action

Spring Meeting

Tuesday, April 18th

3–6 PM

Colorado Convention Center

Room 405-407

ACTION Spring Meeting

Tuesday, April 18th, 2023
3 – 6 pm MT

ACTION @ ISHLT
Colorado Convention Center
Room 405-407

TIME (MT)	AGENDA TOPIC
3:00 – 3:10 PM	**WELCOME & INTRODUCTIONS**
3:10 – 3:20 PM	**NETWORK UPDATES**
3:20 - 4:00 PM	**HOW DO WE GET DEVICES & MEDICATIONS TO KIDS FASTER?** • Leveraging ACTION Data | *Angela Lorts* • Real World Data Example: HM3 | *Matt O'Connor* • Prospective Device Trial Update: Active Driver | *Bob Kroslowitz* • Defining Adverse Events for Pediatrics | *Angela Lorts* • ACTION HF Registry for Baseline Trial Outcome | *Joseph Spinner* • ACTION Wearables | *David Peng* • ACTION Global | *Angela Lorts & Christina VanderPluym*
4:00 – 5:00 PM	**BREAKOUTS**
5:00 – 6:00 PM	**CLOSING & DISCUSSION**

INTRODUCTIONS | Something in Common

Introduce yourselves and work with your table to find something that you all have in common.

Get creative! Ideas to get your conversation started…

- Hobby
- Unique food you have tried
- Favorite place you have traveled to
- Favorite Book/TV Show/Movie/Musician
- Least favorite food

When time is up…

Choose one commonality to share with the group.

The table with the most unique answer will receive a prize!

Network Updates

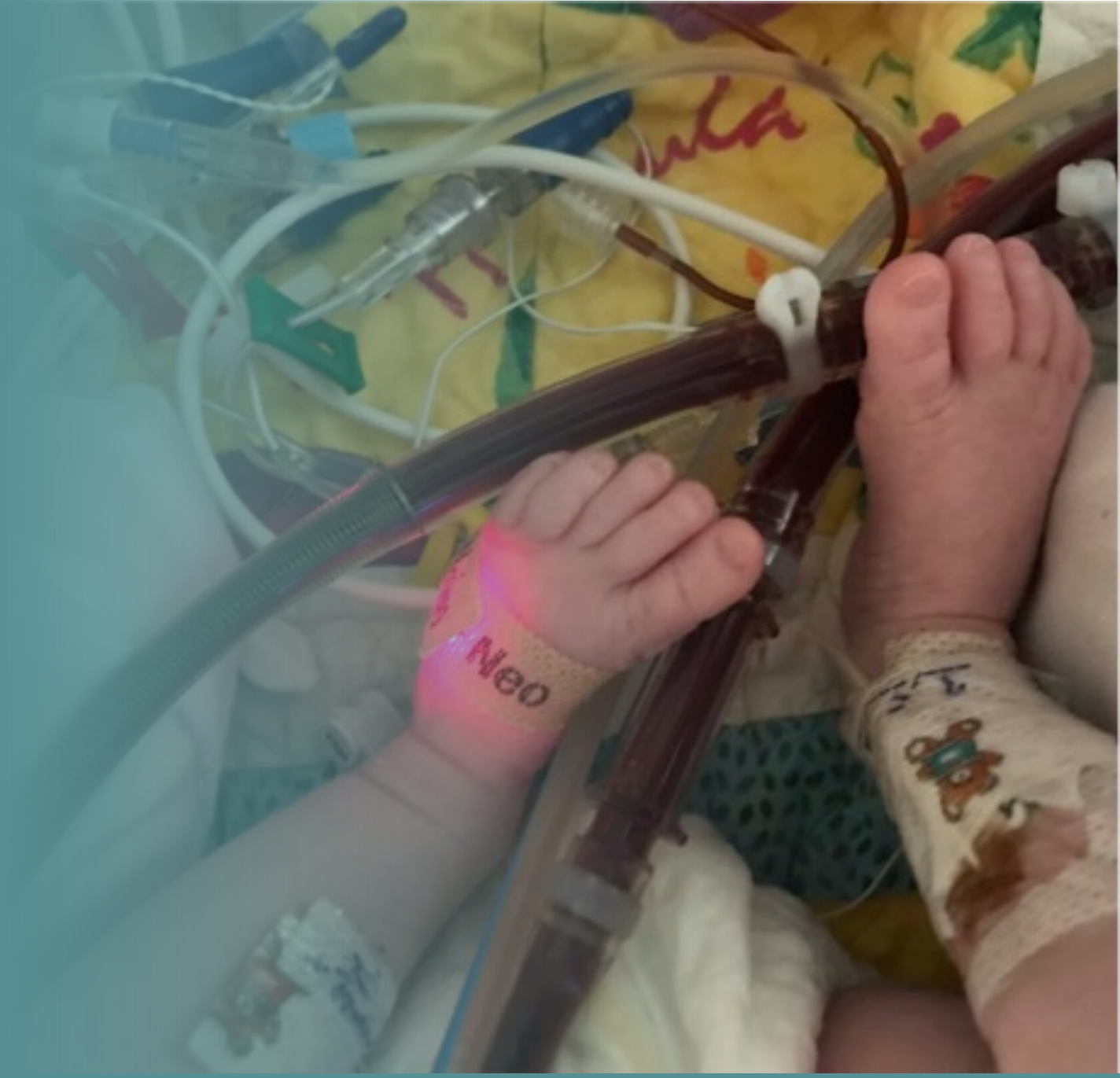
Pitch Deck & Data Updates

action

Working together to improve critical outcomes for all cardiac patients.

Despite the prevalence of pediatric heart failure…. it is **underfunded** and **understudied.**

Cardiac devices and medicines are **not developed** for children.



This leads to an increase in

pediatric heart failure-related:

mortality

hospitalizations

adverse events

We don’t always have the right treatments...

- Most heart failure medicines are not approved for pediatrics
- 1 in 5 children with heart failure will need a VAD or transplant
- 50% of children needing a VAD are too small for advanced continuous flow technology

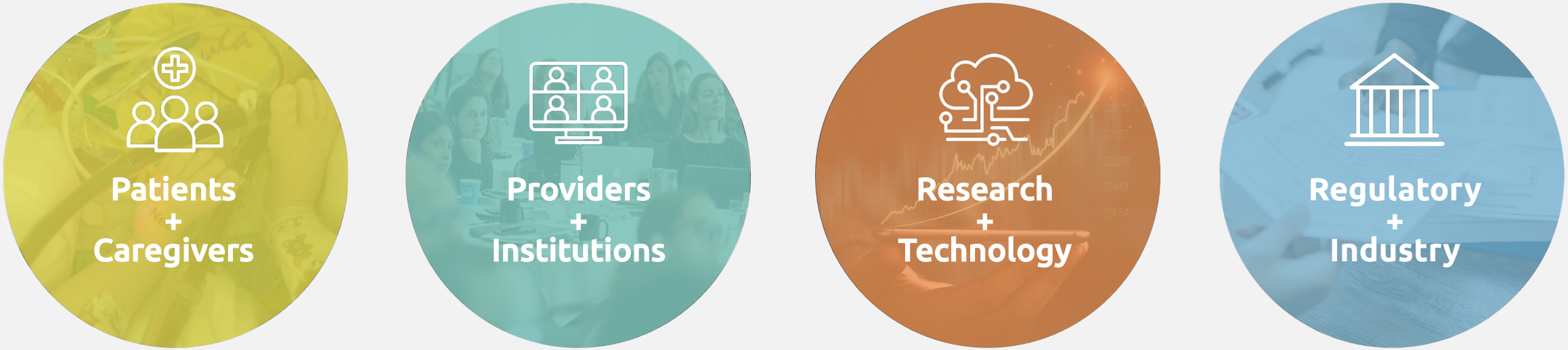
The best therapies are not developed for children due to…

- Relatively small patient numbers
- Lack of economic incentive
- Burden of data collection
- Suboptimal awareness of the problem

Now is the time
for ACTION.

Our Solution

A learning health network to bring everyone together



Our Principles

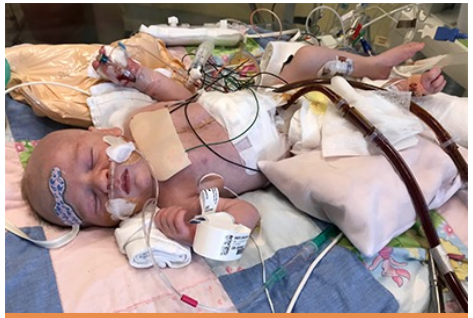
To tackle the problem, ACTION will:

- Build a cohesive community with all stakeholders
- Bring new technologies to pediatrics
- Be cost efficient while being effective
- Focus on the outcomes that matter

Our Patient Populations & Registries

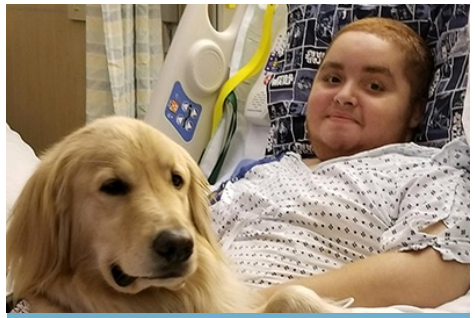
Cardiomyopathy/ Congenital Heart Disease

ACT HF



Ventricle Assist Device (VAD)

ACT VAD



Muscular Dystrophy

ACT MD

Pediatric & Adult Fontan Circulatory Failure

ACT FON

Our Growth

60+
North American Network Sites

Countries represented
8

1,158+
Network members

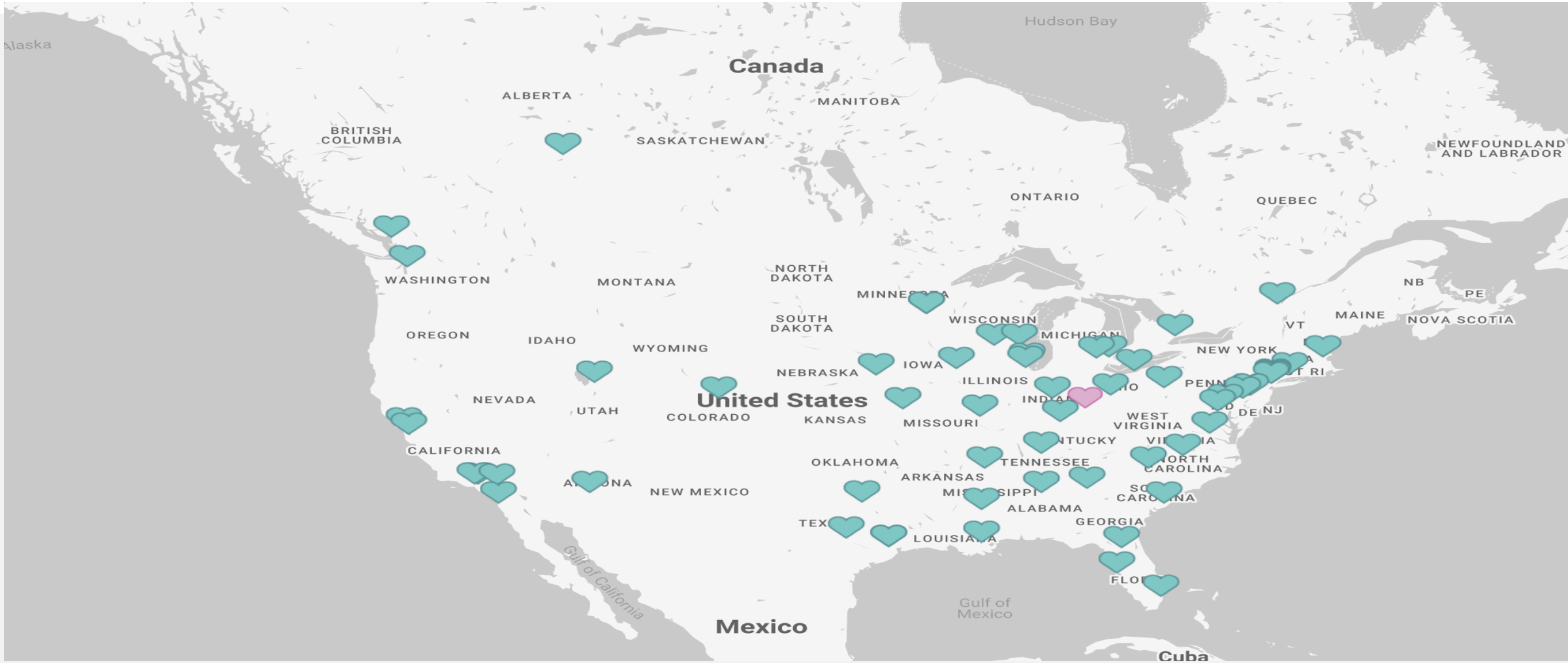
10
Network-wide initiatives

22
Manuscripts published

40+
Abstracts accepted

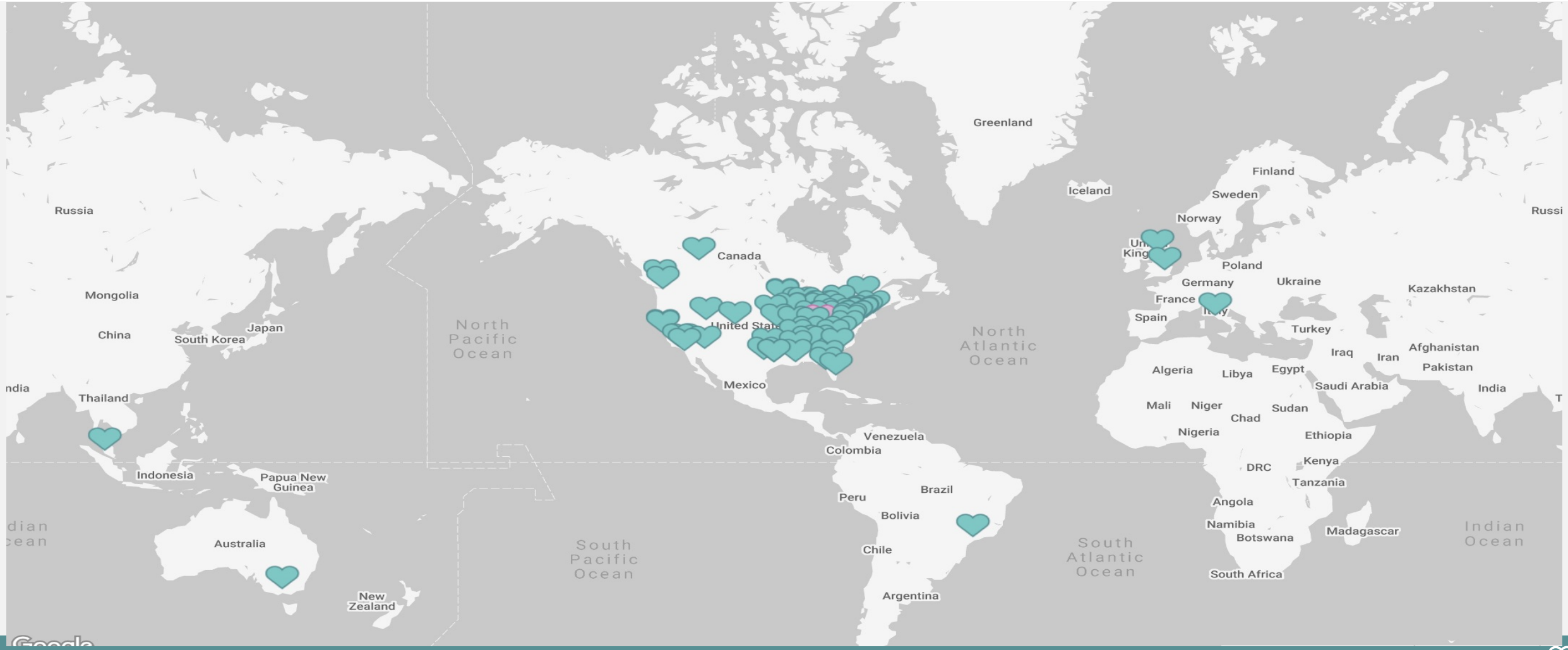
35+
Harmonized Protocols

Our Growth


Hudson Bay
Canada
ALBERTA
MANITOBA
BRITISH COLUMBIA
SASKATCHEWAN
NEWFOUNDLAND AND LABRADOR
ONTARIO
QUEBEC
WASHINGTON
MONTANA
NORTH DAKOTA
NB
PE
MAINE
NOVA SCOTIA
SOUTH DAKOTA
WISCONSIN
VT
OREGON
IDAHO
WYOMING
MICHIGAN
NEW YORK
NEBRASKA
IOWA
ILLINOIS
United States
NEVADA
UTAH
COLORADO
KANSAS
MISSOURI
WEST VIRGINIA
DE
NJ
CALIFORNIA
OKLAHOMA
TENNESSEE
ARKANSAS
NEW MEXICO
ALABAMA
GEORGIA
Gulf of California
Gulf of Mexico
Mexico
Cuba

Our Future

Our Global Progress



With help, we aim to:

1

Share ACTION models and methodologies to improve outcomes for other rare diseases

2

Collaborate with other organizations that will help further our mission

3

Global Expansion to international heart failure centers

4

Conduct trials to bring new devices and medications to children with heart failure

5

Improve outcomes for all pediatric and adult patients with heart failure

action

actionlearningnetwork.org | myactioneducation.org

Action-Learning-Network @Action4HF

- ACTION Global
- ACTION Foundation
- VAD discharge toolkit
- AE trial endpoints
- PRO for DMD
- Revamp Fontan work
- DEI & Access Planning

Leveraging ACTION Data

More sites and More data = More Possibilities

Our Data

ACTION will have the reliable regulatory data at the lowest cost.
To ensure that this is true we will:

- Audit site data
- Adjudicate adverse events
- Link to other data sources, including wearable data
- Format data for use as Real World Data
- Collect patient reported data and outcomes

ACT HF

ACT VAD

ACT MD

ACT FON

action VAD DATA summary

Sites Entering Data

44

		LVAD	RVAD	SVAD
1304	**Total Devices**	1081	254	402
1234	**Total Patients**	902	199	272

Number of patients being supported on

Berlin Heart EXCOR®

582

HeartMate 3™

238

HVAD™ System

198

Impella®

118

CentriMag™

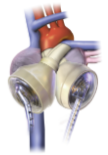
188

PediMag™

176

Rotaflow

63



SynCardia TAH

11

Stroke Rate

12.6%

Bleeding Rate

19.4%

Infection Rate

27.1%

Malfunction Rate

6.9%

Mortality Rate

12.7%

ACT VAD

as of April 2023:

44
sites

1200
patients

ACT VAD

as of April 2023:

44
sites

1200
patients

Goal for December 2023:

ALL
VAD sites

1500
patients

ACT HF

as of April 2023:

14
sites

153
patients

ACT HF

as of April 2023:

14
sites

153
patients

Goal for December 2023:

25
sites

500
patients

ACT MD

as of April 2023:

22
sites

275
patients

ACT MD

as of April 2023:

22 sites

275 patients

Goal for December 2023:

400 patients

Manuscripts

22
manuscripts published

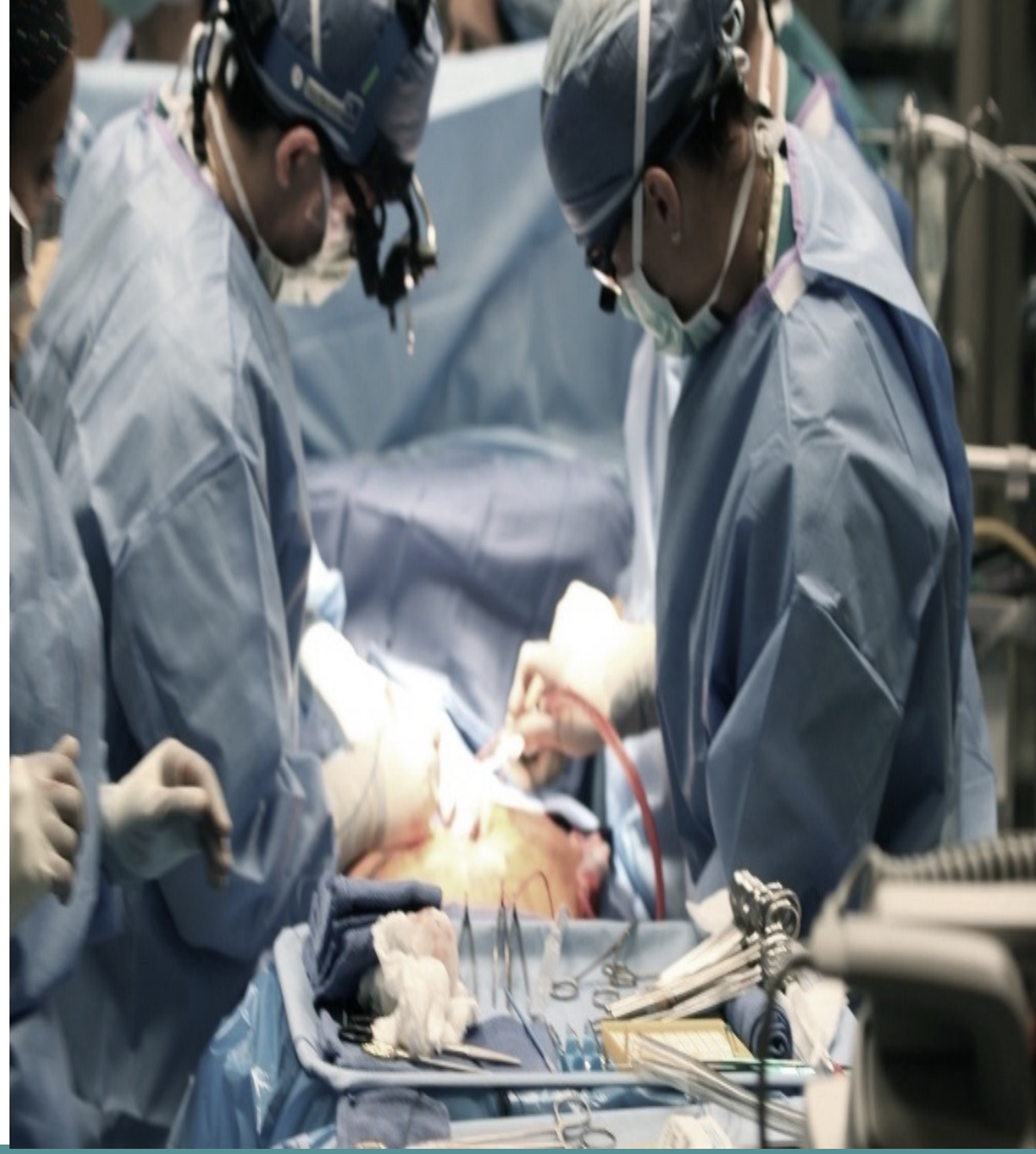
35
harmonized protocols

Real World Data Example: HeartMate 3™

Matthew O'Connor, CHOP

Benefits of FDA Labeling

- Pediatric Surgical training
- Education for children
- Insurance and hospital acceptance



Real World Data Sources

HeartMate 3™ Pediatric Expanded Labeling

- ACTION Registry Data
- Adjudication
- Application submitted to FDA
- 2-year post surveillance study by ACTION

ELSEVIER

The Journal of Heart and Lung Transplantation
http://www.jhltonline.org

Early experience with the HeartMate 3 continuous-flow ventricular assist device in pediatric patients and patients with congenital heart disease: A multicenter registry analysis

Matthew J. O'Connor, MD,[a] Angela Lorts, MD, MBA,[b] Ryan R. Davies, MD,[c] Francis Fynn-Thompson, MD,[d] Anna Joong, MD,[e] Katsuhide Maeda, MD,[f] Christopher E. Mascio, MD,[g] Patrick I. McConnell, MD,[h] Michael C. Mongé, MD,[i] Deipanjan Nandi, MD,[j] David M. Peng, MD,[k] David N. Rosenthal, MD,[l] Ming-Sing Si, MD,[m] David L. Sutcliffe, MD,[n] Christina J. VanderPluym, MD,[o] Melita Viegas, MD,[p] Farhan Zafar, MD,[b] Matthew Zinn, DO,[q] and David L.S. Morales, MD[b]

From the [a]Division of Cardiology, Departme Perelman School of Medicine, Philadelphia, Cincinnati, Ohio; [c]Department of Cardiova Health, Dallas, Texas; [d]Department of Car Boston, Massachusetts; [e]Division of Pedia nois; [f]Departments of Cardiothoracic Surg California; [g]Division of Pediatric Cardioth University of Pennsylvania School of Med Nationwide Children's Hospital, Columbu Lurie Children's Hospital, Chicago, Illino Hospital, Columbus, Ohio; [k]Department o Arbor, Michigan; [l]Division of Pediatric C nia; [m]Department of Cardiac Surgery, D Arbor, Michigan; [n]Department of Pediatri Texas; [o]Department of Cardiology, Boston of Pediatric Cardiothoracic Surgery, Depa Medical Center, Pittsburgh, Pennsylvania; a Pittsburgh, University of Pittsburgh Medical

Table 4 Clinical Outcome

Outcome	*n*
Alive on device	13
Deceased on device	1
Transplanted, alive	20
Transplanted, deceased	0
Ventricular recovery, wean	1
Explanted (apart from transplant), alive	0
Explanted (apart from transplant), deceased	0

18 months from Idea to Approval

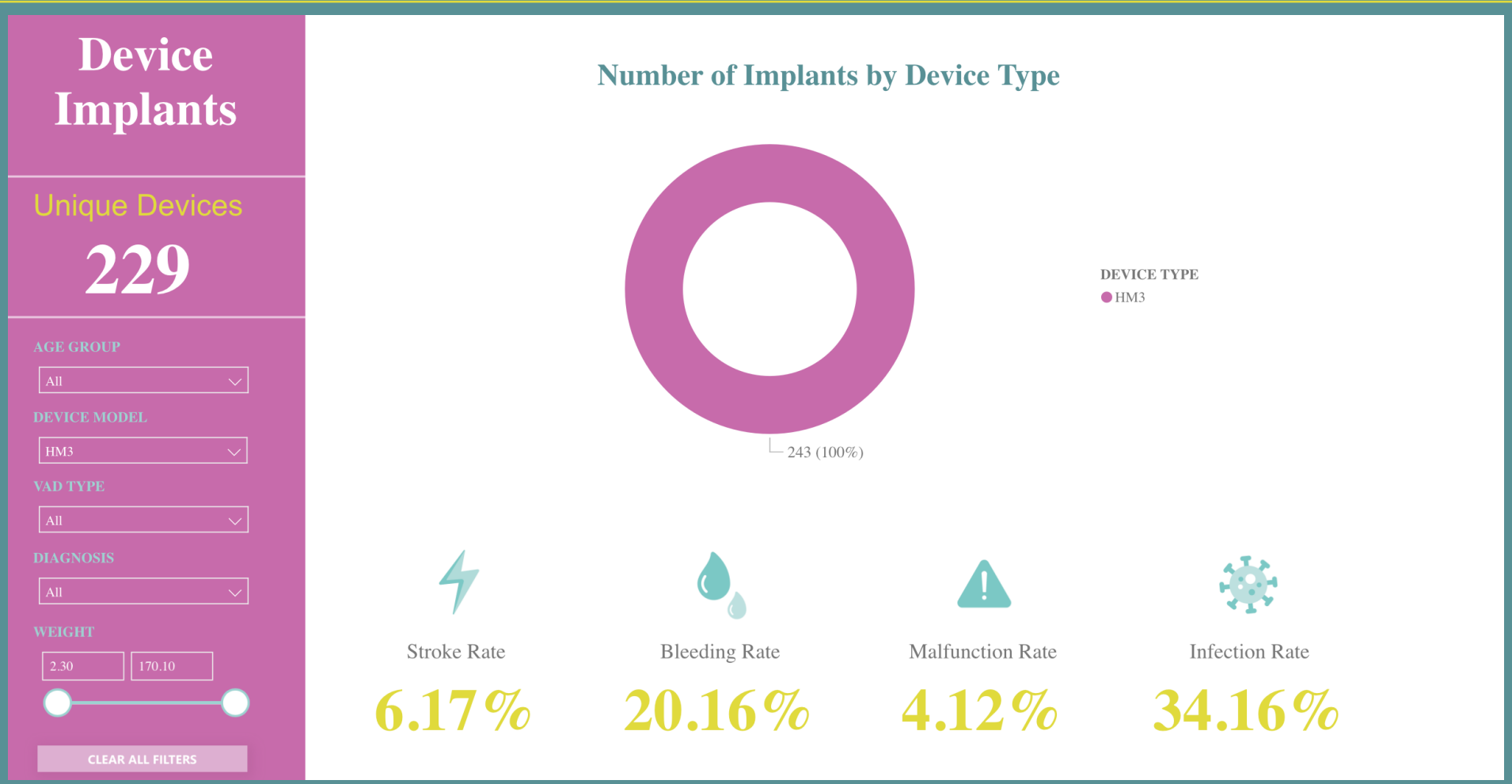
The HeartMate 3™ VAD Expanded Label

(sponsored by Abbott, using the ACTION registry)

The HeartMate 3™ VAD was used in pediatrics for compassionate use as it was not approved for children, leading to a lack of pediatric training and pediatric specific educational materials. ACTION collaborated with Abbott to collect and adjudicate safety and efficacy data from 20 sites. The data was used for an application to the FDA, and in December 2020, the HeartMate 3™ VAD received an expanded label to include children. After the indication was broadened, pediatric educational materials were co-created through a partnership between Abbott and ACTION. ACTION is currently collecting the post surveillance data.

Where are we now? HeartMate 3™ Data

Not Adjudicated – Do not reproduce or distribute



Prospective Device Trial Update: Berlin Active Driver

Bob Kroslowitz, Berlin Heart

Berlin Heart EXCOR® Report

action
ADVANCED CARDIAC THERAPIES
IMPROVING OUTCOMES NETWORK

Patient Population

Number of Patients With a Berlin Heart Excor from April 2018 to December 2022

382

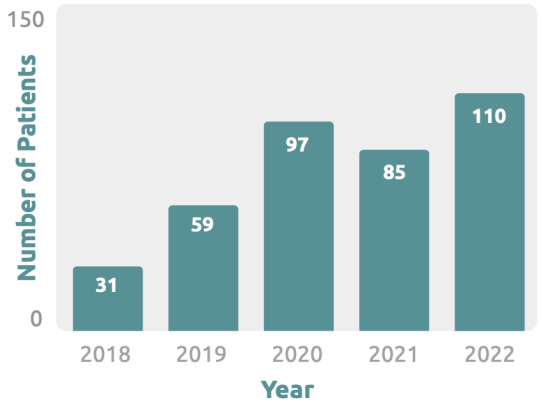
Devices Implanted

Berlin Heart Excor Devices Implanted from April 2018 to December 2022

496

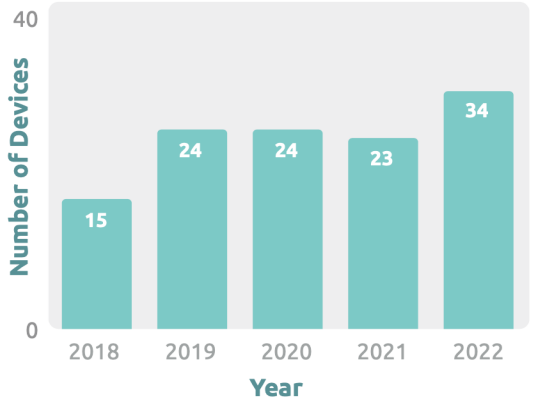
Patient Population by Year

Number of Patients with a Berlin Heart Excor Per Year from April 2018 to December 2022



Centers

Number of Centers with Berlin Heart Excor Patients from April 2018 to December 2022



Berlin Heart® | action

The Berlin Heart ACTIVE Driver Trial

(sponsored by Berlin Heart, Inc., using the ACTION registry)

action | Berlin Heart®

The Berlin Heart ACTIVE Driver Trial is sponsored by Berlin Heart, Inc. ACTION is serving as the clinical research organization (CRO) and the trial data is being collected through the ACTION registry.

The goal of the trial is to study the ACTIVE driver, which will be replacing the current IKUS (driving unit that powers the pump). The device/blood pump is still the same Berlin Heart EXCOR® device. Out of the 60 sites in ACTION, 17 sites have been chosen to be part of the trial.

As of April 4, 2023

19
Patients Enrolled
19/40
48%

15
Sites Enrolled
15/15
100%

Enrolled Sites

15
Sites Activated
15/15
100%

Active Sites

As of today –
20 patients and
10 have met 90-day end point or were explanted.

as of April 2023:

15
sites

20
patients

Goal for Fall 2023:

15
Sites

40
patients

ACTION HF Registry for Baseline Trial Outcome

Joseph Spinner, Texas Children's

What Don't We Know?

- What doses are we using?
- Are we titrating to goal doses?
- Is there a difference in outcomes based on reaching "target dose"
- If we don't get to "target dosing"…WHY? Inertia or side effects?
- Does switching from ACEi/ARB ⟹ ARNI improve outcomes?
- Do MRAs improve outcomes in children? Why is use so low?
- Are we using **SGLT2 inhibitors**? What are the side effects?

Where We Are Going: Let's Figure This Out

- How can we best answer these questions?
  - We have the infrastructure within ACTION
  - We have a track record of rapidly acquiring and sharing information, initiating protocols, HM3 FDA approval (!)
  - **Collaborating TOGETHER, we can work with drug companies to increase access to and study new (and old?) drugs in our patients**

Recent HF related Projects

Admissions/Enrollment

CardioMEMS

Communication Checklist

DMD

Discharge

Education

PHIS-ACTION linkage and report cards

Medication Titration

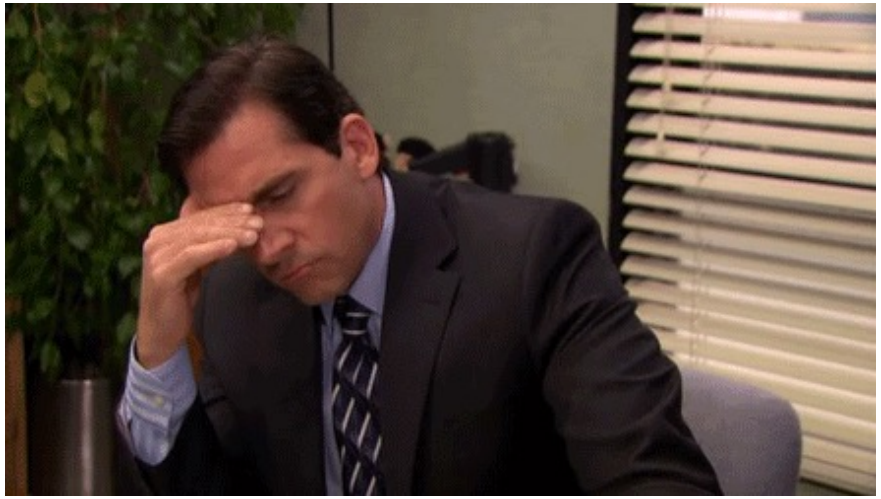
VAD “Recovery”

Wearables

Let's Simplify This

For all Heart Failure projects:

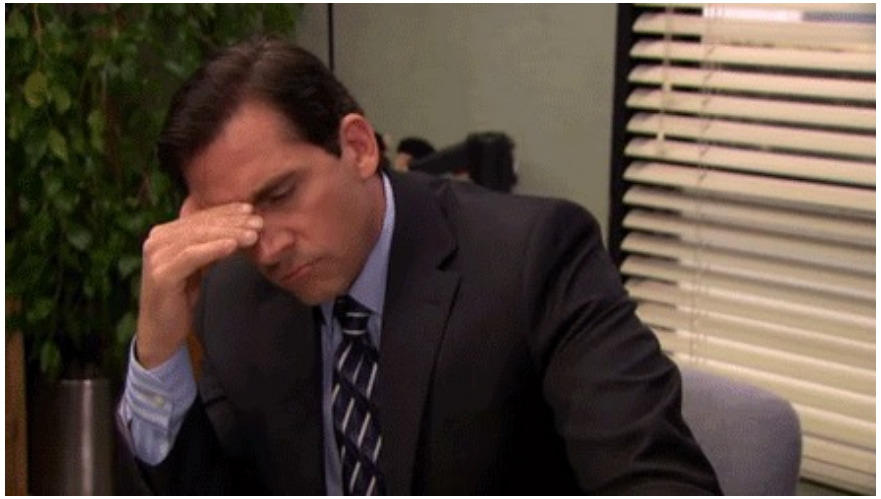
- **1 shared Enrollment REDCap**
- **1 ACTION HF ID to link all projects**



Let's Simplify This

For all Heart Failure projects:

- **1 shared Enrollment REDCap**
- **1 ACTION HF ID to link all projects**
- **Exception: Dystrophinopathy**



Who Do We Include?

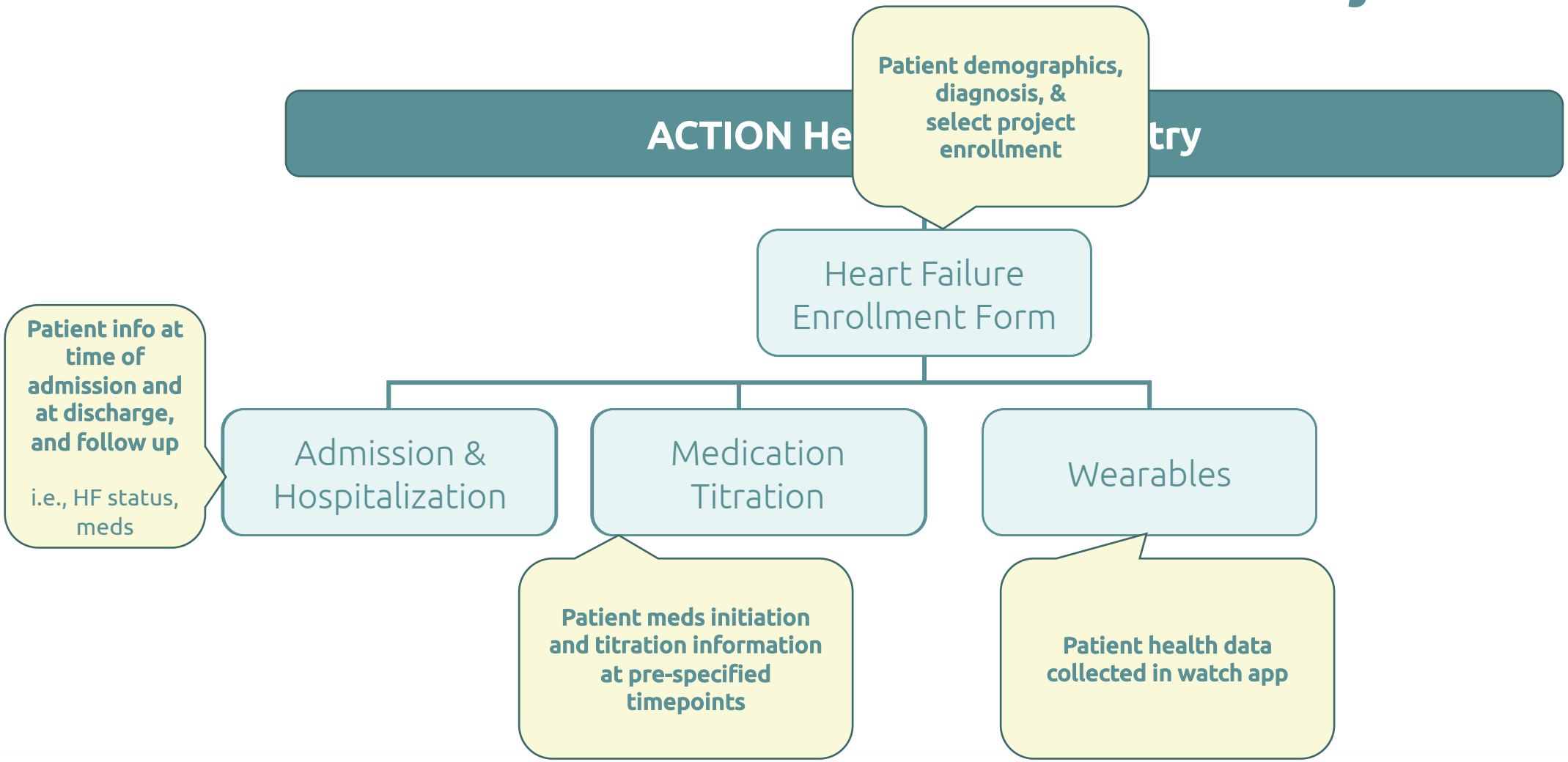
- **All** patients admitted to the hospital to receive treatment for heart dysfunction or symptoms of heart failure
  - We have specific questions to capture their “phenotype” (including Fontan)
- Patients ”participating” in Outpatient Medication titration

Who Do We Include?

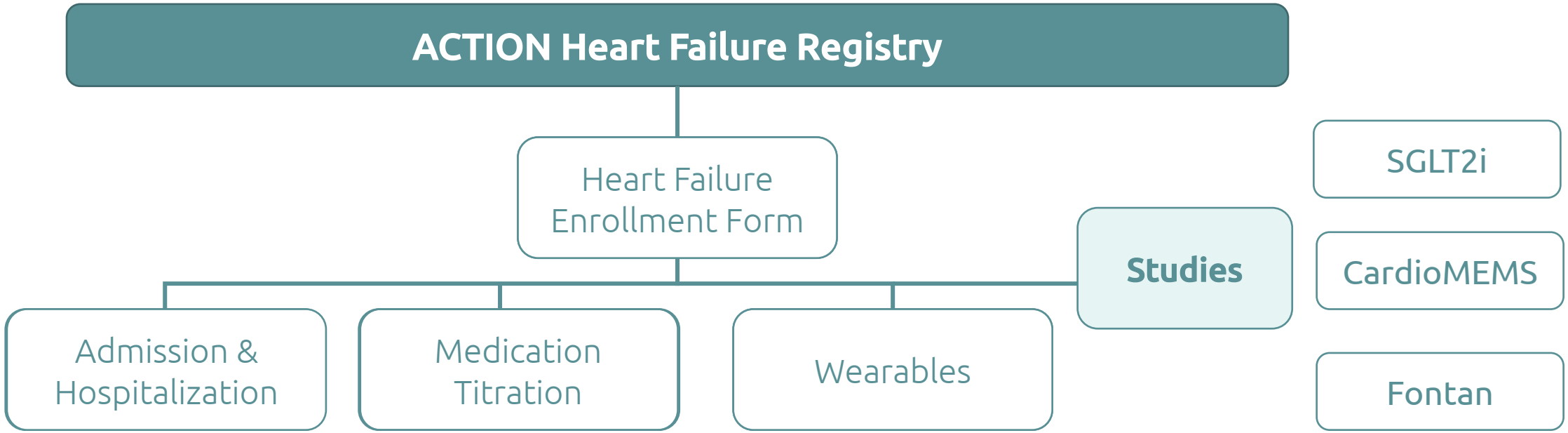
- **All** patients admitted to the hospital to receive treatment for heart dysfunction or symptoms of heart failure
  - We have specific questions to capture their “phenotype” (including Fontan)
- Patients ”participating” in Outpatient Medication titration
- Any patient who had received an Apple Watch
- Any patient with HF who has received an SGLT2-inhibitor
- Any patient with HF who has received a CardioMEMS

HF Registry - Data Entry

A Centralized Registry to Connect ACTION Heart Failure Related Projects



A Centralized Registry to Connect ACTION Heart Failure Related Projects



SGLT2 Inhibitor Use In Pediatric Heart Failure

R. Butts[1], D. Nandi[2], B. Hong[3], A. Lorts[4], J. Spinner[5].
[1]Children's Medical Center of Dallas/University of Texas Southwestern, Dallas, TX,
[2]Nationwide Children's Hospital, Columbus, OH,
[3]Seattle Children's Hospital, Seattle, WA,
[4]CincinnatiChildren's Hospital Medical Center, Cincinnati, OH,
[5]Baylor College of Medicine, Houston, TX,

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ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

Background

SGLT2 Inhibitors

- Improve survival in adults with heart failure
- Rapid adoption to guideline directed medical therapy for adults with heart failure
- Minimal evidence for use in Pediatric Heart Failure
- Have been utilized in Pediatric Heart Failure despite lack of evidence

Aim: To describe the current practice patterns of SGLT2 inhibitor use in pediatric heart failure

Methods

Survey

20 Questions REDCap survey regarding:

- Indications for use
- Patient population
- Medication management
- Laboratory monitoring

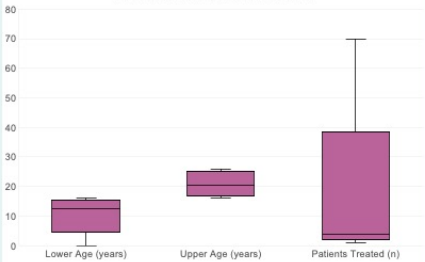
Sent to all ACTION sites

First response from each site analyzed

Results

18 of 29 (62%) institutions reported utilizing SGLT2i in approximately 185 patients

Figure 1. Lower and Upper Age of SGLT2 Initiation
Number Patients Treated at Each Institution

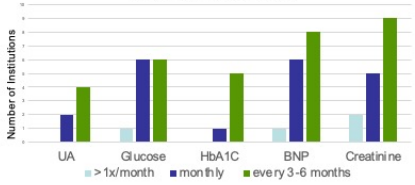


13 institutions report utilizing dapagliflozin
10 institutions reported utilizing empagliflozin

Table 1. Practice Patterns in Institutions Utilizing SGLT2i

	Number of Insitutions (n=18)
Physiological Class of Heart Failure	
Systolic Heart Failure	12 (66.7%)
Diastolic Heart Failure	8 (44.4%)
Combined Systolic and Diastolic	15 (83.3%)
Acute Heart Failure	8 (44.4%)
Chronic Heart Failure	15 (83.3%)
Acute on Chronic Heart Failure	7 (38.9%)
Cardiac Diagnosis	
Dilated Cardiomyopathy	16 (88.9%)
Hypertrophic Cardiomyopathy	0 (0%)
Restrictive Cardiomyopathy	3 (16.7%)
Non-Compaction Cardiomyopathy	3 (16.7%)
Post-Transplant Systolic Graft Dysfunction	7 (38.9%)
Fontan Ventricular Systolic Dysfunction	6 (33.3%)
Biventricular CHD Systolic Dysfunction	6 (33.3%)
Medications Utilized Prior to SGLT2i	
ACE/ARB/ARNi	18 (100%)
Beta Blocker	16 (88.9%)
MRA	17 (94.4%)
Digoxin	2 (11.1%)
Diuretics	9 (50%)
Laboratories Obtained Prior to Initiation	
Urinalysis	11 (61%)
HbA1c	12 (66.7%)
BNP	16 (88.9%)
Hemoglobin	8 (44.4%)
Creatinine	17 (94.4%)
Cystatin C	9 (50%)
Blood Glucose	14 (77.8%)

Frequency of Lab Monitoring After SGLT2 Initiation
(Within first 6 months of therapy)



Of the **11** institutions who reported **not** utilizing SGLT2i
2 are likely to utilize them in the **next 0-3 months**,
5 in the **next 3-6 months**,
3 in **greater than 6 months**, and
only 1 without any current plans to utilize SGLT2i.

Conclusions

SGLT2i **have been** incorporated into the management of pediatric heart failure at **many centers**

SGLT2i tend to be utilized in **older** pediatric patients with **dilated cardiomyopathy and systolic heart failure** as a **4th line** agent.

Institutions frequently monitor **renal function and BNP at least quarterly** and are less likely to monitor urine analysis, HbA1c and glucose

In centers where SGLT2i have not been used, **most plan to utilize SGLT2i soon**

Next Steps

Given SGLT2i **are being utilized in many pediatric centers** for the treatment of heart failure and there is a **lack of pediatric specific data**,

there should be dedicated retrospective and prospective **studies** to determine the **safety and efficacy of SGLT2i in pediatric heart failure**

ACTION SGLT2i Retrospective Study

1. REDCap Study utilizing pediatric heart failure registry

2. Study aimed at understanding safety profile, granular data regarding dosing, outcomes

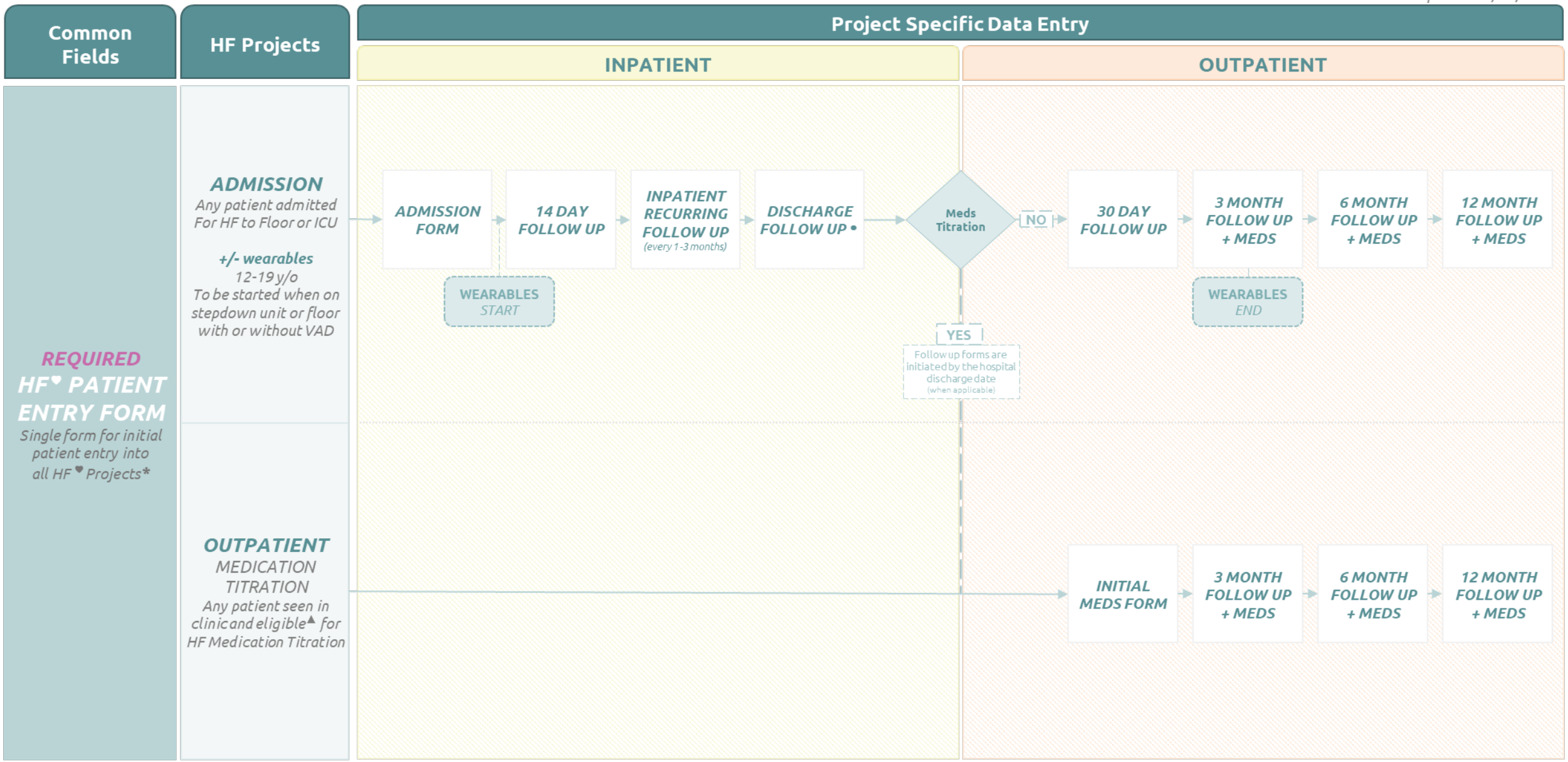
3. Three forms per patient
   - Intake
   - Last follow-up
   - Adverse Events

Email ryan.butts@utsouthwestern.edu with questions

actionlearningnetwork.org | myactioneducation.org

ACTION HF Registry – Data Entry Process

Last Updated: 7/25/2022



♥ Heart Failure Definition: A clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection. Cardinal symptoms include breathing difficulty, feeding intolerance, and decreased activity.

▲ Eligible for HF Medication Titration: Patients whose clinicians will use GDMT to achieve maximally tolerated doses of ACEi/ARB/ARNI, BB and MRA.

● When discharged the patient can be enrolled in medication titration.

* DMD/BMD patients are to be generally excluded from the HF studies as their data is being collected through the ACTION DMD registry.

ACT HF

as of April 2023:

14
sites

153
patients

16
meds titration

25
CardioMEMS™

3
wearables

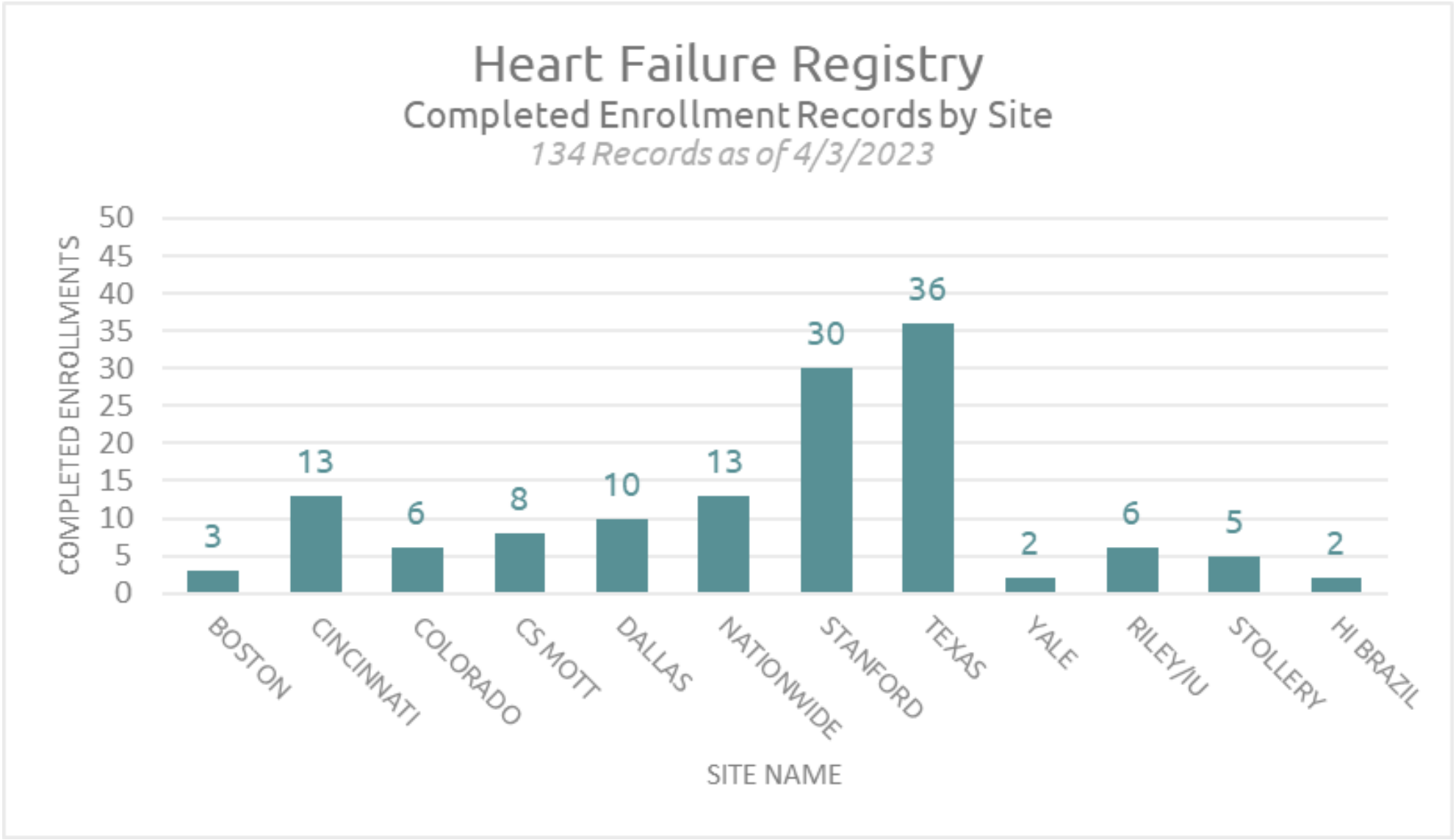

Heart Failure Registry
Completed Enrollment Records by Site
134 Records as of 4/3/2023
COMPLETED ENROLLMENTS
50
45
40
35
30
25
20
15
10
5
0
3
13
6
8
10
13
30
36
2
6
5
2
BOSTON
CINCINNATI
COLORADO
CS MOTT
DALLAS
NATIONWIDE
STANFORD
TEXAS
YALE
RILEY/IU
STOLLERY
HI BRAZIL
SITE NAME

Table 1. Patient characteristics and diagnosis at enrollment

	All patients N=136
<2 years of age at enrollment	42 (31%)
Sex – Female	69 (51%)
Race	
White	85 (62%)
Black or African American	27 (20%)
Asian	5 (3.7%)
Hawaiian / Pacific Islander	5 (3.7%)
Other	8 (5.9%)
Unknown	6 (4.4%)
Ethnicity	
Hispanic or Latinx	39 (29%)
Diagnosis	
Dilated cardiomyopathy	45 (33%)
Hypertrophic cardiomyopathy	3 (2.2%)
Restrictive cardiomyopathy	7 (5.1%)
Left ventricular non-compaction	5 (3.7%)
Isolated active myocarditis	11 (8.1%)
Cardiomyopathy - Mixed phenotype	9 (6.6%)
Congenital heart disease	39 (29%)
Biventricular	16/39 (41%)
Univentricular	23/39 (59%)
Norwood stage	2/23(8.7%)
Bidirectional Glenn stage	4/23 (17%)
Fontan stage	17/23 (74%)
Coronary abnormality	3 (2.2%)
Others	4 (2.9%)
Transplant Graft Dysfunction	10 (7.3%)

Table 2. Clinical presentation and heart failure evaluation data at admission

	All patients N=136
Age at admission (years)	8.6 (IQR 0.7-15.8, range 0-27)
Height/length	121 (IQR 63-160, range 16-198)
Weight (kg)	24 (IQR 7.8-62.2, range 2-188)
Number of previous hospitalizations for heart failure	
1 previous hospitalization	15 (11%)
2 previous hospitalizations	13 (9.6%)
3 previous hospitalizations	3 (2.2%)
5 previous hospitalizations	1 (0.7%)
Location of admission for hospitalization	
ICU	95 (70%)
Floor/ Stepdown Unit	40 (29%)
Unknown	1 (0.7%)
NYHA heart failure Classification	
NYHA class I	0 (0%)
NYHA class II	18 (13%)
NYHA class III	34 (25%)
NYHA class IV	62 (46%)
Not applicable/Unknown	22 (16%)
ACC/AHA heart failure Classification	
Stage A	1 (0.7%)
Stage B	12 (8.8%)
Stage C	51 (37%)
Stage D	63 (46%)
Not applicable/Unknown	9 (6.6%)
Cardiac imaging performed	127 (93%)
Ejection fraction(%, n=86)	29 (IQR 22-38, range 7-63)
Qualitative assessment of systemic ventricle systolic function	41 (30%)
Normal Systolic Function	21/41 (51%)
Mild Systolic Dysfunction	2/41 (4.9%)
Moderate Systolic Dysfunction	4/41 (9.8%)
Severe Systolic Dysfunction	14/41 (34%)
BNP (pg/ml, n=69)	1425 (IQR 399-4276, range 12-15736)
NT-proBNP (pg/ml, n=64)	5784 (IQR 1910-24963, range 37-123000)
Creatinine (mg/dl, n=120)	0.6 (IQR 0.3-0.9, range 0.1-24)
Cystatin C (mg/L, n=49)	0.9 (IQR 0.8-1.3, range 0.6-5)
Potassium (mEq/L, n=128)	4.2 (IQR 3.8-5, range 1.9-6.9)
Sodium (mEq/L, n=128)	137 (IQR 134-139, range 123-149)
Bilirubin total (mg/dl, n=118)	0.7 (IQR 0.4-1.3, range 0-5.5)
Hemoglobin (mg/dl, n=126)	12.8 (IQR 10.5-14.7, range 1.9-20)

Table 3. Medications during hospitalization

	All patients N=136
Medications present at time of admission	79 (58%)
Ace Inhibitor / Angiotensin Receptor Blocker / ARNI	37 (27%)
Captopril	2 (1.4%)
Enalapril	18 (13%)
Lisinopril	4 (2.9%)
Losartan	3 (2.2%)
Sacubitril/Valsartan	10 (7.3%)
Beta blocker	34 (25%)
Carvedilol	15 (11%)
Metoprolol	15 (11%)
Propranolol	1 (0.7%)
Other	3 (2.2%)
Aldosterone antagonist	38 (30%)
Eplerenone	2 (1.4%)
Spironolactone	36 (26%)
Anticoagulants	
Aspirin	35 (26%)
Enoxaparin	6 (4.4%)
Warfarin	3 (2.2%)
Apixaban	4 (2.9%)
Rivaroxaban	1 (0.7%)
Other	1 (0.7%)
Other medications	
Digoxin	6 (4.4%)
Milrinone	27 (20%)
SGLT-2 inhibitor	8 (5.9%)
Sildenafil	3 (2.2%)
Furosemide	47 (34%)
Torsemide	7 (5.1%)

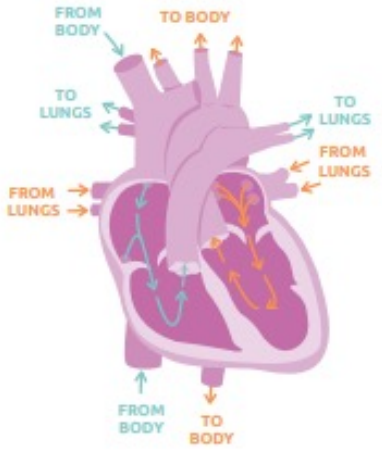
	All patients N=84
Outcome of heart failure admission	
Died during hospitalization	5 (5.9%)
Patient discharged without transplant or VAD	49 (58%)
Patient discharged with VAD	3 (3.6%)
Patient discharged with HeartMate 3	3/3 (100%)
Patient underwent heart transplant this admission	15 (18%)
Other	12 (14%)
Other events during hospitalization	
Patient was listed for heart transplant	11 (13%)
Patient already listed for heart transplant	6 (7.1%)
Patient evaluated for VAD but declined	6 (7.1%)
Patient evaluated for heart transplant but declined	3 (3.6%)
Patient on VAD during hospitalization	13 (15%)
Cardiac surgery during hospitalization	
Congenital heart surgery repair or palliation	8 (9.5%)
ECMO	5 (5.9%)
Temporary VAD	7 (8.3%)
Durable VAD	8 (9.5%)
Heart transplant	11 (13%)
Other	2 (2.4%)
Complications during hospitalization	
Cardiac arrest	7 (8.3%)
Dialysis	2 (2.4%)
Required mechanical ventilation	22 (26%)
Patient admitted to ICU during hospitalization	61 (73%)
ICU days	13 (IQR 6.2-24, range 1-200)
Patient on IV inotropes during hospitalization	57 (68%)
Epinephrine	30 (36%)
Norepinephrine	1 (1.2%)
Dopamine	3 (3.6%)
Milrinone	56 (67%)
Calcium	1 (1.2%)

An Introduction to Pediatric Heart Failure

action
ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

WHAT IS THE HEART & HOW DOES IT WORK?

The heart is a muscle that pumps blood around the body. The four chambers in the heart are separated into the right and left sides.



The right side
of the heart fills with blood from the body and squeezes to pump blood to the lungs to get oxygen.

The left side
of the heart fills with blood from the lungs, and squeezes to pump blood with oxygen to the body.

WHAT IS HEART FAILURE?

A group of symptoms that occur when the heart doesn't squeeze enough to move blood out or relax enough to let blood in.

COMMON CAUSES OF HEART FAILURE?

CONGENITAL HEART DISEASE
Stress and damage to the heart muscle caused because the heart chambers and connections are not formed properly during fetal life.

CARDIOMYOPATHY
An abnormality of the heart muscle that may be present from birth or can be caused by other diseases. There are many types of cardiomyopathy.

MYOCARDITIS
A heart muscle injury often caused by certain infections.

CARDIOTOXICITY
A heart muscle injury often caused by certain medications and treatments, such as chemotherapy or radiation.

actionlearningnetwork.org info@actionlearningnetwork.org Action-Learning-Network @Action4HF

Heart ~~Failure~~ Success Medicines

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People with decreased heart function often have elevated levels of **neurohormones.** Neurohormones are proteins that are released from your cells into your blood and can be harmful to the heart, blood vessels, and circulation system. This may lead to worsening symptoms of heart failure. The following medicines, **often used in combination,** help by blocking or lowering the effect of the neurohormones on your heart. **Please let your care team know of any changes in how you are feeling while taking these medicines.**

ANGIOTENSIN

- **ACE inhibitors**
  Medicines that end in "-pril" *(ex: captopril, enalapril, lisinopril)*
- **Angiotensin Receptor Blockers (ARBs)**
  Medicines than end in "-artan" *(ex: losartan, valsartan)*
- **Angiotensin Receptor Blocker Neprolysin Inhibitor (ARNIs)**
  This is a combination of sacubitril + valsartan *(ex: Entresto®)*

Your provider/care team will help decide which Angiotensin medicine is right for you.

What they do: These medicines help the blood vessels relax (easier for the heart to pump), help preserve or potentially improve heart function, and help decrease salt and water in the body.

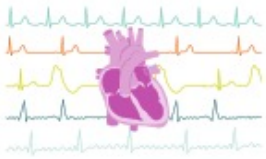
Possible side effects: Lower blood pressure (light-headedness or dizziness), elevated levels of potassium, a dry cough, swelling of the lips, and change in kidney function.

BETA BLOCKERS

- Medicines that end in "-olol" *(ex: metoprolol, carvedilol)*

What they do: These medicines help slow the heart rate (relaxes the heart), help the blood vessels relax (easier for the heart to pump), and help preserve or potentially improve heart function. They can also be used to treat arrhythmias, or abnormal heart rhythms.

Possible side effects: Lower blood pressure (light-headedness or dizziness), lower heart rate (light-headedness or dizziness), and feeling tired or drowsy.

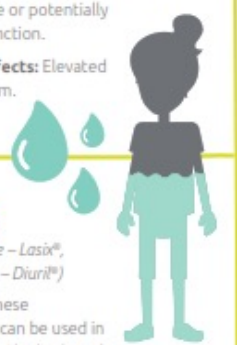


MINERALOCORTICOID RECEPTOR ANTAGONISTS (MRA's)

- *(ex. spironolactone and eplerenone)*

What they do: These medicines are also known as "potassium sparing diuretics", but they do much more than help remove excess water and salt from the body. They also help preserve or potentially improve heart function.

Possible side effects: Elevated levels of potassium.



DIURETICS

- *(ex. furosemide – Lasix®, chlorothiazide – Diuril®)*

What they do: These medicines, which can be used in combination, help the body make more urine, which gets rid of excess water and salt. This helps improve swelling and can help reduce the amount of fluid in the lungs. They can also help lower blood pressure.

Possible side effects:
Decreased levels of potassium and sodium, dehydration, as well as other electrolyte changes, and decreased blood pressure (light-headedness or dizziness).

Learn more about heart medicines at: **myactioneducation.org/courses/medicines**

Heart ~~Failure~~ Success Discharge Plan

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ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

for _____ FIRST _____ LAST

My next follow-up visit is:

?? _____ DATE at _____ TIME

with _____ CARE PROVIDER at _____ LOCATION

My care team can be reached at:

_____ - _____ - _____

Your heart medicines may change often. At your next visit, **ask your care team** if any of your medicine doses need to change.

I am on the following types of heart medicine:

- ☐ ACE/ARB/ARNI: _____
- ☐ Beta Blocker: _____
- ☐ Aldosterone Antagonist: _____
- ☐ Diuretic: _____
- ☐ Heart Rhythm: _____
- ☐ Other: _____

*Please see the **discharge summary** for exact dose of each heart failure medicine your child should be taking.*

My vital signs at discharge:

Blood Pressure: _____

Oxygen Saturation: _____

Heart Rate: _____

Weight: _____ lbs _____ kg

My activity and diet:

My care team recommends a: ☐ Normal diet

☐ Restricted diet: _____

My feeding plan is: _____

My fluid intake goal is: ☐ Normal intake

☐ Set by my care team as follows:

Daily Minimum: _____ *Daily Maximum:* _____

My physical activity is: ☐ Not restricted

☐ Restricted: _____

Next >

Heart ~~Failure~~ Success Discharge Plan

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ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

for _____ FIRST _____ LAST

For children between the ages of 1–18, use the zones below as a guide to monitor your child after discharge and as a reference for when to contact your care team. **In case of emergency, call 911.**

GREEN ZONE

Your child is doing great!

My child has:

- No trouble breathing, or breathing is normal for my child
- Ability to continue their normal activity
- No swelling in their face, eyelids, legs, feet, or stomach
- No trouble with eating, and has their normal appetite
- Weight is within goal range

What to do: Continue current plan.

YELLOW ZONE

Your child may have worsening heart failure.

My child has:

- Shortness of breath, especially with physical activity
- Weight: gained _____ lbs in _____ days OR lost _____ lbs in _____ days
- Increased fatigue (tiredness), need to take a more than normal amount of breaks while playing or exercising
- Mild swelling in their face, eyes, legs, feet, or stomach
- Difficulty lying down or sleeping flat
- Nausea/vomiting or poor appetite

What to do: (check all that apply)

☐ Make the following changes to your diuretic medicine: _____

☐ Call your care team for further advice.

RED ZONE

Your child has concerning signs of heart failure, requiring evaluation.

My child has:

- Rapid breathing, faster than normal even when sitting or resting
- A lot of swelling in their face, eyelids, legs, feet, or abdomen
- Nausea, vomiting, complaints of abdominal pain, especially after eating
- Continued weight gain, or weight gain more than _____ lbs in _____ days
- Continued weight loss, or weight loss more than _____ lbs in _____ days
- No relief of symptoms after using the extra diuretics in yellow zone for _____ days

What to do: Call your care team for further advice.

Heart ~~Failure~~ Success Discharge Plan

action
ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

for _____ FIRST _____ LAST

For infants between 0–12 months, use the zones below as a guide to monitor your child after discharge and as a reference for when to contact your care team. **In case of emergency, call 911.**

GREEN ZONE

Your infant is doing great!

My infant has:

- No trouble breathing or breathing is at baseline
- Ability to eat normally and complete their feeds
- No swelling in their face, eyelids, legs, feet, or abdomen
- Been gaining weight appropriately

What to do: Continue current plan.

YELLOW ZONE

Your infant may have worsening heart failure.

My infant has:

- Shortness of breath, especially with feedings or activity
- Increased fatigue, taking more breaks than normal when feeding but is still able to complete
- Mild swelling in their face, eyes, legs, feet, or abdomen
- Not gained weight appropriately

What to do: (check all that apply)

☐ Make the following changes to your diuretic medicine: _____

☐ Call your care team for further advice.

RED ZONE

Your infant has concerning signs of heart failure, requiring evaluation.

My infant has:

- Shortness of breath or trouble breathing at rest
- No energy and is unable to eat
- A lot of swelling in their face, eyelids, legs, feet, or abdomen
- Nausea, vomiting, especially after eating
- Not gained weight appropriately and has lost weight
- No relief of symptoms after using the diuretic action plan for _____ days

What to do: Call your care team for further advice.

ACT HF

as of April 2023:

14
sites

153
patients

16
meds
titration

25
CardioMEMS™

ACTION Wearables

David Peng, CS Mott

We are up and running!

Now actively collecting physiologic and activity data (HR, RR, steps, etc) from our patients using the watch!

Will correlate with data from HF Registry to better understand our HF patients

Now open to ALL sites participating in the single IRB!

Yale NewHaven Health
Yale New Haven Children's Hospital

Lucile Packard Children's Hospital Stanford

IOWA

Texas Children's Hospital®

Boston Children's

>11yo-19yo hospitalized with acute decompensated heart failure (can use patient/parent iphone)

Signing up patients is easy!

Please reach out to me to participate.


action
GLOBAL

- Data
- Webinars
- Advocacy
- Educational materials
- Trials

action GLOBAL

Defining Adverse Events for Pediatrics

Angela Lorts on behalf of David Rosenthal

Our Trial End-Points

ACTION will have the most reliable adverse event definitions and trial end-points:

- **Up to date Adverse Event Definition**
- **Reliable Patient Reported Outcomes**
- **Wearable data to determine QOL**

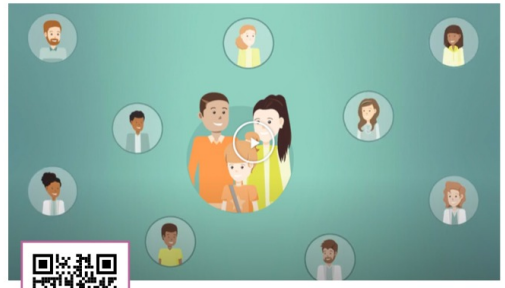
Taking ACTION on Outcomes that Matter Most to You

action
ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

Patient and Parent Reported Outcomes (PROs)

What are PROs?

Patient reported outcomes (PROs) are measures of health, symptoms, behavior, or experiences as reported by a patient or parent. PROs provide helpful information allowing us to improve care provided. Your heart team may think they know what matters most to you, but the best way to really know is to ask you! This is why ACTION and your heart team have teamed up to collect your PROs. We will ask about your physical and emotional health, as well as how your family is coping.



Watch our short video to learn more about PROs.

Why is it time?

1. Clinical Trial Safety Measures

2. Clean “anchors” in registry data collections (often used as endpoints in registry analyses)

History of the Peds MCS AE definitions

- AE definitions emerged from conversations with FDA and device manufacturers in a trial-specific manner
- ISHLT MCS database was initial effort to standardize
- Followed by Intermacs and Pedimacs
- MCS-ARC is current classification of MCS AE's but is light on pediatric input

Benefits of FDA Labeling

- Pediatric Surgical training
- Education for children
- Insurance and hospital acceptance

ELSEVIER

OPINION

The darker side of device evolution: Children get left behind

Seth A. Hollander,[a] David N. Rosenthal,[a] and Angela Lorts,[b],
On Behalf of the ACTION Network

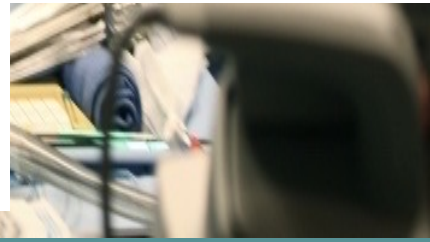
ASAIO Journal 2023

Editorial

Ventricular Assist Device Development: Women and Children Should No Longer Be Last!

ANGELA LORTS* AND MIRNELA BYKUT

trics (Cardiology), Stanford Uni-
o Alto, California; and the [b]De-
ati Children's Hospital Medical
Cincinnati, Ohio.



- AE definitions emerged from conversations with FDA and device manufacturers in a trial-specific manner
- ISHLT MCS database was initial effort to standardize
- Followed by Intermacs and Pedimacs
- MCS-ARC is current classification of MCS AE's but is light on pediatric input

Goals of the 2020 MCS ARC:

1. Refine/Clarify AE definitions
2. Classify by type/severity/location/timing
3. Harmonize with other ARC initiatives e.g. Neuro-ARC
4. Provide guidance for data abstractors
5. Assign cause
6. Review every 2 years and update as needed

The Journal of Heart and Lung Transplantation
http://www.jhltonline.org

EDITORIAL COMMENTARY

Updated definitions of adverse events for trials and registries of mechanical circulatory support: A consensus statement of the mechanical circulatory support academic research consortium

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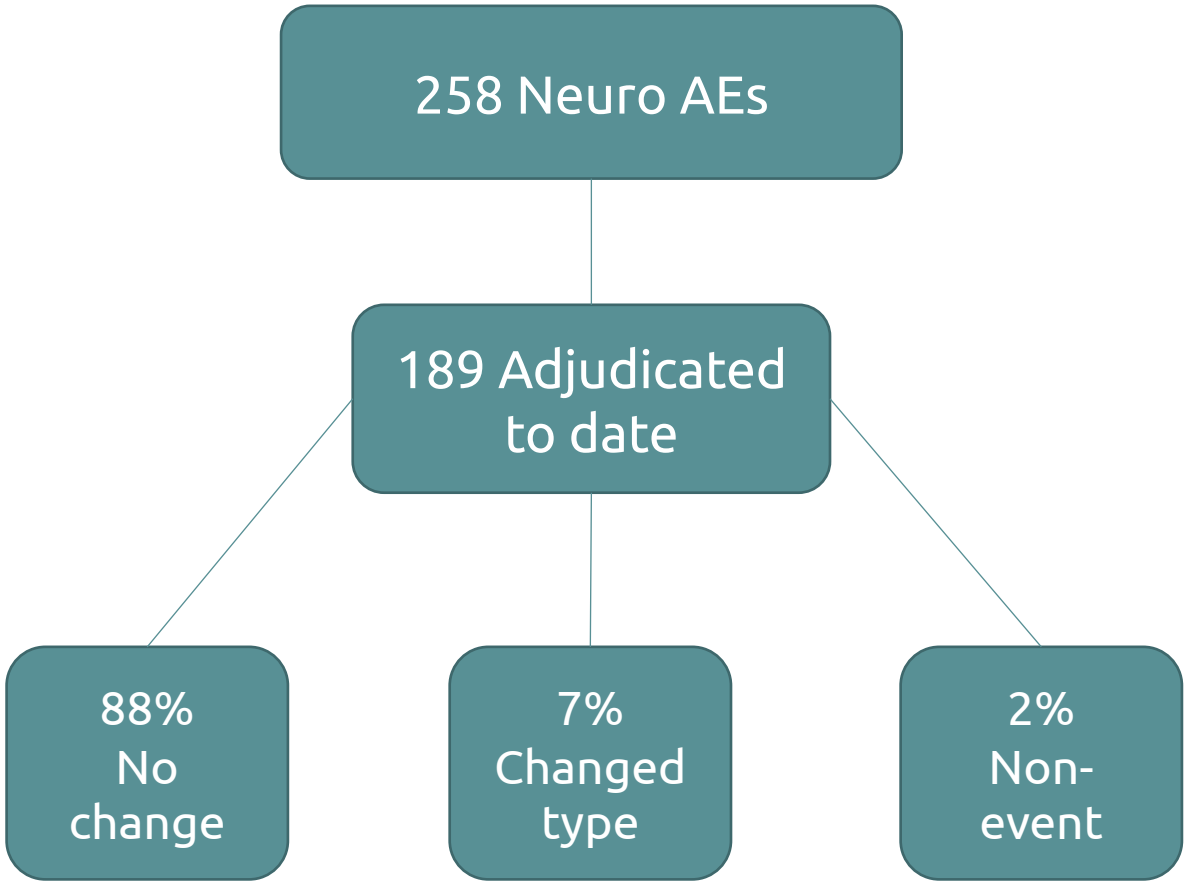
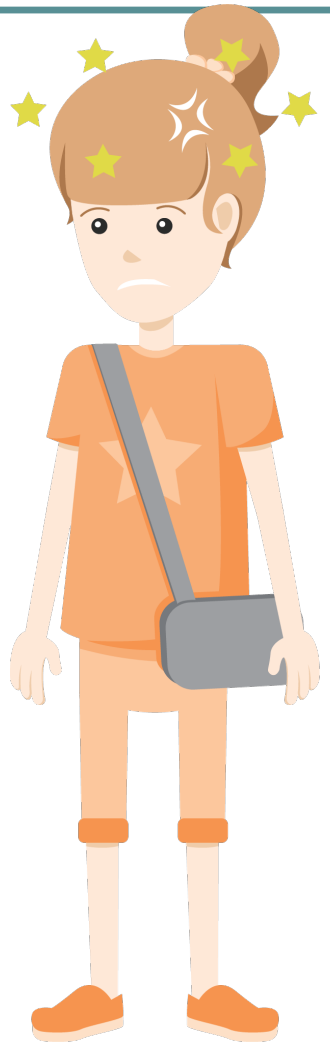
Randall C. Starling, MD, MPH,[e] James K. Kirklin, MD,[f]
J. Eduardo Rame, MD, MPhil,[g] David Rosenthal, MD,[h] Martha L. Mooney, MD,[i]
Kadir Caliskan, MD,[j] Steven R. Messe, MD,[k] Jeffrey J. Teuteberg, MD,[l]
Paul Mohacsi, MD,[m] Mark S. Slaughter, MD,[n] Evgenij V. Potapov, MD,[o]
Vivek Rao, MD,[p] Heinrich Schima, PhD,[q] Josef Stehlik, MD,[r]
Susan Joseph, MD,[s] Steve C. Koenig, MD,[n] and Francis D. Pagani, MD, PhD[t]

ACTION AE Definitions

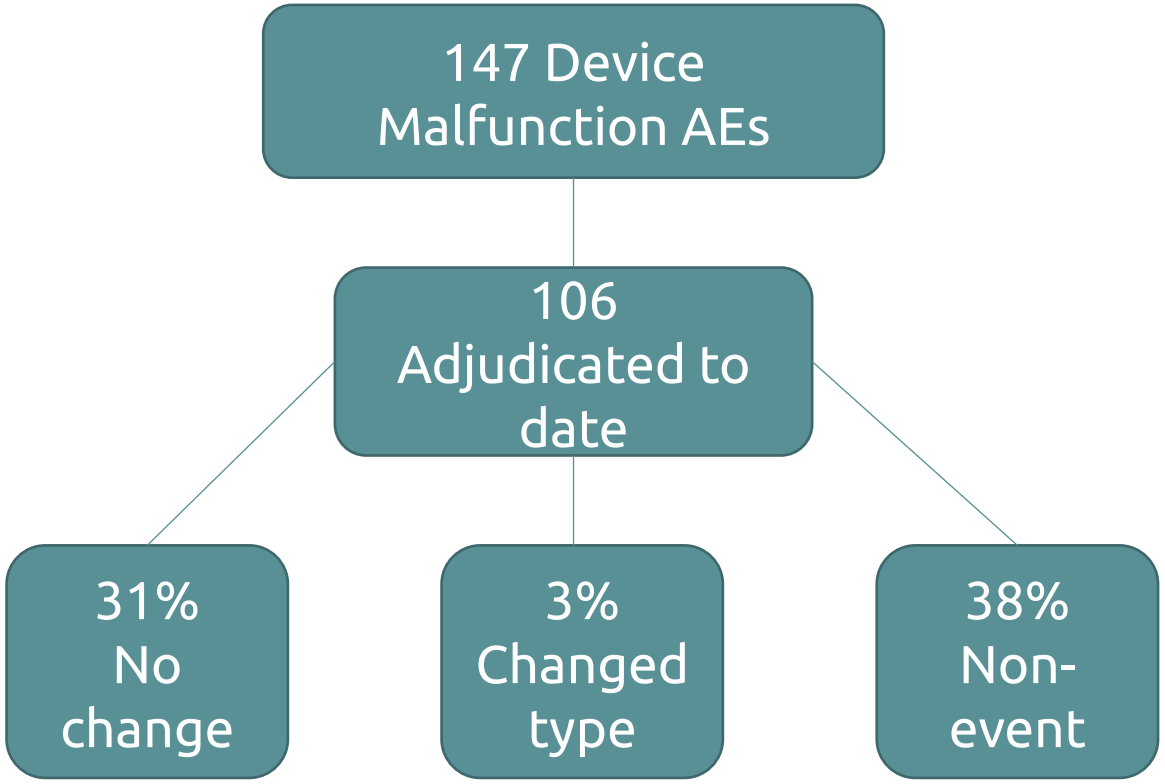
- Based upon Pedimacs which were in turn based on Intermacs
- We now have considerable experience using these definitions and understanding more about how Pediatric MCS has different requirements

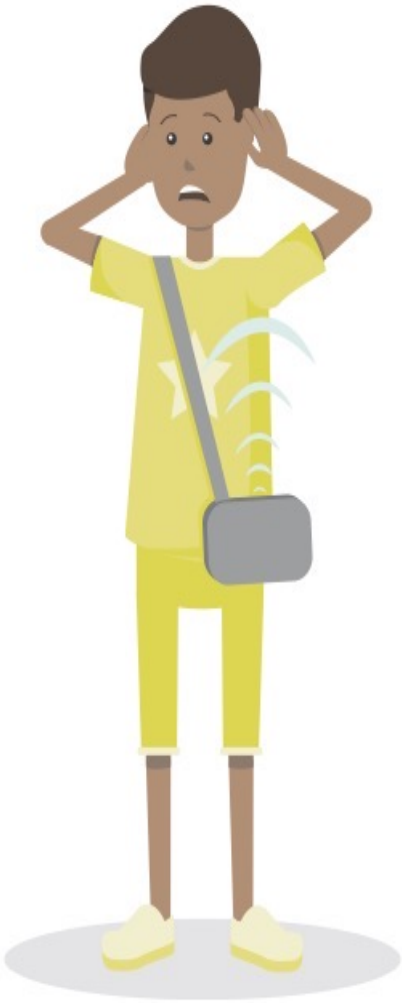
ACTION Adverse Event Adjudication





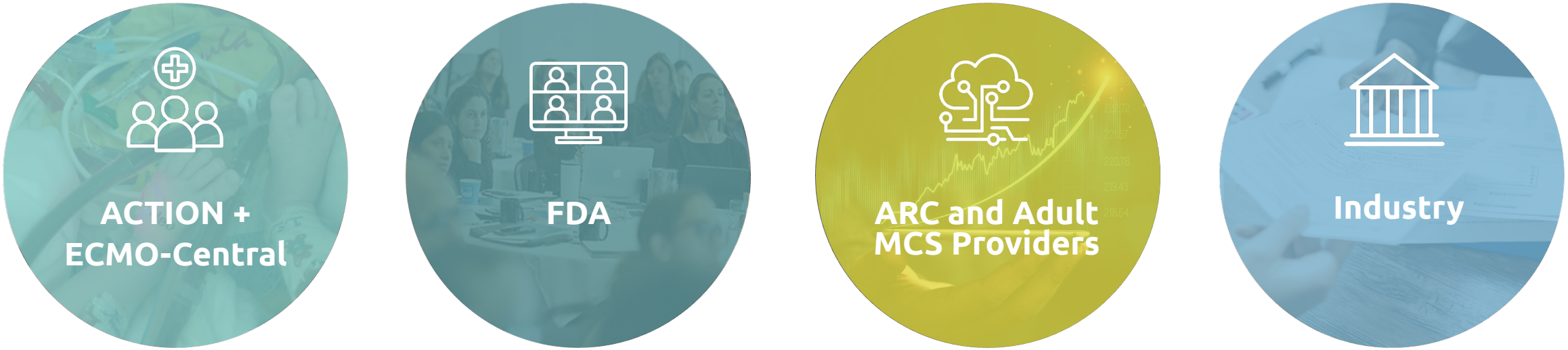
ACTION Adverse Event Adjudication





Our Solution to AE Definitions…..

ACTION MCS ARC Initiative



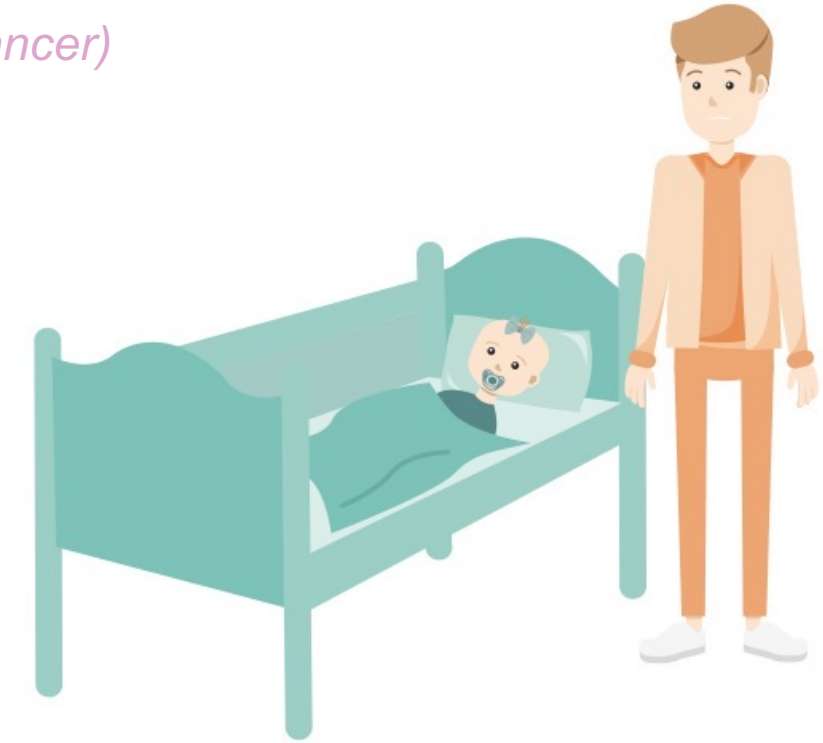
Our Goals

- Reliable definitions relevant to current VAD practice
- **Pediatric** specific definitions
- Elimination of irrelevant definitions
- Refine and clarify definitions
- Incorporate severity and cause

AE Severity

Based upon CTCAE categories (well-established, in wide use in cancer)

- **Grade 1 (mild)**: Asymptomatic or mild symptoms. Clinical or diagnostic observation indicated but no intervention.
- **Grade 2 (moderate):** Local or noninvasive intervention indicated
- **Grade 3 (severe):** Medically significant but not immediately life-threatening. Hospitalization or prolongation of hospitalization indicated.
- **Grade 4 (life-threatening):** Life-threatening consequences; urgent intervention indicated
- **Grade 5 (fatal):** Death resulting from AE



AE Cause (Probably related to)

1. **Device/Procedure:** Direct consequence of either the medical device or procedure required for implantation (includes device malfunction and user error)

2. **Patient/Treatment:** Direct consequence of underlying clinical condition of patient including organ dysfunction and its consequences, and of the treatment provided to the patient including treatment used to support the device

Breakouts

BREAKOUTS: Global and AE definitions

GROUP 1	GROUP 2	GROUP 3	GROUP 4	GROUP 5
Global ideas Bleeding AE Stroke AE	Global ideas Pump Thrombosis Hemolysis	Global ideas Device Malfunction	Global ideas Liver Respiratory Renal	Global ideas Inadequate support Right heart Dysfunction

Global: People to involve, ideas, things you have seen that we should adopt

AE: Does the definition define the problem? What is missing in the definition?

Other: Any ideas you have for ACTION?

Thank you to our collaborators!

ADDITIONAL VENTURES

Abbott

ABIOMED

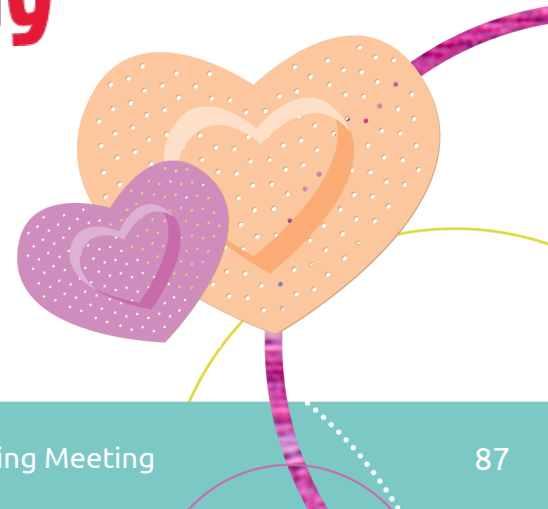
BAYER

Medtronic

Parent Project Muscular Dystrophy

Berlin Heart®

SynCardia SYSTEMS, INC.



Closing & Next Steps