

CRISP: Catheterization RISk score for Pediatrics: A Report from the Congenital Cardiac Interventional Study Consortium (CCISC)

n=18,564

David G Nykanen [1], Thomas J Forbes [2], Wei Du [3], Abhay A Divekar [4], Jaxk H Reeves [5], Donald J Hagler [6], Thomas E Fagan [7], Carlos A C Pedra [8], Gregory A Fleming [9], Danyal M Khan [10], Alexander J Javois [11], Daniel H Gruenstein [12], Shakeel A Qureshi [13], Phillip M Moore [14], David H Wax [15]; Congenital Cardiac Interventional Study Consortium (CCISC)

2019 Validation of CRISP Score

Multicenter Study > Catheter Cardiovasc Interv. 2019 Jan 1;93(1):97-104.

doi: 10.1002/ccd.27837. Epub 2018 Sep 9.

n = 29,830

Validation and refinement of the catheterization RISk score for pediatrics (CRISP score): An analysis from the congenital cardiac interventional study consortium

Kevin D Hill [1 2], Wei Du [3 4], Gregory A Fleming [1 2], Thomas J Forbes [3 4], David G Nykanen [5 6], Jaxk Reeves [7], Yan Du [7], Daisuke Kobayashi [3 4]

2021 – Validation of CRSIP Score | UK/Ireland

Cardiol Young. 2021 Oct 14:1-8. doi: 10.1017/S1047951121004170. Online ahead of print.

Validating a risk assessment tool in United Kingdom and Irish paediatric cardiac catheterisation practice

Barry O'Callaghan [1 2], Emma Shepherd [2], Demetris Taliotis [2], James Bentham [3], Damien Kenny [4], Benjamin Smith [5], Salvador Rodriguez Franco [1], Gareth J Morgan [1 6]

CONCLUSION

- The CRISP score accurately predicts significant complications in congenital catheterisation practice in the United Kingdom and Ireland.
- Our data validated the CRISP assessment tool in five congenital centres.

2024 Spain

Use of a pediatric risk score for cardiac catheterization in a Spanish population with congenital heart disease

REC Inter Cardiol

Aplicación de una puntuación de riesgo pediátrico para cateterismo cardiaco en una población española con cardiopatía congénita

Paulo Éden Santos,[a] Fernando Ballesteros,[b] Alexandro Rodríguez,[b] and José Luis Zunzunegui[b]

CONCLUSIONS

- *The CRISP system is a relatively simple tool for risk assessment before catheterization in the CHD domain.*
- *Despite …, this model has proven accurate.*
- *We are confident that this score could also be extrapolated to all pediatric populations in Spain.*
- *We strongly believe that this scoring system can become a handy tool for risk prediction, thus planning and preparing procedures in advance.*
- *Finally, we suggest the use of CRISP before cardiac catheterization for procedural risk assessment planning.*

2019 CRISA Score

Multicenter Study > Am J Cardiol. 2019 May 1;123(9):1527-1531.
doi: 10.1016/j.amjcard.2019.01.042. Epub 2019 Feb 8.

A Model for Assessment of Catheterization Risk in Adults With Congenital Heart Disease

n=7317

Nathaniel W Taggart [1], Wei Du [2], Thomas J Forbes [3], David G Nykanen [4], David F Wax [5], Allison K Cabalka [6], Jaxk H Reeves [7], Yan Du [7], Daisuke Kobayashi [3]

CCISC | Device Approval Effort | Research

- In May 2018, FDA approached CCISC to develop a method of using Registries to further device approval in the US.
- CCISC/CRISP Registry is a QI/QA registry having a RESEARCH component, that goes through a formal IRB approval process.
- Emphasis on device approval projects, collaborating with FDA and vendors.

CCISC Research Project – KA Microplug

Retrospective Data Collection for IDE Application for Limited Prospective Clinical Trial for PMA

January 2023 planned for Discontinuation

Submitted retrospective data per CCISC June 21st, 2024

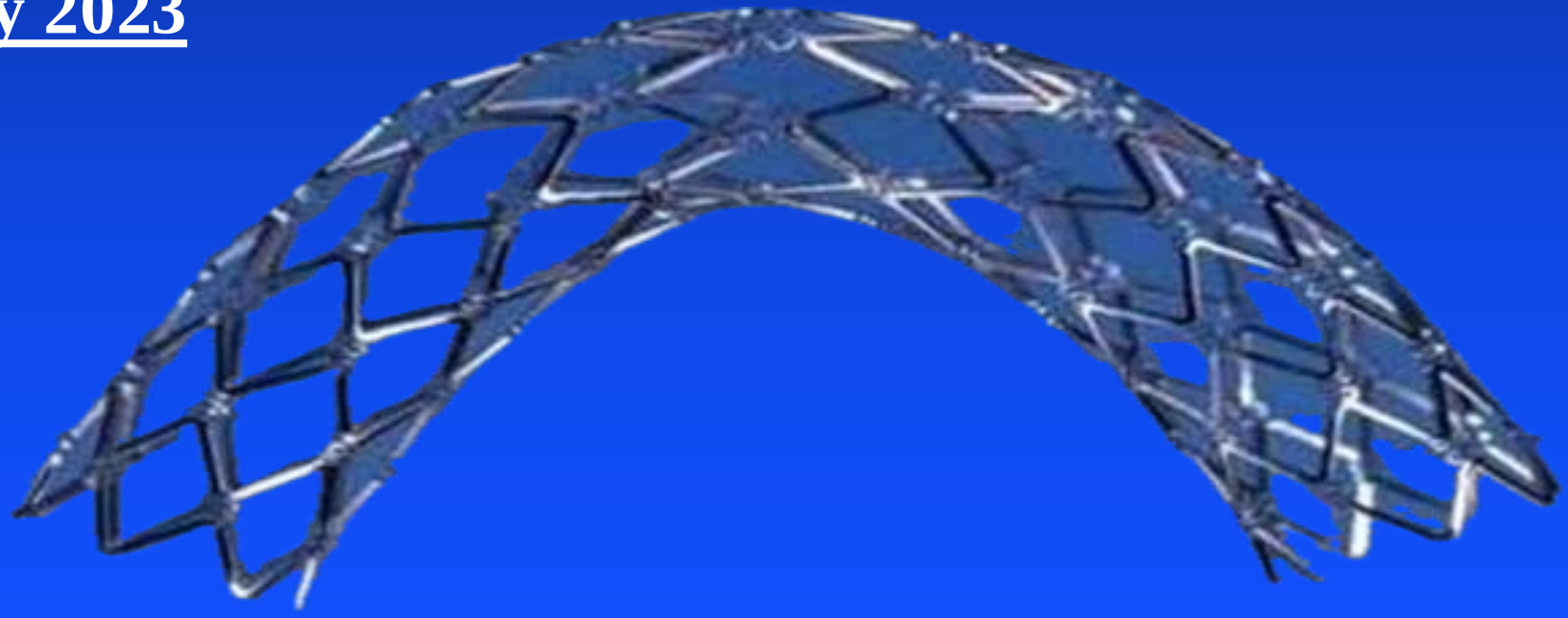
January 2025 Launch Prospective trial

CCISC Research Project – Genesis XD stent

PMA for Genesis XD stent based on retrospective Data Collection

PALMAZ MULLINS XD Pulmonary Stent

PMA granted in July 2023



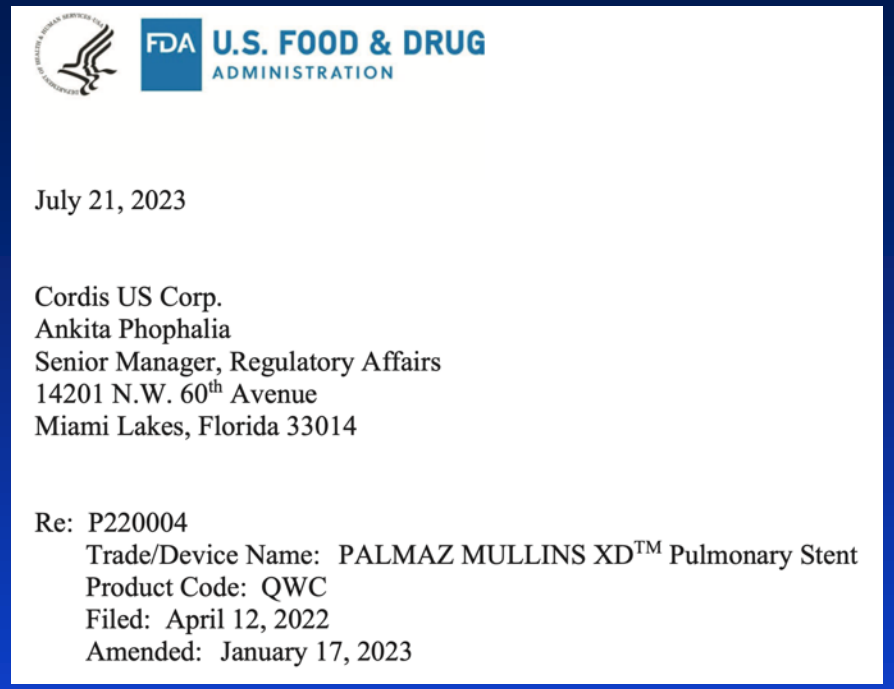
FDA Document
(Summary of Safety and Effectiveness Data)

- The PASS (Pulmonary Artery Stent Study) was the basis of the PMA approval decision.

- The PASS study was based on a retrospective data captured in the CCISC Registry.

FDA Approval Letter (July 21, 2023)

"You must obtain approval of your post-approval study (PAS) as noted below"



U.S. FOOD & DRUG ADMINISTRATION

July 21, 2023

Cordis US Corp.
Ankita Phophalia
Senior Manager, Regulatory Affairs
14201 N.W. 60th Avenue
Miami Lakes, Florida 33014

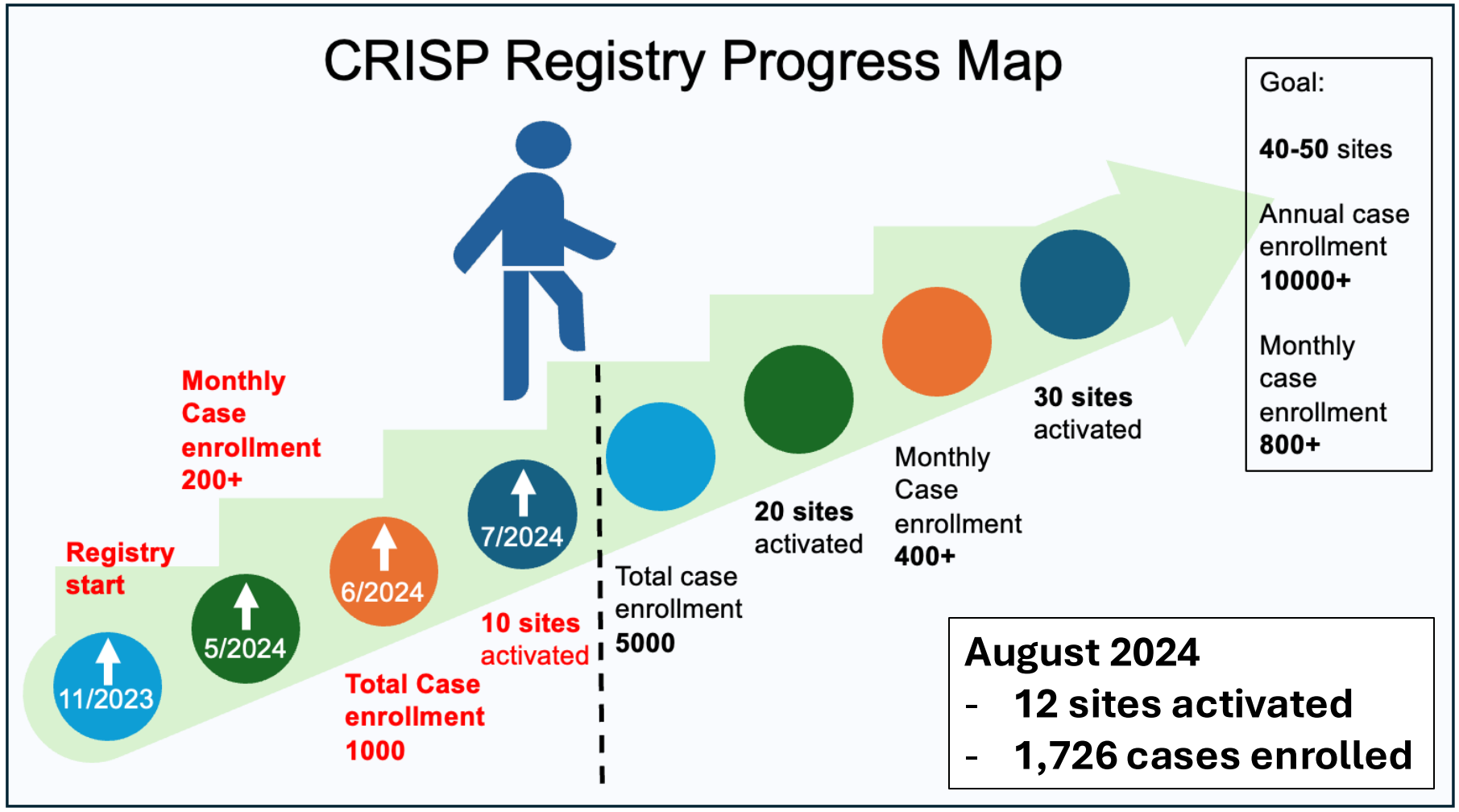
Re: P220004
Trade/Device Name: PALMAZ MULLINS XD™ Pulmonary Stent
Product Code: QWC
Filed: April 12, 2022
Amended: January 17, 2023

PALMAZ MULLINS XD Pulmonary Stent Real-World Use: You have agreed to conduct a prospective, single-arm, multi-center study of consecutive patients treated with the PALMAZ MULLINS XD™ Pulmonary Stent. This study will be carried out to characterize clinical outcomes and to assess the real-world use of the commercial PALMAZ MULLINS XD™ Pulmonary Stent. The study will enroll a minimum of 35 subjects, and will continue until the enrollment of 75 subjects or two years from the time of study activation,

Real-World Use data → CRISP Registry PA stent module

CRISP Registry

CRISP Registry version 3



Site Participation Process

Activated

No.	Site
1	Joe DiMaggio Children's Hospital
2	Children's Minnesota
3	University of Mississippi
4	Ann Lurie Children's Hospital
5	Arnold Palmer Hospital for Children
6	Children's Hospital of New Orleans
7	University of Minnesota
8	Children's Hospital Colorado
9	Atrium Health Levine Children's Hp
10	Duke University
11	Inova Fairfax Children's Hospital
12	Children's Mercy Hospital Kansas City

IRB/contract process

No.	Site
13	University of Virginia
14	Helen DeVos Children's Hospital
15	Wolfson Children's Hospital
16	St. Joseph Children's Hospital Tampa
17	Children's Hospital of Michigan / CMU
18	Advocate Children's Hospital
19	Children's Medical Center Dallas - UTSW
21	St. Louis Children's Hospital / WashU
22	Mayo Clinic
23	Nicklaus Children's Hp Miami
24	Children's Memorial Hermann Hp

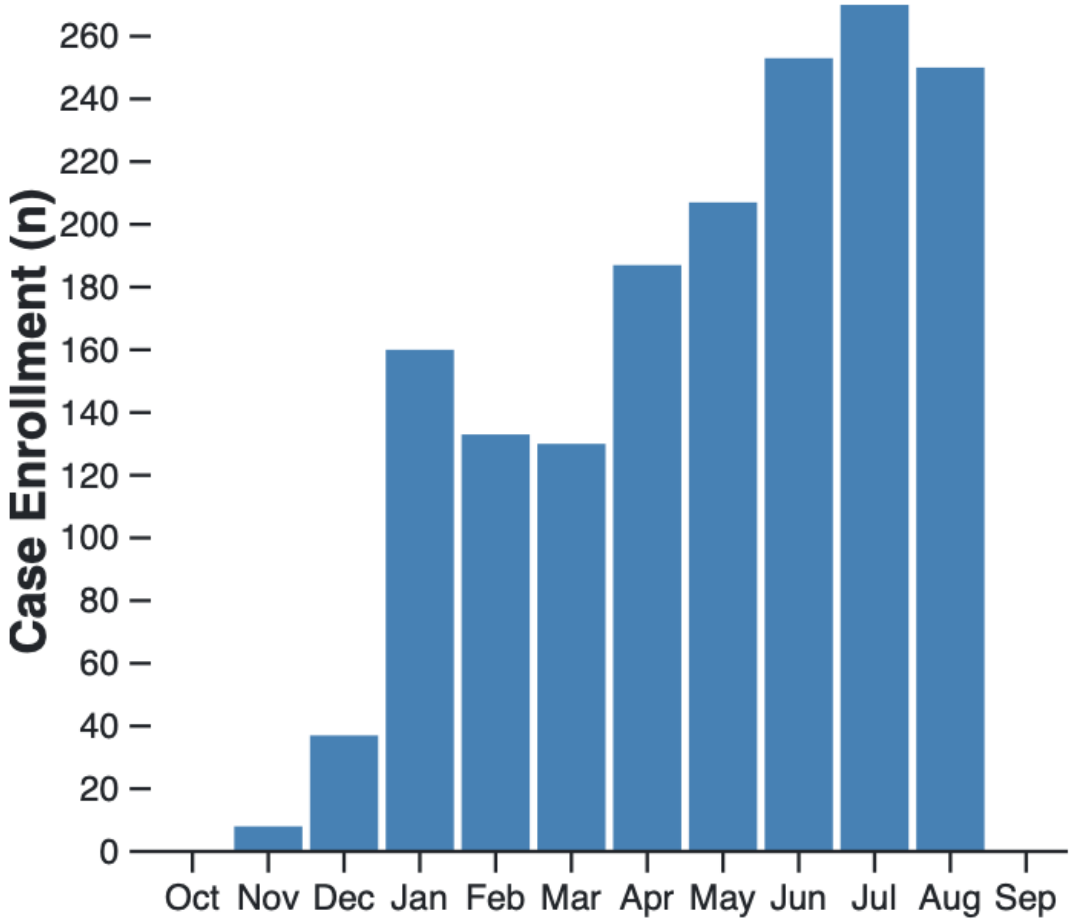
No.	Sites considering participation
25	Medical City, Dallas
26	Driscoll Children's Hospital
27	UCSF
28	Loma Linda University
29	University of Iowa
39	University of Texas at Austin
31	Cardinal Glennon Children's Hospital
32	Cleveland Clinic
33	University of Alabama
34	University of Oklahoma
35	Valley Children's Hospital

12 sites – Activated

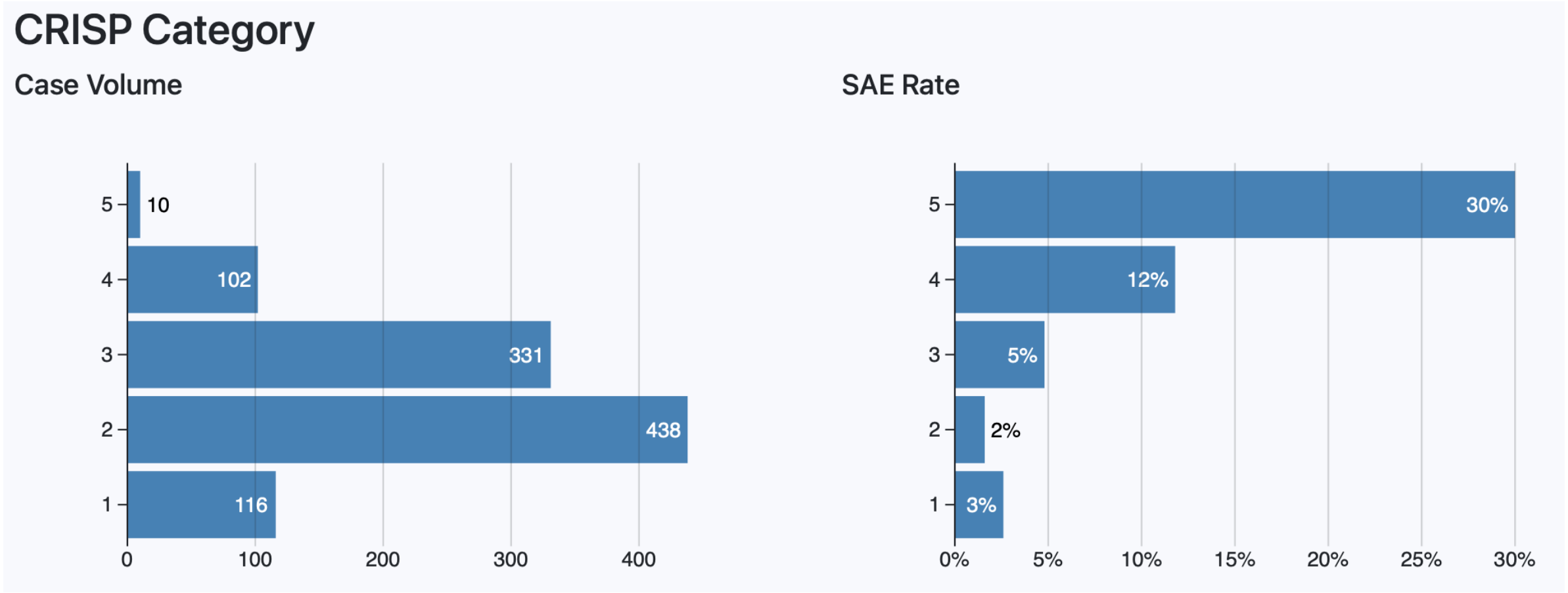
12 sites – IRB/contract process

11 sites – Considering participation

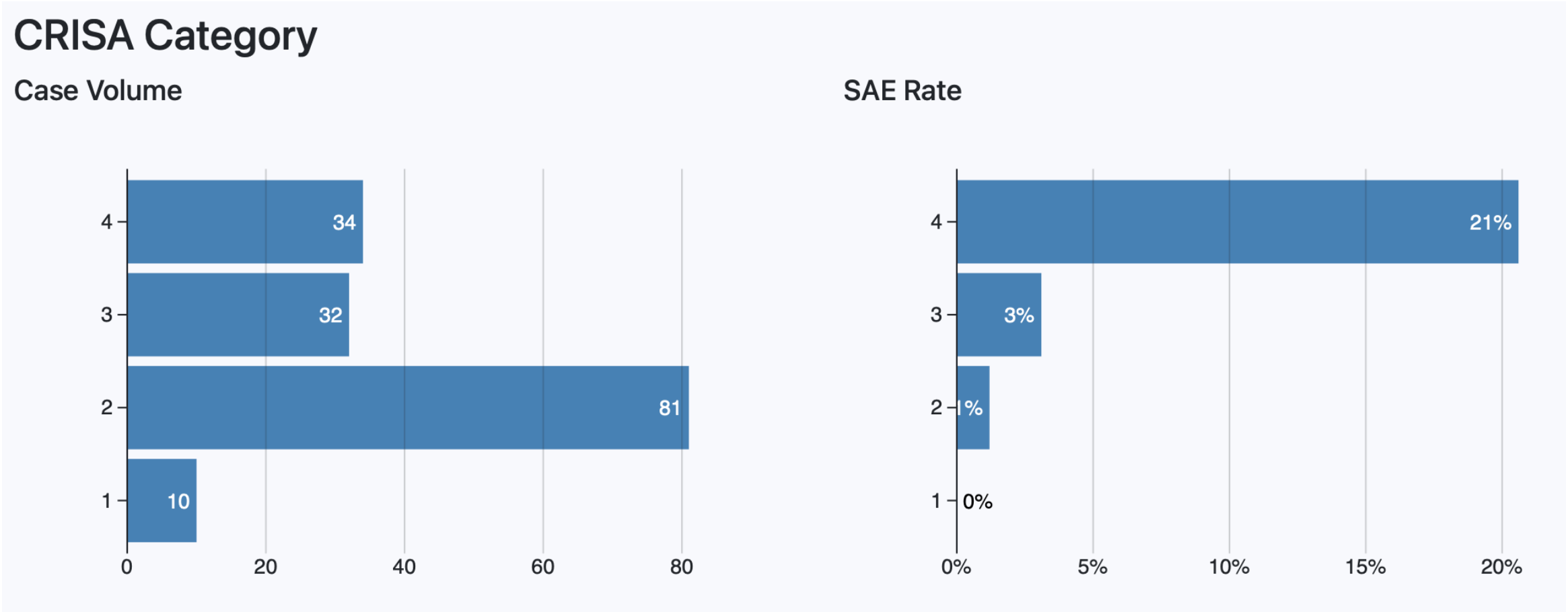
Growth of Case Enrollment



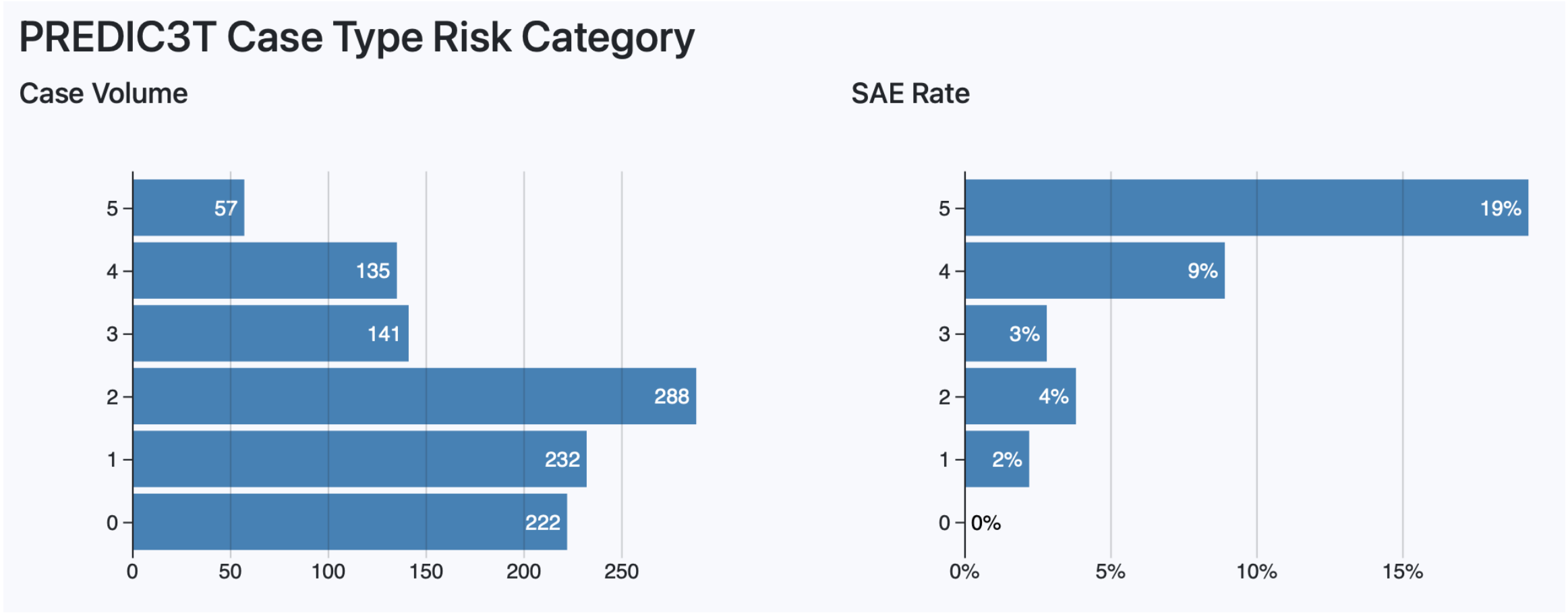
Risk Prediction Performance - CRISP Category (n=997)



Risk Prediction Performance - CRISA Category (n=157)

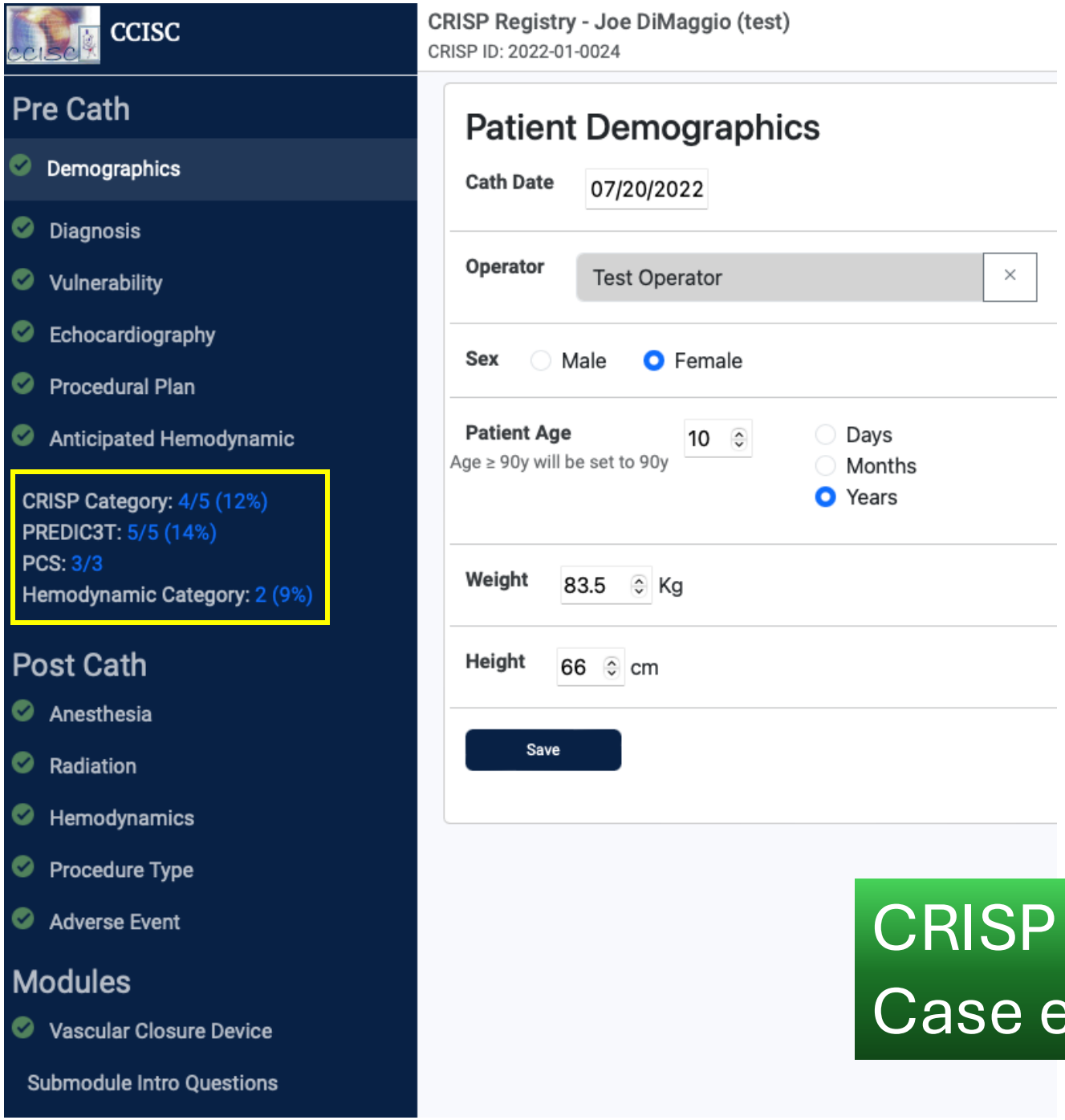


Risk Prediction Performance
- PREDIC^{3}T Case Type Risk Category (n=1,075)



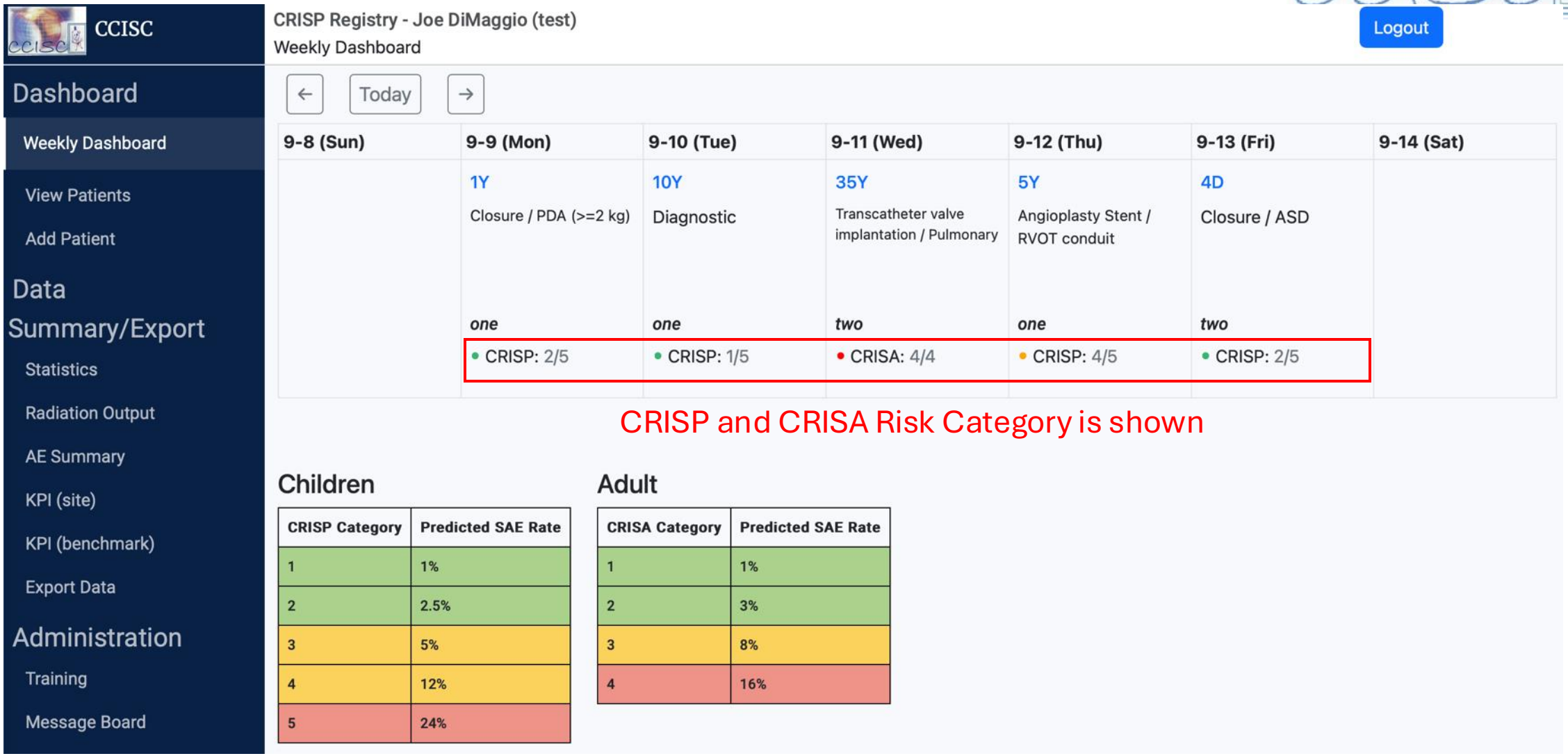
“Pre Cath” data

Risk Prediction Calculator



CRISP Registry
Case entry interface

Risk Prediction - Weekly Dashboard



CRISP and CRISA Risk Category is shown

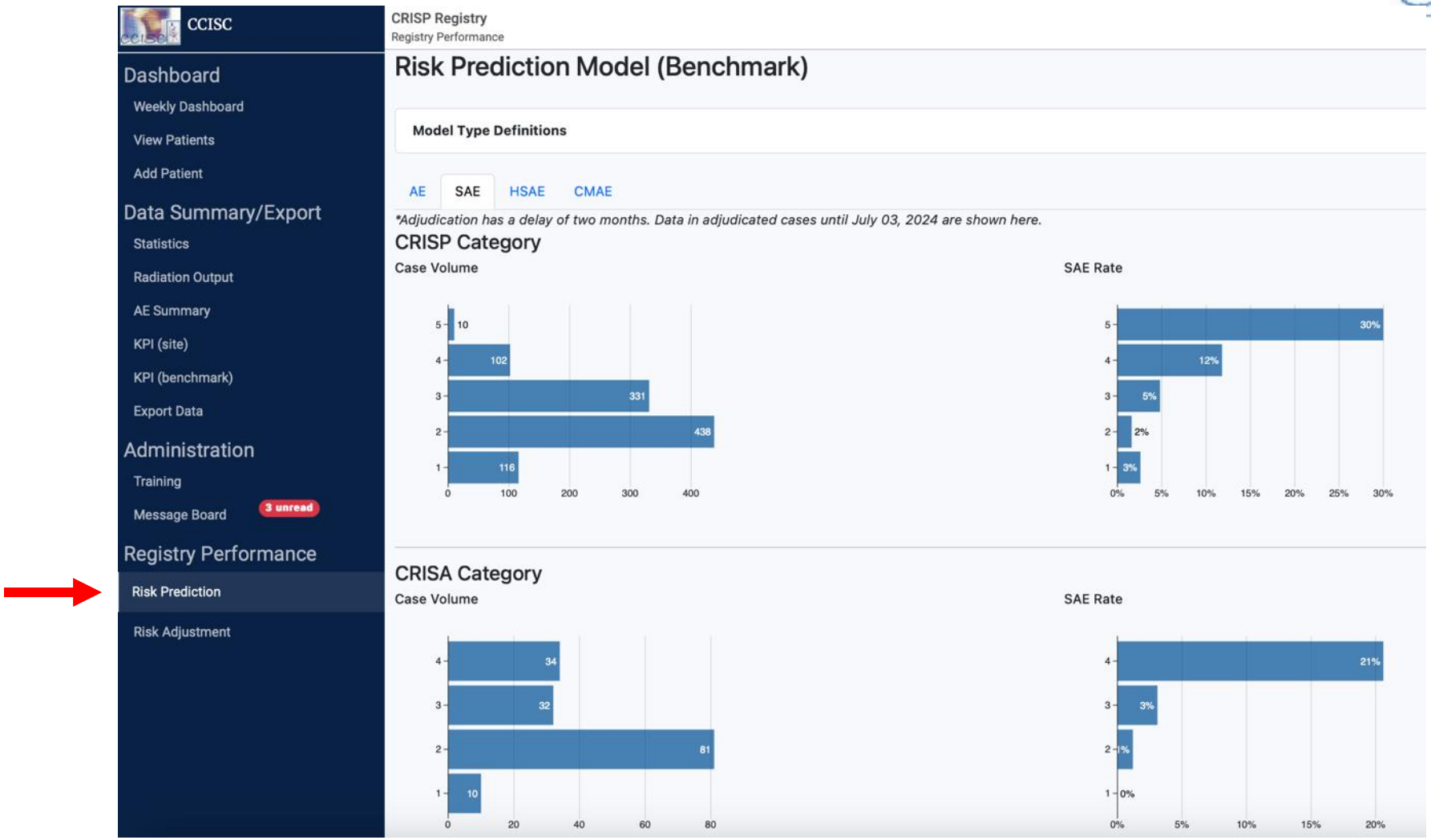
Children

CRISP Category	Predicted SAE Rate
1	1%
2	2.5%
3	5%
4	12%
5	24%

Adult

CRISA Category	Predicted SAE Rate
1	1%
2	3%
3	8%
4	16%

Real-Time Data Output



Interoperability with C3PO and IMPACT Registries

- Data Standards: Use common data elements and definition
- Outcome measures: Adverse event severity grading, radiation dose measure (uGym2/kg)
- Utilization of published classification system:
  - Risk models (CHARM II model, PREDIC3T case type risk category)
  - Radiation exposure category

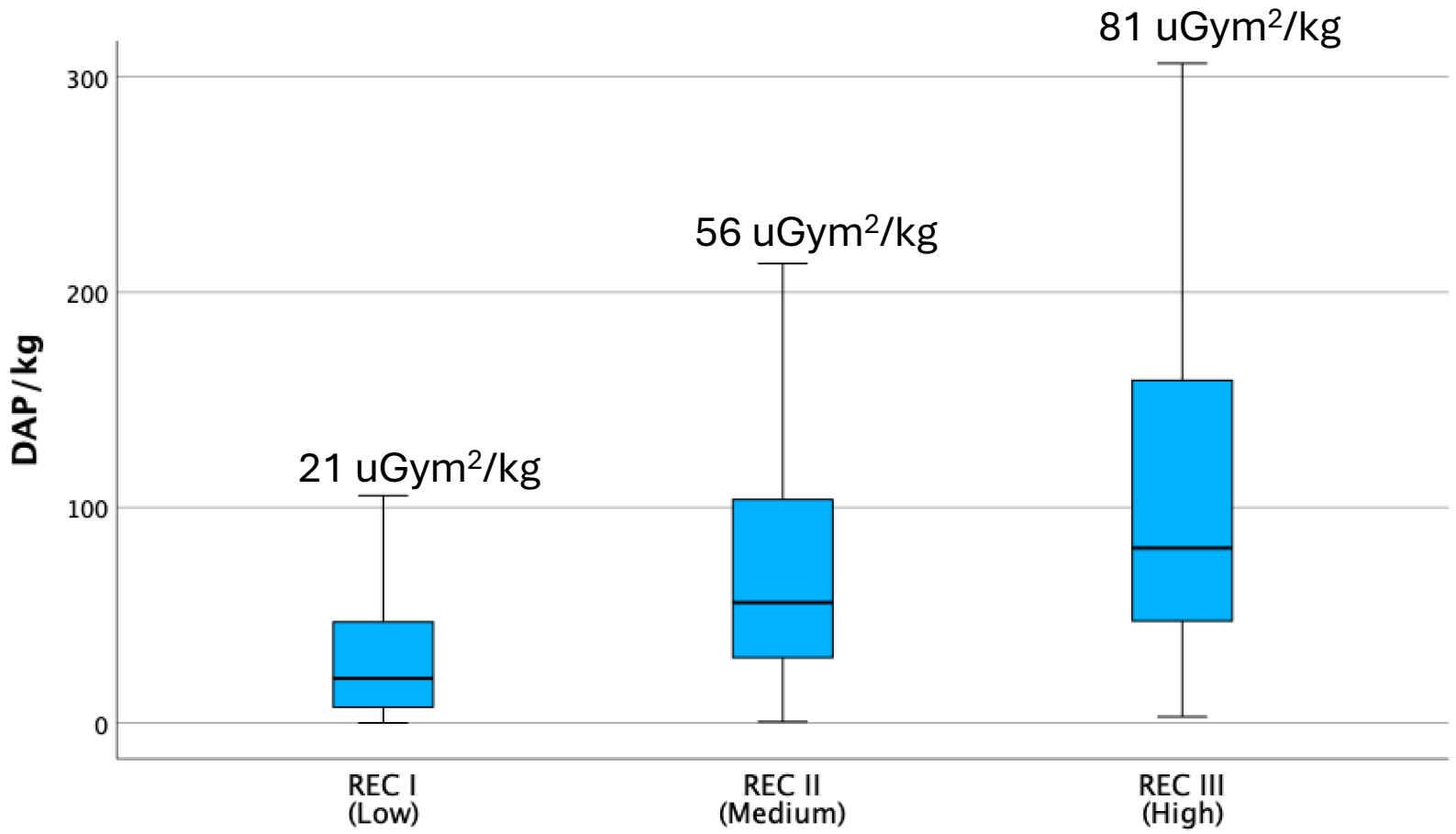
Radiation Dosage Reporting
- C3PO Registry Radiation Exposure Categories

Table 1. Radiation Exposure Categories

Category I (Low)	Category II (Medium)	Category III (High)
Biopsy	Proximal pulmonary angioplasty or stent	Mitral valvotomy+intervention*
ASD or PFO closure	VSD device closure+intervention*	TPV implantation
PDA device or coil closure	RVOT dilation/stent	≥2 vessel proximal or distal angioplasty or stent
Vasodilator testing	ASD or PFO closure+intervention*	Coil systemic pulmonary collateral+intervention*
Atrial septostomy	Venous collateral closure	Aortic valvotomy+intervention*
Pulmonary valvotomy	Distal pulmonary angioplasty or stent	RVOT dilation/stent and ≥2 vessel proximal or distal pulmonary angioplasty or stent
Biopsy+CA	Aorta dilation/stent+intervention*	TPV implantation and PA intervention*
PDA stent placement	Atrial needle transeptal puncture	≥2 vessel proximal or distal pulmonary angioplasty or stent+intervention*
Diagnostic catheterization	Atrial septostomy+intervention*	Pulmonary vein dilation or stent
Fenestration device closure	Coil systemic pulmonary collateral	TPV implantation+intervention*
Aortic valvotomy	Proximal R and L pulmonary angioplasty	Pulmonary vein dilation or stent+intervention*
Aorta dilation and/or stent	Proximal or distal pulmonary angioplasty or stent+intervention*	
Pulmonary valvotomy+intervention*	Atretic valve perforation	
	Atrial septum stent placement	
	Fenestration device closure+intervention*	
	RVOT dilation or stent+proximal pulmonary angioplasty or stent	

Quinn BP 2020 Circ Cardiovasc Interv

Case Stratification Stratified by REC (n=1,436)



n=1,115

n=198

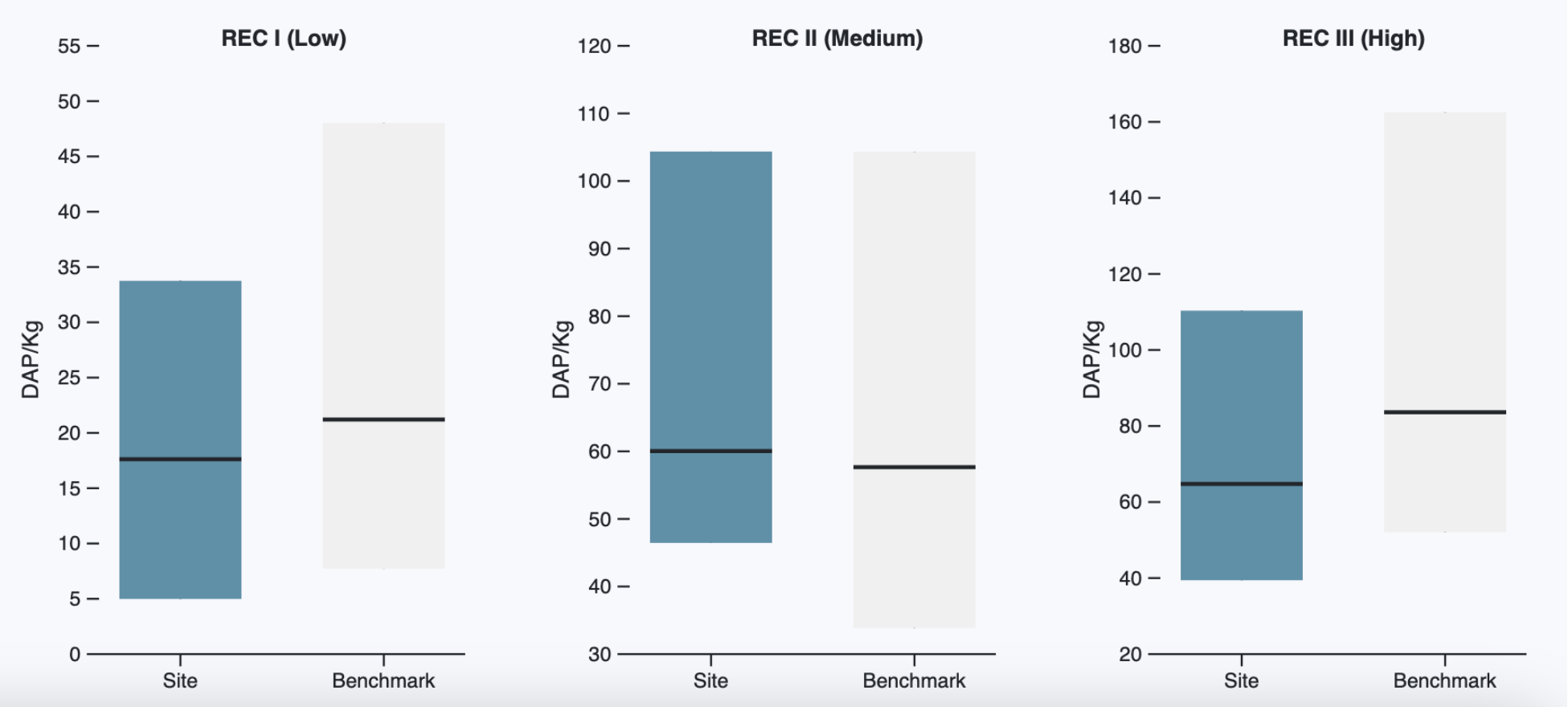
n=123

Not classified (n=193, 12%)

CCISC

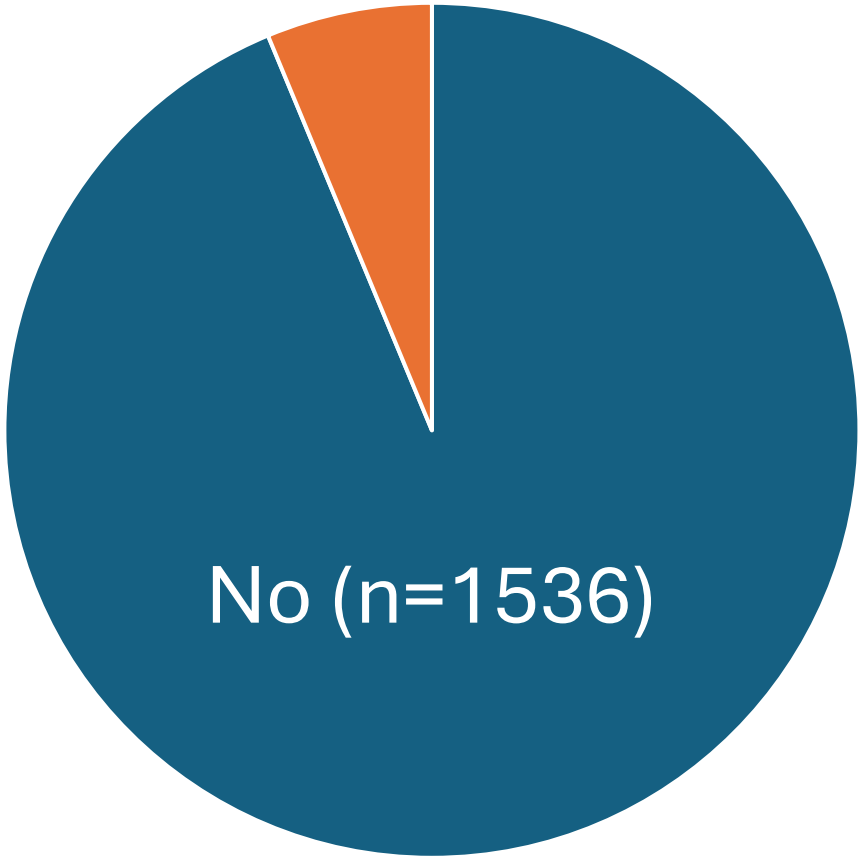
- Dashboard
  - Weekly Dashboard
  - View Patients
  - Add Patient
- Data Summary/Export
  - Statistics
  - Radiation Output
  - AE Summary
  - KPI (site)
  - KPI (benchmark)
  - Export Data
- Administration
  - Training
  - Message Board (3 unread)
- Registry Performance
  - Risk Prediction
  - Risk Adjustment

Radiation Dose Real Time Reporting (Site vs. Benchmark)



All the adverse events are adjudicated

Any AE 6.3%
(n=102)



AE Level (C3PO – CHARM II Paper)

Table 1. Definitions of Adverse Event Severity Including Level 3 Tiers

Level 1: none	No harm, no change in condition, may have required monitoring to assess for potential change in condition with no intervention indicated.
Level 2: minor	Transient change in condition, not life-threatening, condition returns to baseline, requiring monitoring, required minor intervention such as holding a medication or obtaining a laboratory test.
Level 3: moderate	Transient change in condition may be life-threatening if not treated, condition returns to baseline, required monitoring, required intervention such as reversal agent, additional medication, transfer to the intensive care unit for monitoring, or transcatheter intervention to correct condition.
Tier 3A	Event resulting in minimal impact to patient's baseline hemodynamics or condition; requires minor medical or transcatheter therapy to completely reverse the condition with little risk of any long-term impact. Anticipated requirement for medical support during the intervention or in the immediate postcatheterization period necessary to treat the condition. Transient and treatable events related to patient's underlying condition, which are exacerbated by the procedure.
Tier 3B	Transient event that results in moderate change in baseline hemodynamics or condition requiring moderate medical therapy or transcatheter intervention to treat the condition.
Tier 3C	Event resulting in significant impact to patient's baseline hemodynamics or condition requiring major medical therapy or complex transcatheter intervention. May require intensive care unit admission for invasive monitoring or prolonged need for medical or ventilatory support, including follow-up testing and nonsurgical procedures. May result in a life-threatening event if intensive therapy is unable to promptly rescue the patient, preventing a major or catastrophic event from occurring.
Level 4: major	Change in the patient's clinical condition, which is life-threatening and requires intense medical therapy, cardiopulmonary resuscitation, or major invasive transcatheter or urgent/emergent surgical intervention to treat the condition. These conditions may also result in the need for unplanned cardiopulmonary support in the form of heart-lung bypass (ECMO) to prevent a catastrophic event from occurring.
Level 5: catastrophic	Any death and emergent surgery or heart-lung bypass support (ECMO) to prevent death with failure to wean from bypass support.

Circ CV interv 2024

Admin Page – AE Adjudication Process

CCISC Home Publications Admin Audit Trail About Newsletter Risk Calculator ABP MOC

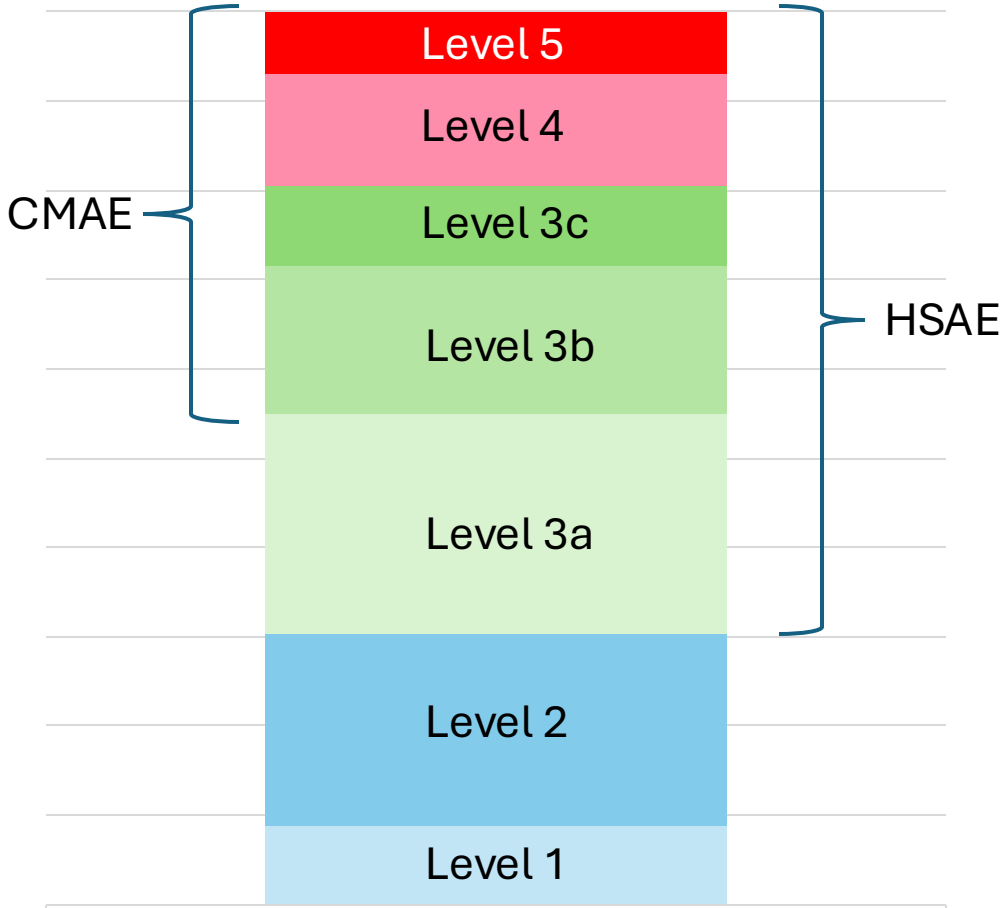
< Go back to Admin page

Adjudication Filter: Need Adjudication

>=30 day after date of cath: Yes

Search:

CRISP ID	Cath Date	AE	Pt. Status	SAE	Need Adjudication	Pending Message Board	Update
2024-03-0504	8/2/2024	Yes (grade 2)	submitted		Need Adjudication	Go to thread	Update
2024-02-0137	7/29/2024	Yes (grade 3a)	submitted		Need Adjudication	Go to thread	Update
2024-03-0474	8/1/2024	Yes (grade 3a)	submitted		Need Adjudication	Go to thread	Update
2024-11-0086	4/9/2024	Yes (grade 3a)	submitted		Need Adjudication	Go to thread	Update
2024-13-0004	7/31/2024	Yes (grade 3a)	submitted		Need Adjudication	Go to thread	Update
2024-03-0497	8/1/2024	Yes (grade 3c)	submitted		Need Adjudication	Go to thread	Update
2024-12-0105	8/1/2024	Yes (grade 4)	submitted		Need Adjudication	Go to thread	Update



	AE
5	7
4	13
3c	9
3b	17
3a	25
2	22
1	9

AE Level in All Cases

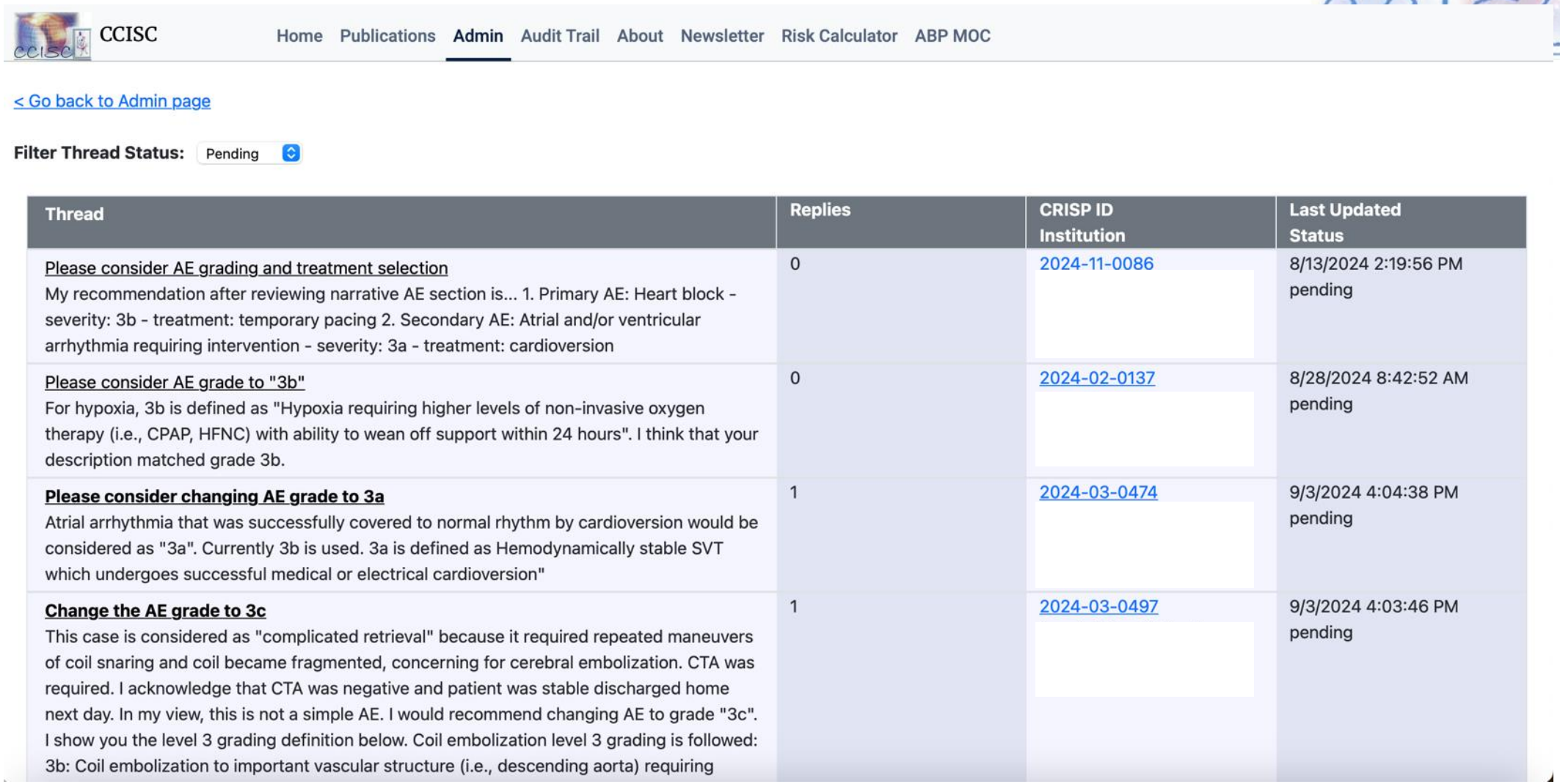
SAE rate 3.1% (50/1629)

↓ Exclude biopsy cases (n=309)

SAE rate 3.8%
Diagnostic + Interventional Cases
(SAE 50/1320)

C3PO AE outcome measures
HSAE (3abc45): 4.1% (54/1320)
CMAE (3bc45): 2.7% (36/1320)

Message Board between Registry and Sites



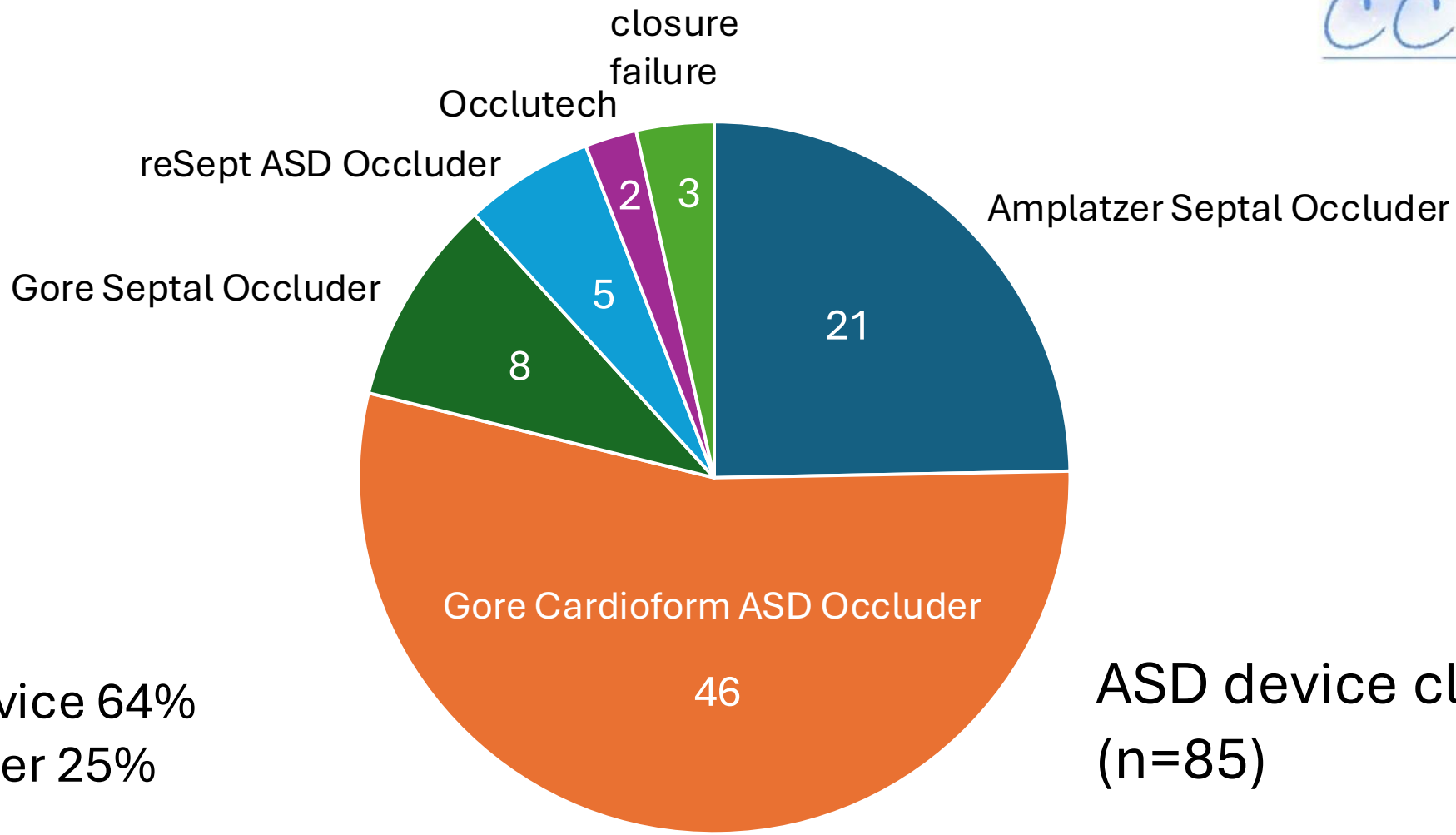
CRISP Registry
- Cardiac Device Use Monitoring

- Device Types
  - PDA closure device
  - CoA stent
  - RVOT stent
  - Pulmonary artery stent
  - Pulmonary vein stent

- Device Types
  - PDA stent
  - TPVI type
  - ASD/PFO closure device
  - Vascular closure device

Device Data – ASD Device Closure

(2024 – limited to 12 sites)

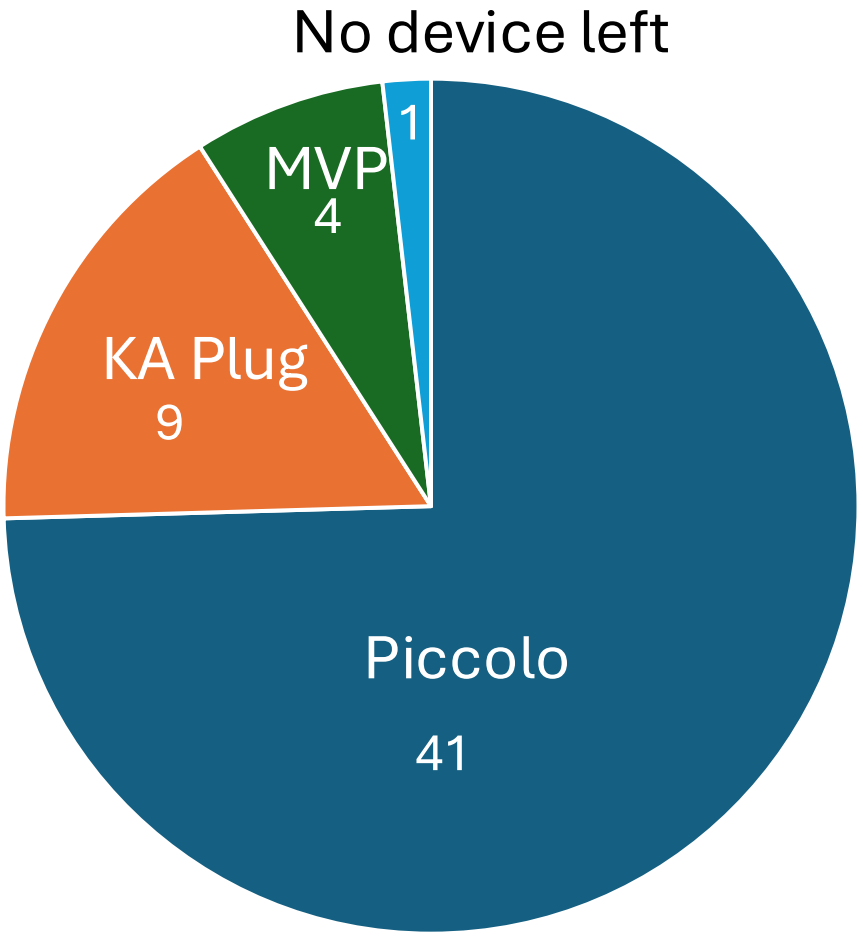


Gore device 64%

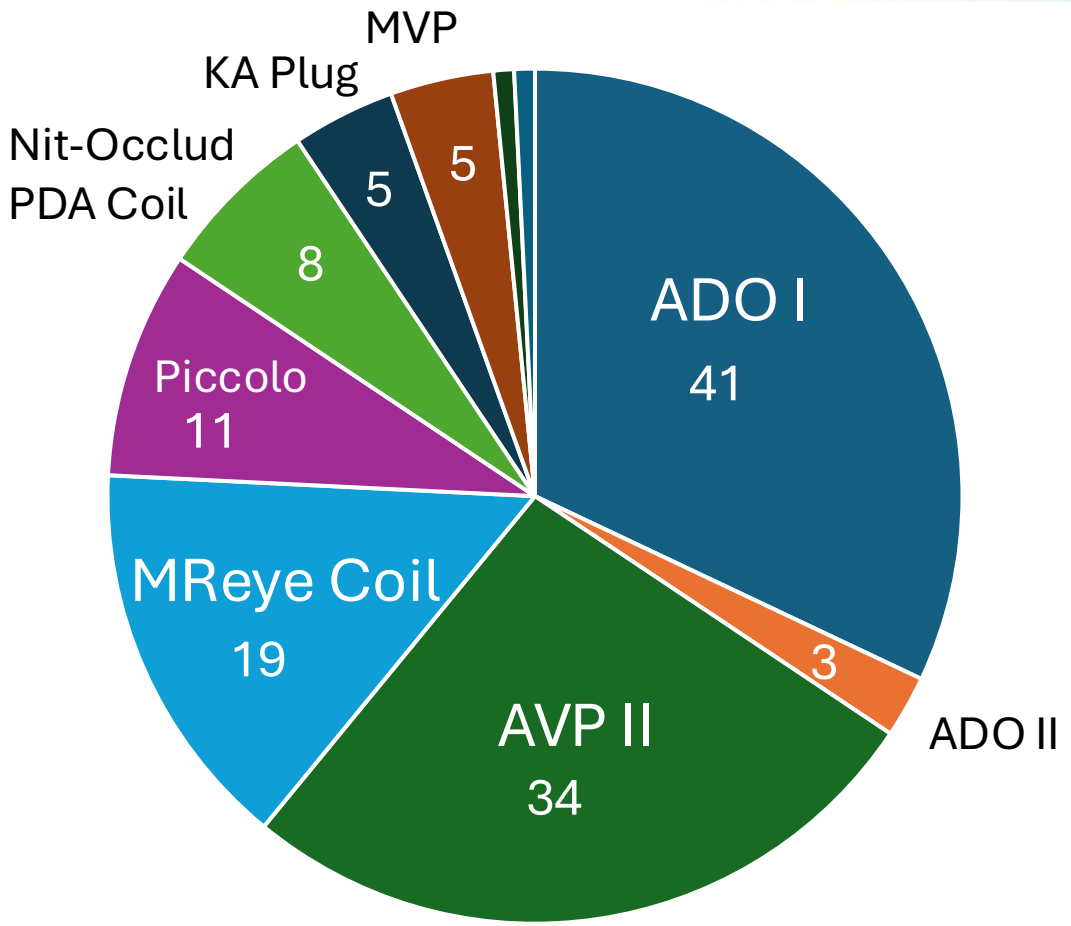
Amplatzer 25%

ASD device closure (n=85)

Device Data – PDA Device Closure
(2024 – limited to 12 sites)

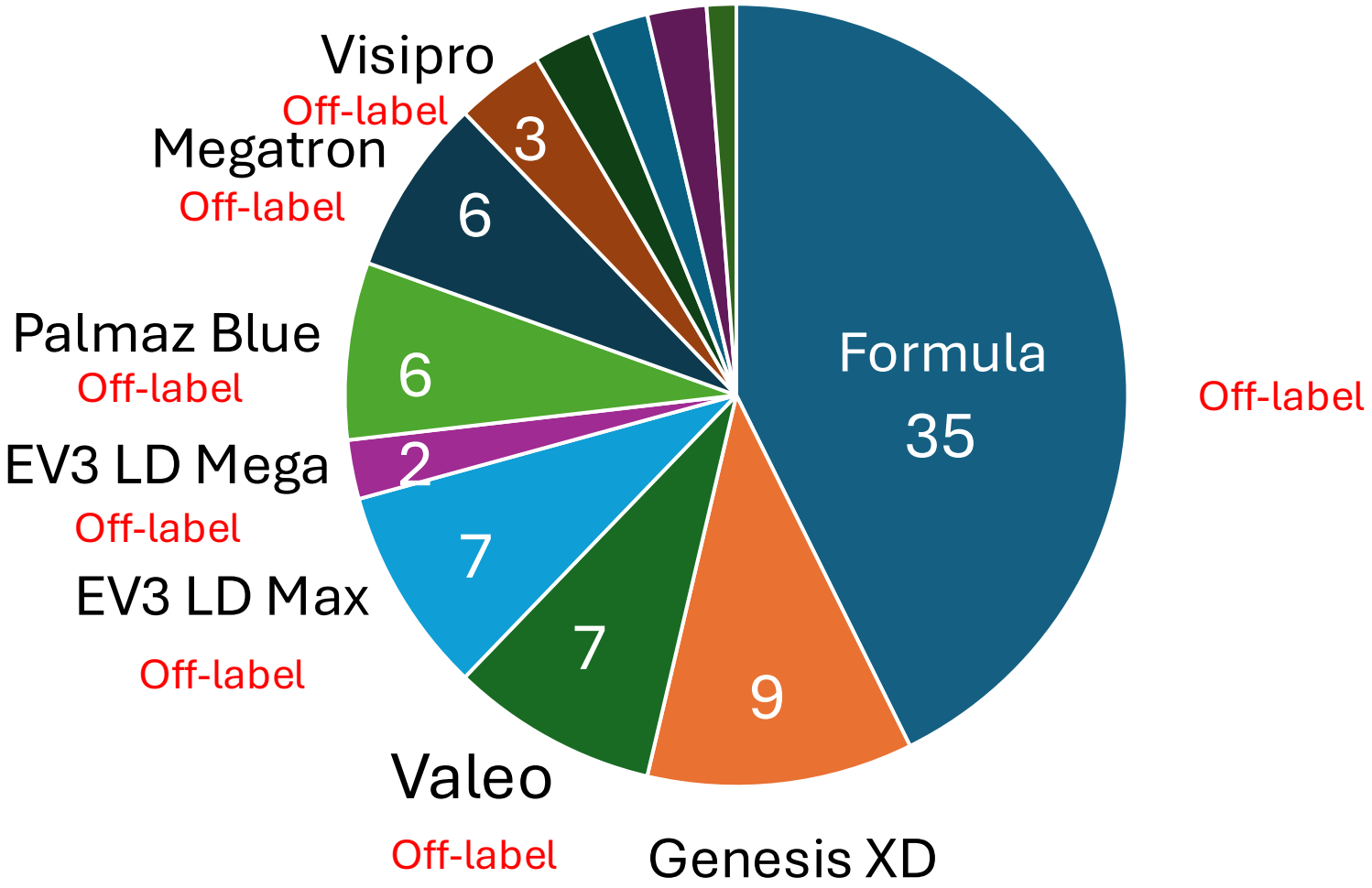


<2 kg (n=55)



>=2 kg (n=128)

Device Data – PA Stent (n=82)
(2024 – limited to 12 sites)



Future Direction – CRISP Registry

- Complete the initial site participation process
- Continue to improve the registry interface
  - Real time data presentation and reporting
    *Users do not need wait until quarterly or annual report
  - Real time practice variation reporting – cardiac devices
- Research projects based on version 3 dataset
  - New risk prediction model
  - Original risk adjustment model
  - Original radiation exposure category
  - Projects targeted on special cohorts and unique case types
- CRISP registry driven radiation reduction initiatives
- New modules
  - ASD device closure
  - PA stent
  - PDA device closure

Please Join the CRISP Registry

- Please contact with
  - ✓Thomas Forbes (National PI)
  - ✓Daisuke Kobayashi (National PI)
  - ✓Nancy Sullivan (Program Manager)
- CRISP Registry is open to **ANY** institutions as far as they commit themselves to enter data consistently, accurately and timely.
- Participation Process
  - Local IRB approval (expedited in nature)
  - Participation agreement with MHS
  - Annual participation fee ($3,500/year)

Jump to CCISC website

new.ccisc.net

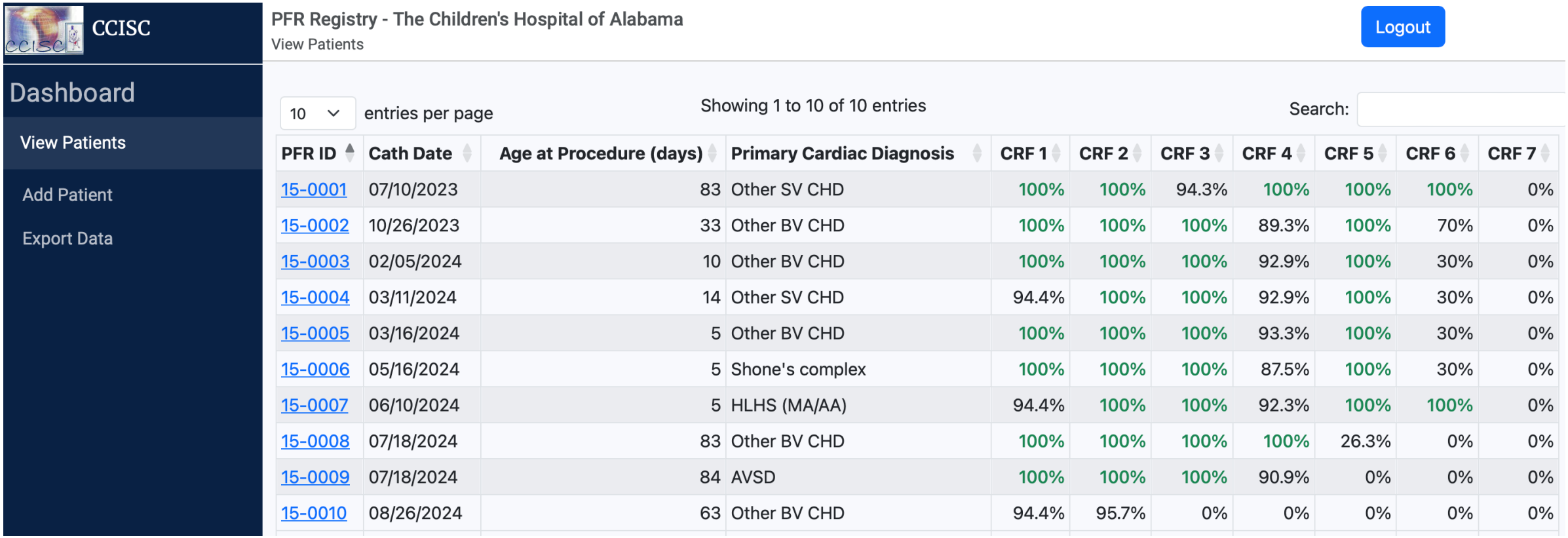
PFR Registry

Site Participation Process

No.	Site	IRB approval	Participation agreement	Site Activation	Number of enrollment
1	Children's Hospital of Colorado	✓	✓	6/26/2024	2
2	Joe DiMaggio Children's Hospital	✓	✓	8/7/2024	5
3	Children's of Alabama at Birmingham	✓	✓	8/22/2024	9
4	Children's Minnesota	✓	✓	8/28/2024	1
5	St. Louis Children's Hospital / WashU	✓	To site		
6	OSF Healthcare Children's Hospital of Illinois	✓	process		
7	Wolfson Children's Hospital	✓	To site		
8	University of Minnesota	✓	process		
9	Vanderbilt University	✓	To site		
10	Ann & Robert H. Lurie Children's Hospital	✓			
11	Columbia Presbyterian Hospital	✓			
12	Children's Hospital of Los Angeles	✓	✓		
13	Phoenix Children's Hospital		✓		
14	University of Texas Memorial Hermann	✓	To site		

Participation preparation	Consideration
- Mayo clinic - Johns Hopkins All Children's Heart Institute - Nicklaus Children's Hospital - Duke University - Texas Children's Hospital - Children's Hospital of Michigan (Detroit)	- Cincinnati Children's Hospital - Advent Health for Children - Children's Hospital of Los Angeles - Children's Hospital of Richmond / VCU

Interface – PFR Registry | View Patients



CCISC

Dashboard

View Patients

Add Patient

Export Data

PFR Registry - The Children's Hospital of Alabama

View Patients

Logout

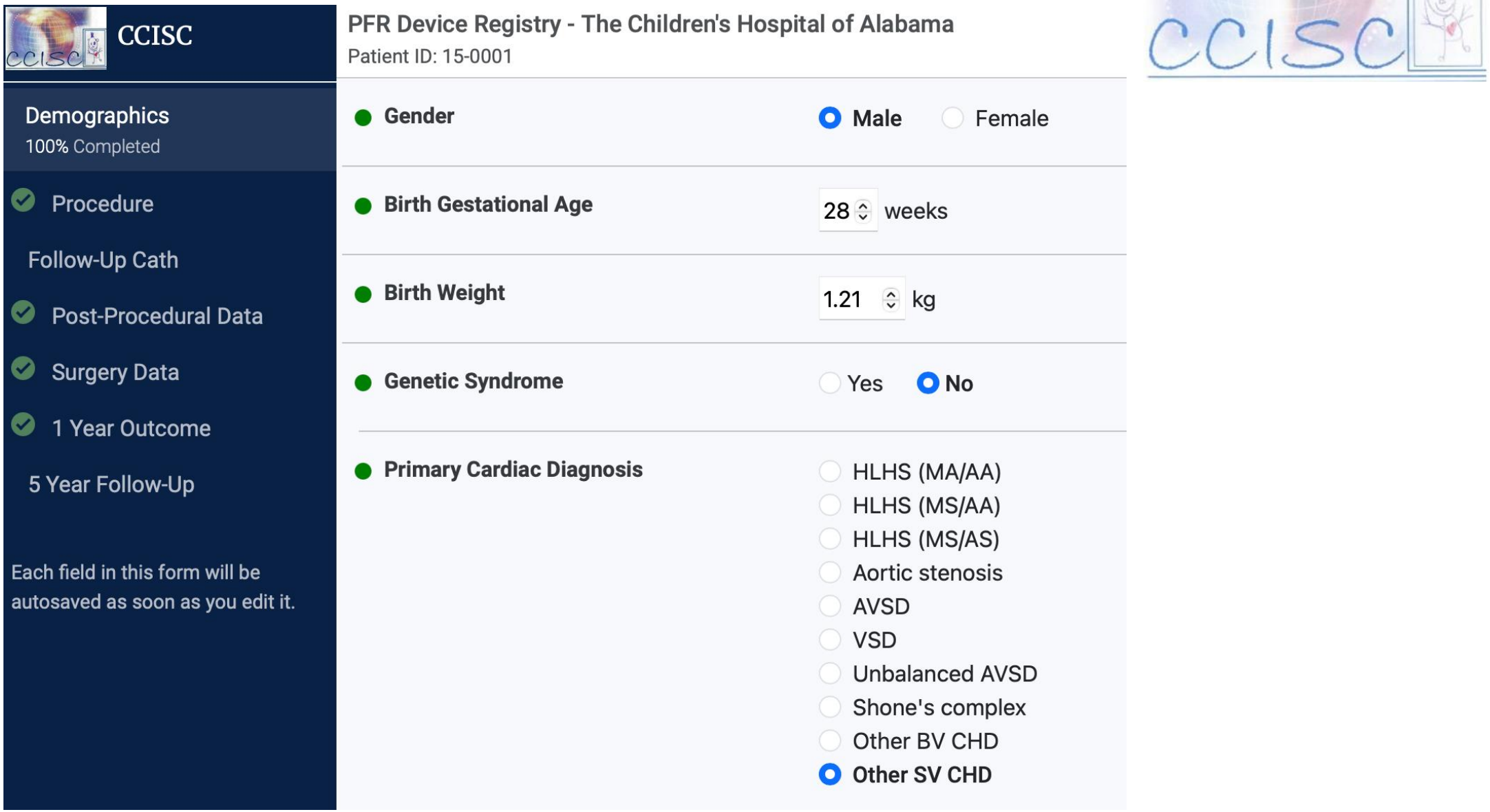
10 entries per page

Showing 1 to 10 of 10 entries

Search:

PFR ID	Cath Date	Age at Procedure (days)	Primary Cardiac Diagnosis	CRF 1	CRF 2	CRF 3	CRF 4	CRF 5	CRF 6	CRF 7
15-0001	07/10/2023	83	Other SV CHD	100%	100%	94.3%	100%	100%	100%	0%
15-0002	10/26/2023	33	Other BV CHD	100%	100%	100%	89.3%	100%	70%	0%
15-0003	02/05/2024	10	Other BV CHD	100%	100%	100%	92.9%	100%	30%	0%
15-0004	03/11/2024	14	Other SV CHD	94.4%	100%	100%	92.9%	100%	30%	0%
15-0005	03/16/2024	5	Other BV CHD	100%	100%	100%	93.3%	100%	30%	0%
15-0006	05/16/2024	5	Shone's complex	100%	100%	100%	87.5%	100%	30%	0%
15-0007	06/10/2024	5	HLHS (MA/AA)	94.4%	100%	100%	92.3%	100%	100%	0%
15-0008	07/18/2024	83	Other BV CHD	100%	100%	100%	100%	26.3%	0%	0%
15-0009	07/18/2024	84	AVSD	100%	100%	100%	90.9%	0%	0%	0%
15-0010	08/26/2024	63	Other BV CHD	94.4%	95.7%	0%	0%	0%	0%	0%

Interface – PFR Registry | Case Entry



Please Join the PFR Registry

- Please contact with
  - ✓Dave Balzer (National PI)
  - ✓Thomas Forbes (National PI)
  - ✓Daisuke Kobayashi (Sub-I)
  - ✓Nancy Sullivan (Program Manager)
- PFR Registry is open to **ANY** institutions.
- No need to be CRISP Registry participants.
- Participation Process
  - Local IRB approval (expedited in nature)
  - Participation agreement with MHS
  - No participation fee

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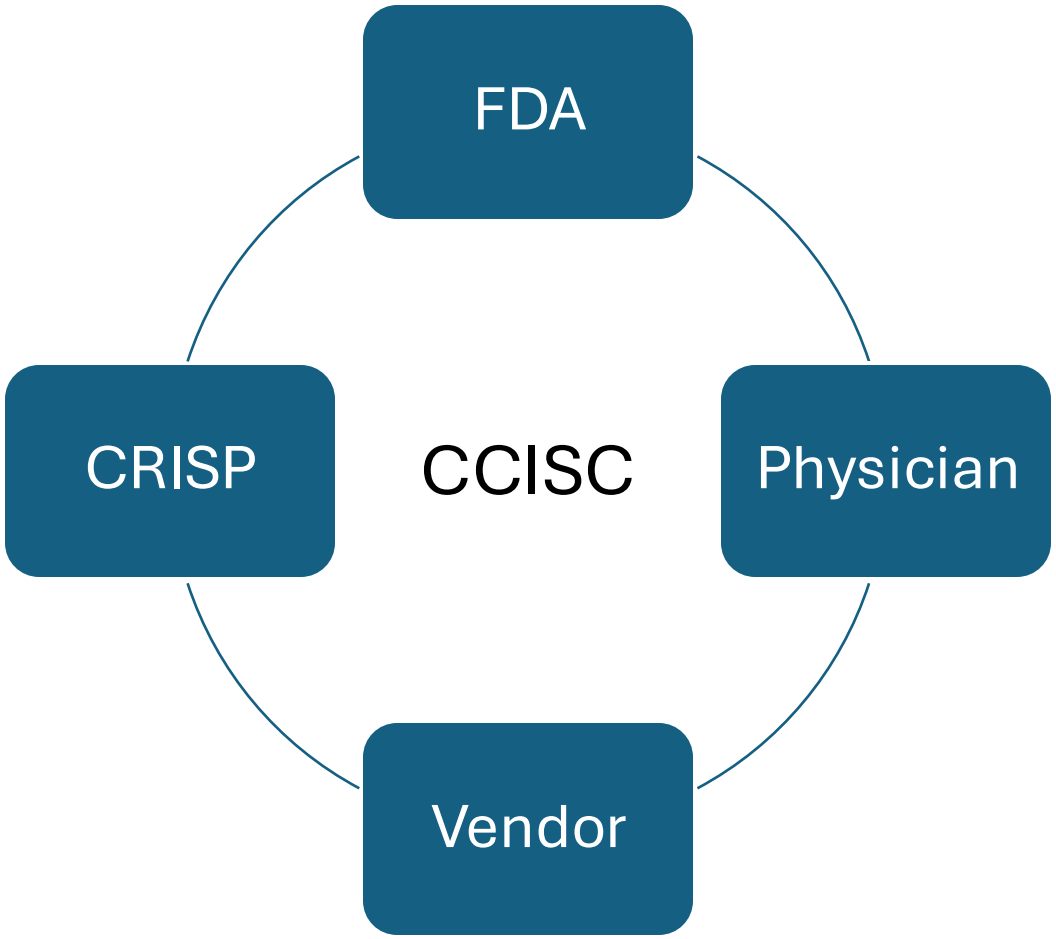
New CRISP Registry Modules

Clinical Study using Real World Data

- Off-label use devices
- Newly approved devices
- Certain unique procedures

Collaboration between key stakeholders

- Objectives
  - ✓Obtain FDA approval for off-label use devices
  - ✓Conduct post-approval study for newly approved devices
  - ✓Use retrospective dataset to facilitate prospective FDA PMA application

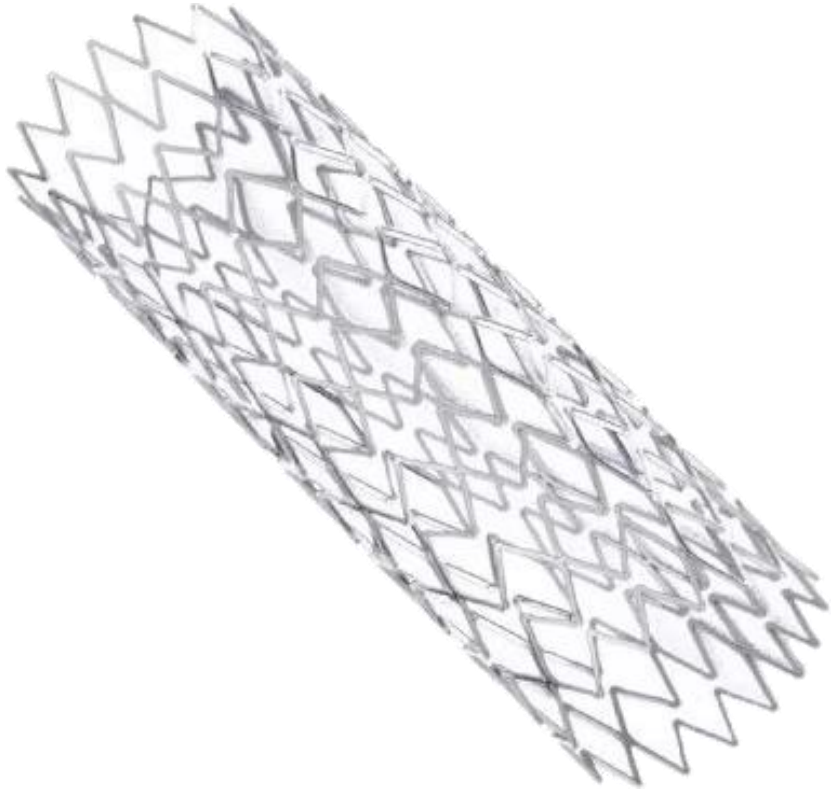


Certain Stents are at Risk for Becoming **Off-Market**

Valeo Biliary Stent

*March 2025
Vendor plans to stop production

EV3 LD Mega/Max Stent



Newly Approved Device - Occlutech ASD Occluder

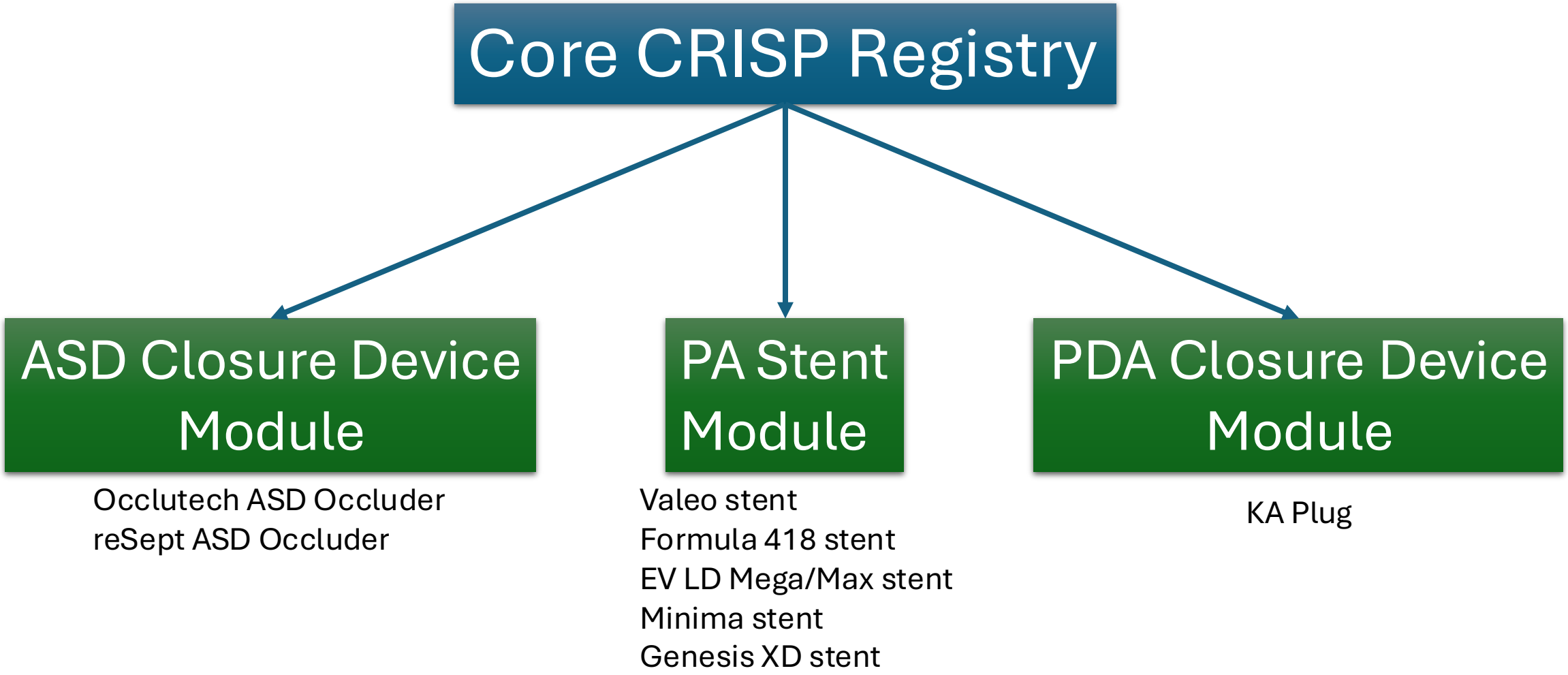
FDA PMA (premarket approval)
December 29, 2023

SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of transcatheter Atrial Septal Defect (ASD) closure with the Figulla Flex II ASD Occluder for transcatheter closure of *ostium secundum*-type ASD in Germany and France. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

→PMA was granted based on non-US data

CRISP Registry – Device Module Design (Real World Data)



ASD Device Closure Module - Occlutech ASD Occluder

- Data collection: Pre-procedural, Procedural, Discharge, and Follow-up (1 month, 6 months, 12 months, and 5 years).
- Primary Effectiveness Endpoint:
  - ✓Successful placement of the ASD closure device, and successful closure of the defect without major complication, surgical re-intervention, embolization or moderate to large residual shunt at discharge from implantation procedure.
- Secondary Effectiveness Endpoint:
  - ✓Closure Success (defined as residual shunt is smaller than or equal to 2 mm) at 12 months post-implant
  - ✓Complete Closure at 12 months post-implant
- Safety Endpoint
  - ✓Major complications within 12 months post-implant. Major complications are defined as stroke, cardiac perforation with tamponade, endocarditis, repeat surgery, death, pericardial effusion with tamponade, arrhythmia requiring major treatment, device embolization requiring surgery.

PA Stent Module (BiV, Proximal PA) - Valeo, EV3 LD Mega/Max, Formula 418

- Data Collection: Pre-procedural, Procedural, Discharge, and Follow-up (1 month, 6 months, 12 months, and late f/u).
- Primary effectiveness endpoint
  - ✓An increase in the stented vessel minimum pulmonary artery diameter >=50% at implantation
- Secondary effectiveness endpoint
  - ✓Ability to maintain relief of stenosis (includes planned re-dilation or re-dilation due to somatic growth) in the stented pulmonary artery at 12 months post-stent implantation by follow-up echocardiography
- Safety:
  - ✓Serious adverse event within 12 months post-implant.

New CRISP Registry Modules

- Modules will be open to the CRISP Registry participants.
- Modules will be optional (not mandatory) for the CRISP registry participants.

- IRB Amendment for CRISP registry v3.2 will be forthcoming.
  - Usually expedited or exempt approval
  - Minor update on Core CRISP Registry CRF
  - New module CRF for ASD device closure and PA stent (BV and SV)

Questions & Answers

Contact regarding CCISC studies

- Thomas Forbes: thforbes@mhs.net
- Nancy Sullivan: NSullivan@mhs.net
- Daisuke Kobayashi: daisuke@wustl.edu

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