Population Health Research Institute
HEALTH THROUGH KNOWLEDGE

ATLAS S-ICD
Avoid Transvenous Leads in Appropriate Subjects S-ICD

The ATLAS trial: Avoid Transvenous Leads in Appropriate Subjects

Heart Rhythm Society 2022

Late-Breaking Clinical Trials Session

Hamilton Health Sciences
McMaster University
Population Health Research Institute is affiliated with the academic teaching hospitals of Hamilton Health Sciences and McMaster University's Faculty of Health Sciences.

Declarations of Interest: Jeff Healey

- Research grants and speaking fees
  - Medtronic, Abbott, Boston Scientific, BMS/Pfizer, Servier, Novartis
- Consulting
  - Bayer, Boston Scientific

Background

- ICDs prolong survival in individuals at high risk of VT/VF
- ICD-related complications occur in up to 3% of recipients
  - Some of which are fatal, and most related to the intra-cardiac lead
- S-ICD was developed to prevent lead-related complications
  - Superiority not yet clearly proven in a RCT
  - PRAETORIAN trial demonstrated non-inferiority for a composite outcome
  - Additional RCTs need to clarify S-ICD performance vs. TV-ICD:
    - Appropriate shock efficacy and inappropriate shocks

ATLAS S-ICD
Avoid Transvenous Leads in Appropriate Subjects S-ICD

Primary Objective

To show that the use of an S-ICD reduces the rate of major lead-related complications, measured at 6-months following implant.

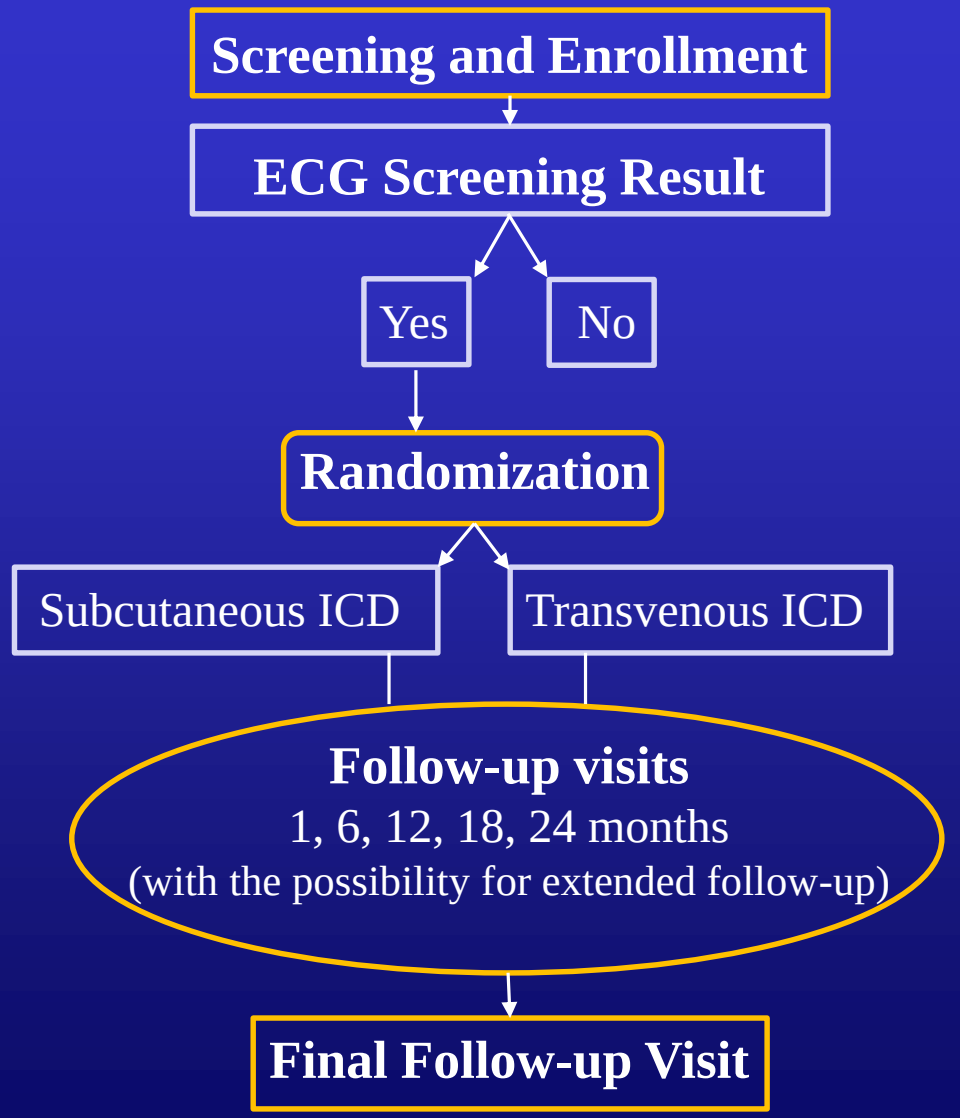
Secondary Objectives

1. To show that the S-ICD has a similar risk of inappropriate shocks

2. To show that the S-ICD has a similar risk of failed appropriate ICD shock and/or arrhythmic death

3. To show that the S-ICD reduces all-cause ICD/lead-related re-operation

ATLAS Trial Design



All patients had a study echocardiogram prior to implant and 6 months post-implant

Standardized device programming as per MADIT-RIT

Investigator Sponsored Trial with funding from Boston Scientific

Inclusion Criteria

ATLAS S-ICD
Avoid Transvenous Leads in Appropriate Subjects S-ICD

Patient must satisfy any ONE of the following two criteria:

1. Patient is ≥ 18 - 60 years old AND has a standard indication for ICD;

OR

2. Patient is ≥ 18 years old AND has any one of the following present:

- An inherited arrhythmia syndrome (i.e. Long QT, Brugada, ARVC, hypertrophic or dilated cardiomyopathy, early repolarization syndrome, etc.)
- Prior pacemaker or ICD removal for infection
- Need for hemodialysis
- Prior heart valve surgery (repair or replacement)
- Chronic obstructive pulmonary disease (with FEV1 < 1.5 L)

Exclusion Criteria

ATLAS S-ICD
Avoid Transvenous Leads in Appropriate Subjects S-ICD

- Mechanical tricuspid valve
- Fontan repair
- Presence of an intra-cardiac shunt
- Known lack of upper extremity venous access
- Need for cardiac pacing for bradycardia indication
- Clinical indication for biventricular pacing
- PR interval > 240 msec.
- Patients with permanent pacemaker

Primary Outcome

ATLAS S-ICD
Avoid Transvenous Leads in Appropriate Subjects S-ICD

Composite of major peri-operative, lead-related complications measured at 6 months, including:

- Hemothorax or pneumothorax
- Cardiac perforation, tamponade, pericardial effusion or pericarditis
- Lead dislodgement or loss of pacing/sensing requiring revision
- New moderate-severe or severe tricuspid insufficiency (3+ or 4+)
- Ipsilateral upper extremity deep venous thrombosis

A secondary 6-month safety composite includes the above plus:

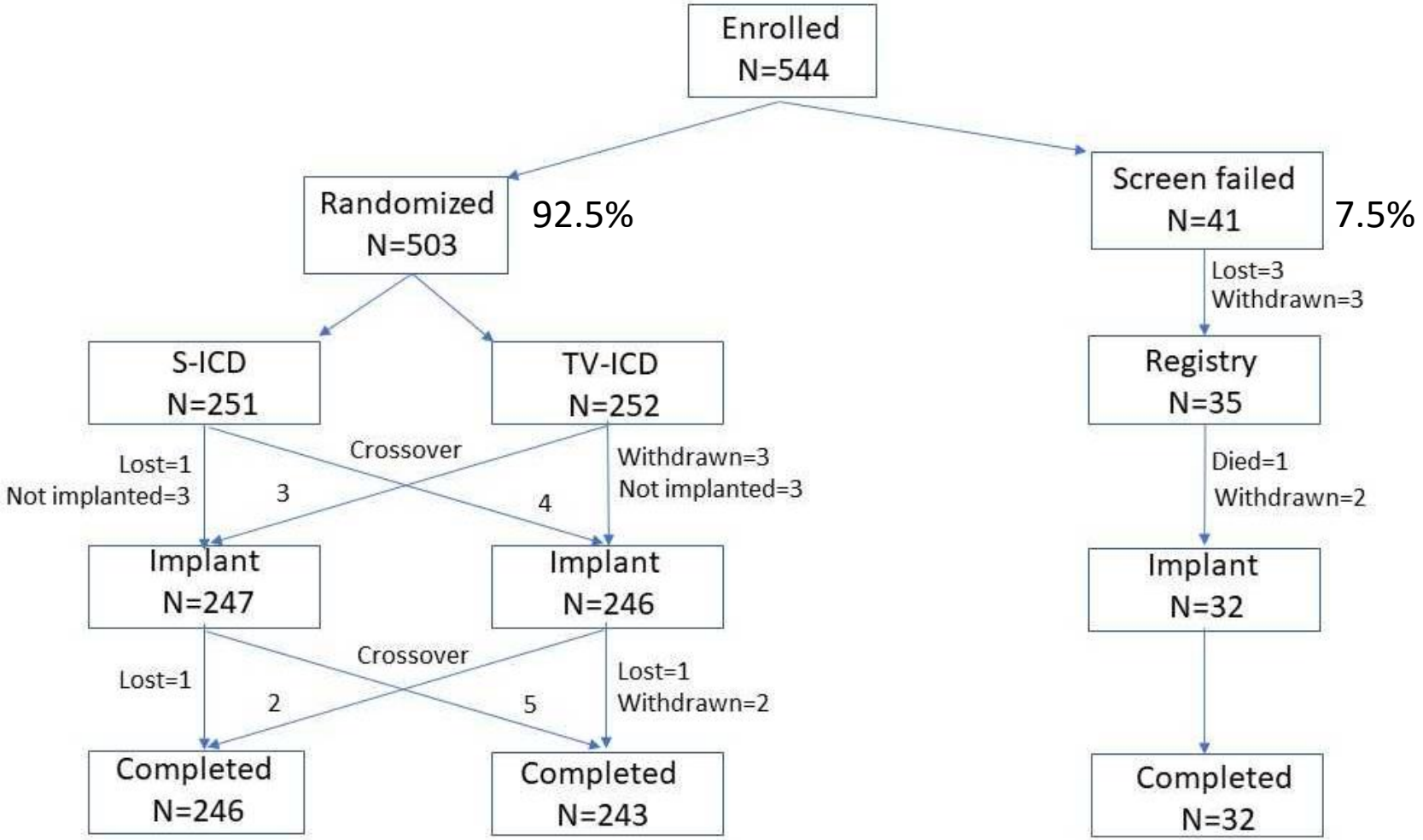
- Device-related infection requiring surgical revision
- Significant wound hematoma (requiring evacuation or interruption of OAC)
- Myocardial infarction, Stroke or Death

*** All clinical and ICD events centrally-adjudicated by a committee of experts**

CONSORT Diagram

mean centre implant volume before ATLAS of **17.1 ± 15.3 S-ICD cases**

mean Follow-up of 2.5 ± 1.1 years



Baseline Characteristics

	Registry	Randomized	S-ICD	TV-ICD
N	35	503	251	252
Age (years) - mean (SD)	48 (13.7)	49 (11.5)	48 (11.9)	50 (11.1)
Male - n (%)	24 (68.6)	373 (74.2)	191 (76.1)	182 (72.2)
Previous cardiac arrest – n (%)	4 (11.4)	113 (22.5)	59 (23.5)	54 (21.4)
Sustained ventricular tachycardia – n (%)	5 (14.3)	46 (9.1)	23 (9.2)	23 (9.1)
Heart failure – n (%)	15 (42.9)	243 (48.3)	126 (50.2)	117 (46.4)
Previous stroke – n (%)	1 (2.9)	18 (3.6)	9 (3.6)	9 (3.6)
Diabetes – n (%)	6 (17.1)	98 (19.5)	49 (19.5)	49 (19.4)
Beta Blocker (other than Sotalol) – n (%)	28 (80.0)	395 (78.5)	197 (78.5)	198 (78.6)
Sotalol – n (%)	0 (0.0)	5 (1.0)	3 (1.2)	2 (0.8)
Amiodarone – n (%)	1 (2.9)	25 (5.0)	13 (5.2)	12 (4.8)
Other Antiarrhythmic Therapy – n (%)	2 (5.7)	16 (3.2)	8 (3.2)	8 (3.2)

* Self-reported ethnicity: Caucasian 83.9%, Asian 6.4%, Black 2.8%, Indigenous 1.4%, Latino 1.2%

Baseline Cardiac Conditions

	Registry	Randomized	S-ICD	TV-ICD
Coronary artery disease - n (%)	11(31.4)	183 (36.4)	87 (34.7)	96 (38.1)
Dilated cardiomyopathy - n (%)	7 (20.0)	116 (23.1)	56 (22.3)	60 (23.8)
Hypertrophic cardiomyopathy - n (%)	10 (28.6)	93 (18.5)	45 (17.9)	48 (19.0)
Idiopathic ventricular fibrillation - n (%)	4 (11.4)	84 (16.7)	47 (18.7)	37 (14.7)
Right ventricular cardiomyopathy - n (%)	1 (2.9)	21 (4.2)	11 (4.4)	10 (4.0)
Brugada syndrome - n (%)	2 (5.7)	12 (2.4)	5 (2.0)	7 (2.8)
Long QT syndrome - n (%)	1 (2.9)	7 (1.4)	4 (1.6)	3 (1.2)
Catecholaminergic polymorphic - n (%)	0 (0.0)	2 (0.4)	1 (0.4)	1 (0.4)
Valvular heart disease - n (%)	0 (0.0)	5 (1.0)	4 (1.6)	1 (0.6)
Congenital heart disease - n (%)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.4)

Primary Outcome

	S-ICD	TV-ICD	OR (CI)	P-value
Composite Primary Outcome – n (%)	**1 (0.4)**	**12 (4.8)**	**0.08 (0.00- 0.55)**	**0.003**
Hemothorax or pneumothorax – n (%)	0 (0.0)	2 (0.8)	0.41 (0.00- 3.48)	0.25
Cardiac perforation, tamponade, pericardial effusion or pericarditis – n (%)	1 (0.4)	4 (1.6)	0.25 (0.01- 2.54)	0.38
Lead dislodgement or loss of sensing or pacing requiring revision – n (%)	0 (0.0)	2 (0.8)	0.41 (0.00- 3.48)	0.25
New moderate-severe or severe tricuspid insufficiency – n (%)	0 (0.0)	3 (1.2)	0.26 (0.00- 1.72)	0.13
Ipsilateral upper extremity deep venous thrombosis – n (%)	0 (0.0)	1 (0.4)	1.00 (0.00-19.08)	0.50

* No difference with per-protocol analysis; no significant sub-group interactions

Secondary Safety Outcome

	S-ICD	TV-ICD	CI
Secondary Safety 6-month composite – n (%)	**11 (4.4)**	**14 (5.6)**	**0.78 (0.35- 1.75)**
Device-related infection requiring surgery – n (%)	2 (0.8)	1 (0.4)	2.01 (0.10-119.4)
ICD wound hematoma – n (%)	3 (1.2)	1 (0.4)	3.03 (0.24-160.0)
Myocardial Infarction – n (%)	2 (0.8)	0 (0.0)	2.43 (0.29- I)
Stroke or transient ischemic attack – n (%)	1 (0.4)	0 (0.0)	1.00 (0.05- I)
Death – n (%)	3 (1.2%)	0 (0.0)	3.89 (0.59-I)

Inappropriate Shocks

	S-ICD	TV-ICD	OR (CI)
N	251	252	
Any inappropriate shock – n (%)	**16 (6.4)**	**7 (2.8)**	**2.38 (0.96- 5.90)**
T-wave oversensing – n (%)	6	0	
Atrial arrhythmia – n (%)	2	5	
Electromagnetic Interference – n (%)*	5	2	
Myopotentials **	3	0	
Any inappropriate shock – rate/yr.	2.7% per yr.	1.2% per yr.	HR = 2.37 (0.98- 5.77)

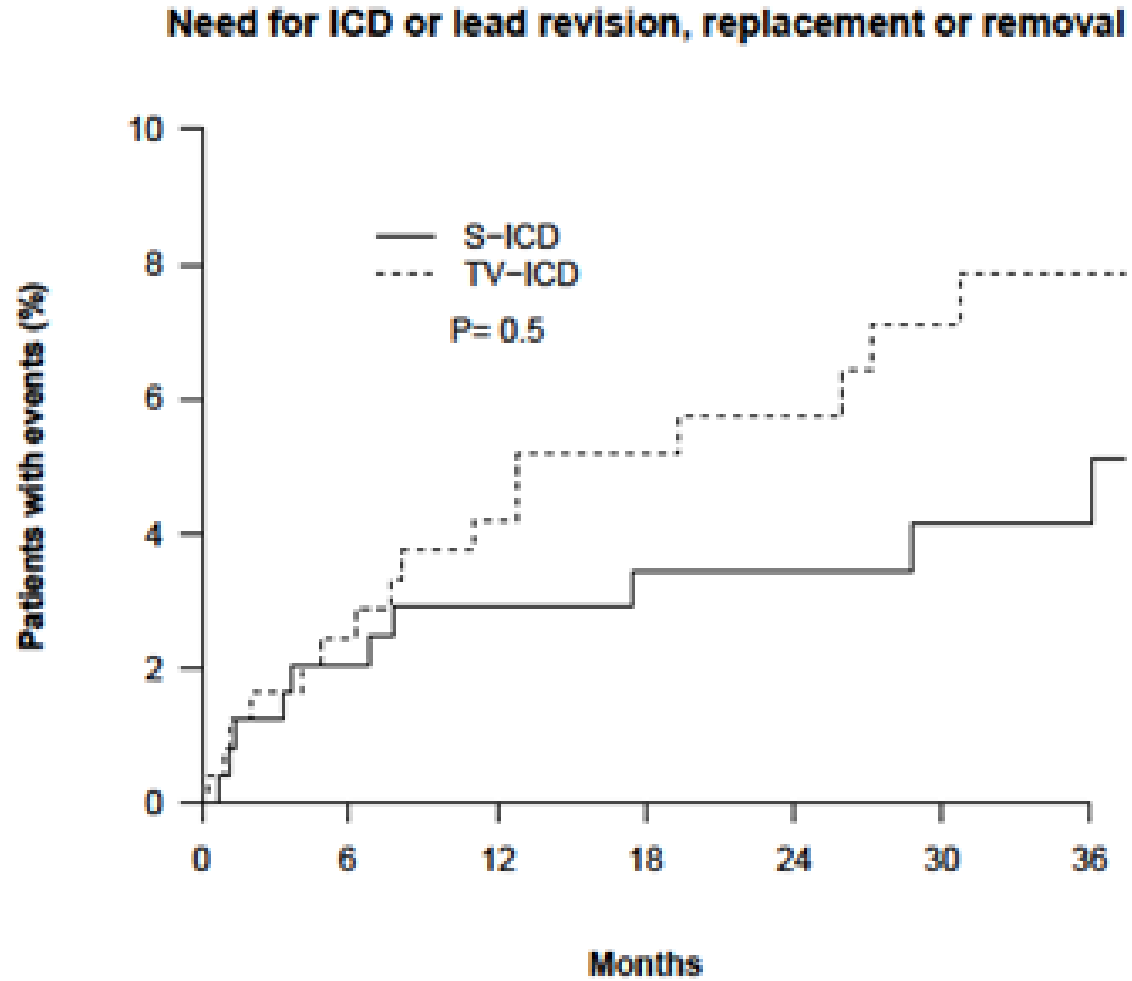
*** 4 cases in S-ICD and 2 cases in TV-ICD arm due to T.E.N.S., one case each in S-ICD due to LVAD**

**** No lead fractures due to advisory**

ICD Effectiveness

	S-ICD	TV-ICD	HR (CI)
Failed first shock or arrhythmic death %/yr.	**1.7**	**1.1**	**1.47; 95% CI, 0.56-3.87**
Failed first shock - %/yr.	1.4	0.8	1.64; 95% CI, 0.54-5.03
Arrhythmic death - %/yr.	0.3	0.5	0.68; 95% CI, 0.11-4.08
All-cause morality - %/yr.	0.8	0.8	1.02; 95% CI, 0.30-3.52
Heart failure hospitalization - %/yr.	3.6	5.2	0.69; 95% CI, 0.30-1.62

All-Cause Re-Operation for ICD or Lead



Conclusions

- S-ICD reduces the rate of major, lead-related complications by 92%
- No significant reduction in ICD performance with S-ICD
  - Inappropriate shocks and appropriate shock success
  - Additional, longer-term data give additional precision
- The S-ICD can be considered an alternative to the TV-ICD
  - Particularly when prevention of lead-related complications is desired

Many thanks to our collaborators!

- **Executive Committee:** Jeff S. Healey (Principal Investigator), **Blandine Mondesert (co-Principal Investigator),** Andrew D. Krahn (Steering Committee Chair, and Jamil Bashir.
- **Adjudication Committee:** John Sapp (Chair), William F. McIntyre, Amir Janmohamed, Guy Amit, Jason Roberts and Francois Philippon.
- **Data Safety and Monitoring Committee:** Andrew Epstein (Chair), John Cairns, and Kevin Thorpe.
- **Echocardiographic Core Lab:** Darryl P. Leong, Naif Saad, Harry Klimis, Felipe Cirne, Osama Eltebi, Aditya Khetan, and Hisham Dokainish.
- **Site investigators**: Guy Amit, Bernice Tsang, Jacqueline Joza, Derek V. Exner, David H. Birnie, Mouhannad Sadek, Dr. Chris Lane, Marc Dubuc, Vidal Essebag, Darryl Leong, Chris Lane, Markus Sikkel, Victoria Korley, John Sapp, Amir Janmohamed, Jean-Francois Roux, Danna Spears, Eugene Crystal, Rupi Sandhu and Tom Hruczkowski.
- **Coordinating Centre (PHRI):** Angie Djuric, Kim Simek, Roberta Napoleoni, Brook Snider, Shun Fu Lee, Gloria Wong, Kailey Howell, and Lauren Christmas.
- **Observers from Boston Scientific**: Ken Stein, Tim Stivland, Mark Mosley, Peter Aitkins.