

Modern ICD Therapy: Reducing Shocks

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HRC 2011*

Negative Publicity Due to ICD Shocks

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Florida: Partly to mostly sunny skies with isolated rain showers, mainly in the southern areas. Highs in lower to mid-40's. Tomorrow, sunny, highs in the 80's. Weather map is on Page D7.

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ONE DOLLAR

Extending Life, Defibrillators Can Prolong Misery

By GINA KOLATA

The patient, a man in his 60's, arrived at the Cleveland Clinic Foundation hospital in acute discomfort. His defibrillator, a tiny device implanted in his chest to correct abnormal heart rhythms, was going off six times a day or more, with a jolt that felt like a boxer's punch to the chest.

The defibrillator was working properly; the man's heart disease was so advanced that his heart rhythms kept going awry. As the man lay in his hospital bed about two years ago, "it was getting to the point where it was happening once an hour," his cardiologist, Dr. Michael

Lauer, recalled.

The doctors tried to calm the man's heart, to no avail. "We were all gathered around his bed, five or six doctors, and we didn't know what to do," Dr. Lauer said.

It was Dr. Lauer's first experience with a condition that he and other medical experts say they are seeing more often. It was unforgettable.

Finally, the man spoke up. "He said: 'I've had enough. It's time to stop,'" Dr. Lauer said. "He knew exactly what that meant."

The doctors turned off the man's defibrillator. Shortly afterward, he died.

Defibrillator storms, as doctors call the condition the patient was

experiencing, are still rare. Still they create a painful predicament that is expected to become more common with results from a study released last week. The study suggested that implantable defibrillators may improve survival rates in millions of heart patients. But what happens when an advance that prolongs life also prolongs a patient's misery?

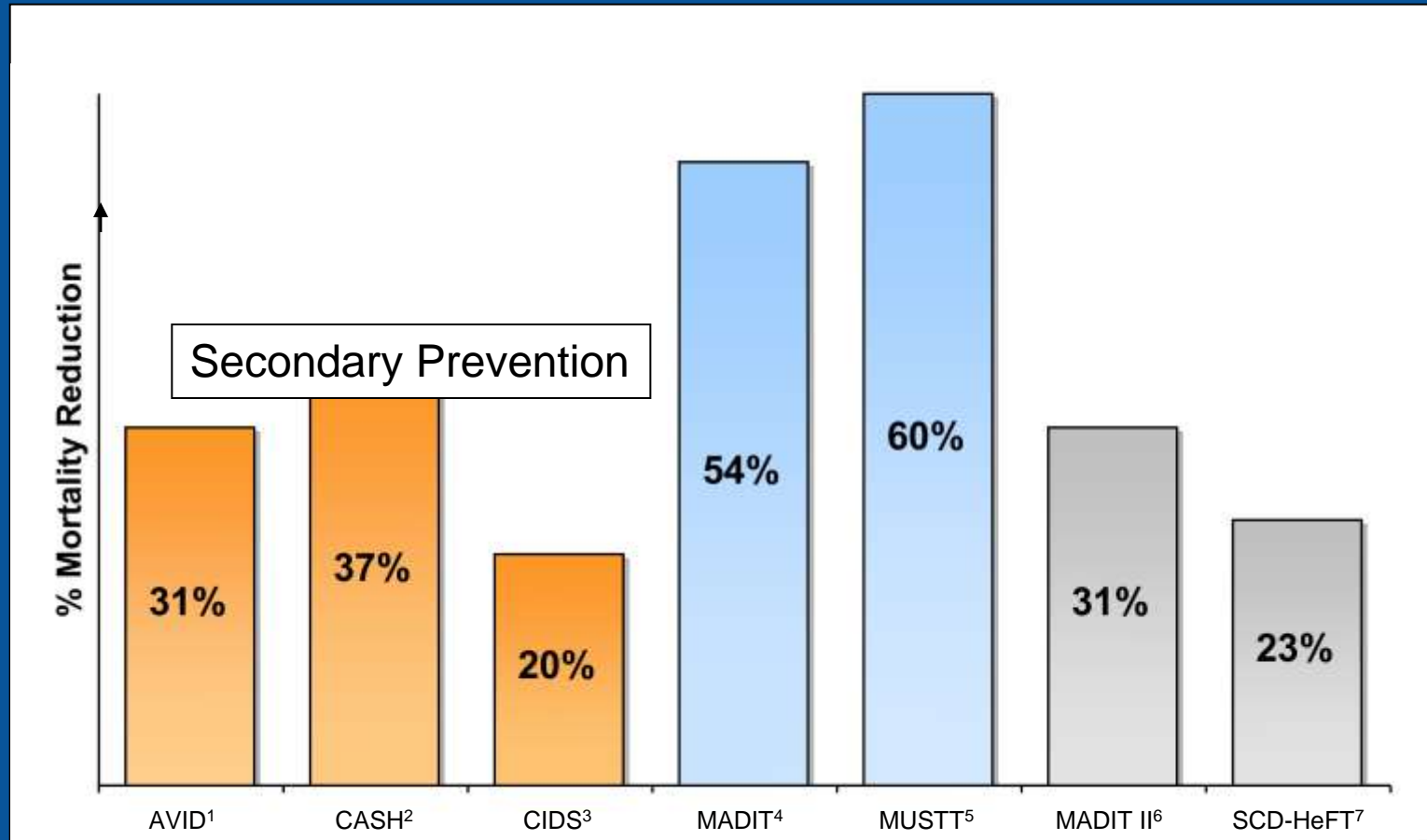
The device, which costs \$20,000, plus \$10,000 for the operation to insert it, is already approved for people (including Vice President Dick Cheney) who have heart rhythm disturbances that can be corrected by electric shocks to the heart. About 80,000 Americans have the devices, and since 1996, when they were approved for patients like Mr. Cheney, their use has been increasing by about 50 percent a year.

The new study, reported in *The New England Journal of Medicine*, found that the device could also help a much larger group of patients, those who have serious damage from heart attacks and are at risk for arrhythmias, but have not had them.

About four million patients in the United States fall into this category, with 400,000 added each year. In the new study, the devices reduced the



Mortality Reduction with ICDs

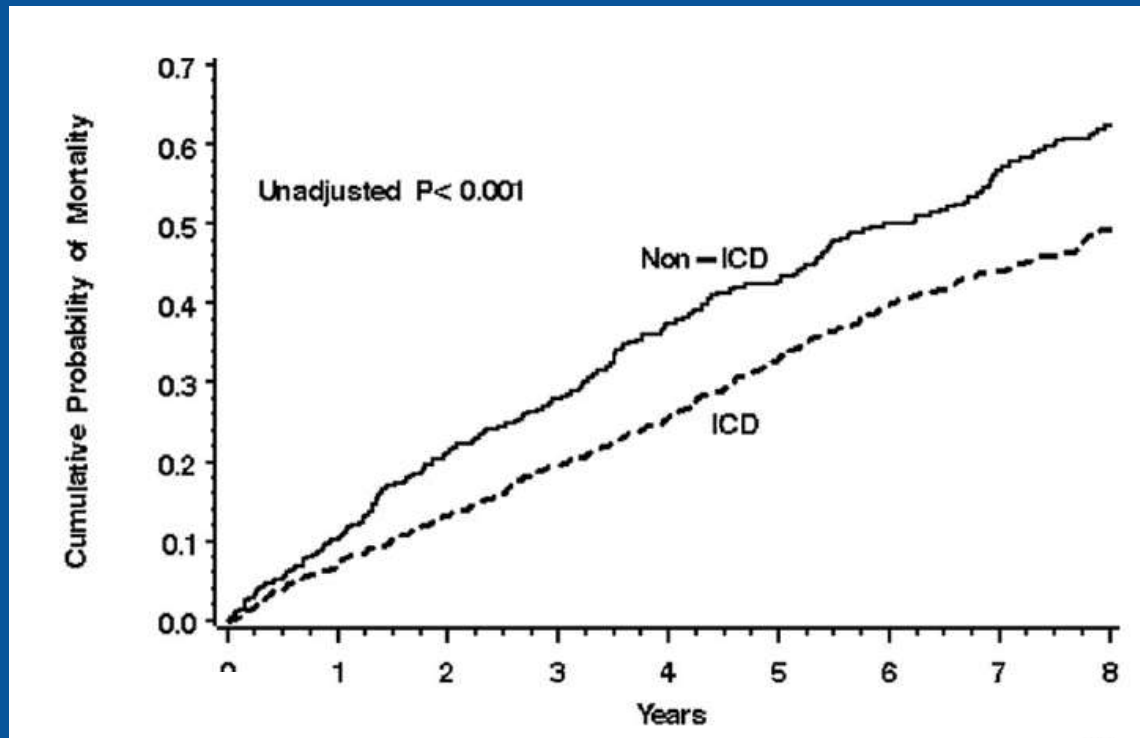


but many more patients receive shocks than lives are saved

1. The AVID Investigators. *N Engl J Med.* 1997;337:1576-1583. 2. Kuck KH. *Circulation.* 2000;102:748-754. 3. Connolly. *Circulation.* 2000;101:1297-1302. 4. Moss AJ, et al. *N Engl J Med.* 1996;335:1933-1940. 5. Buxton AE, et al. *N Engl J Med.* 1999;341:1882-1890. 6. Moss AJ, et al. *N Engl J Med.* 2002;346:877-883. 7. Bardy GH, et al. *N Engl J Med.* 2005;352:225-237.

MADIT II: Long-Term Follow-up

- Sustained survival benefit of ICD therapy
 - NNT with ICD to save 1 life: 17 at 2 years and 6 at 8 years
 - 34% mortality reduction at 8 years



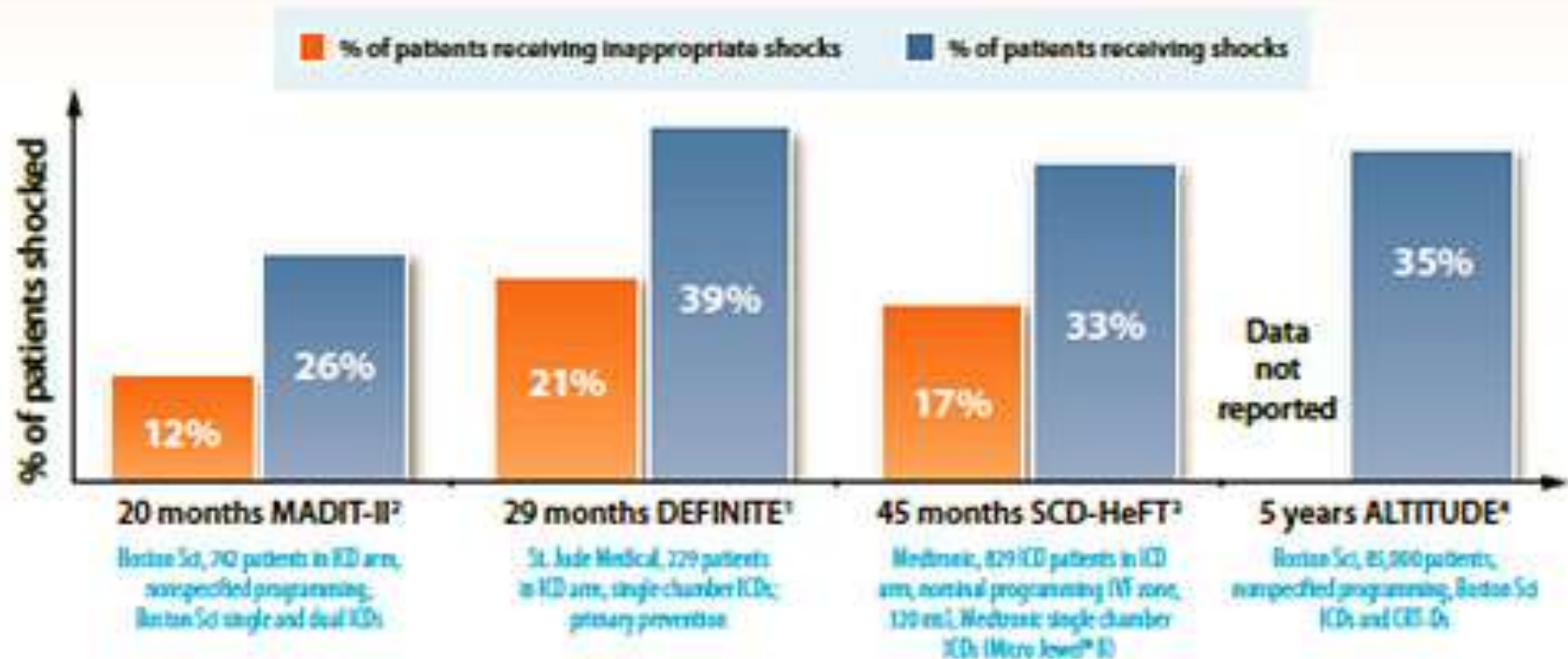
ICD Therapy

**Appropriate, inappropriate and
unnecessary Shocks**

ICD Shocks

- **Appropriate** shocks: Shocks triggered by potentially life-threatening arrhythmias
 - **Unnecessary** shocks: Other painless therapy can be used to terminate arrhythmia
 - Necessary shocks : Shock for arrhythmias not terminated by other means
- **Inappropriate** Shocks: Shocks triggered by an inappropriate detection

Inappropriate Shocks in Clinical Practice



Shocks Affect Patients' Quality of Life

- Psychological impact of shocks on patients has been clinically studied
- For patients, simply the fear of shocks can be disruptive to a normal, active life
- Shock reduction has been shown to improve ICD patient's quality of life

Inappropriate Shocks in Clinical Practice

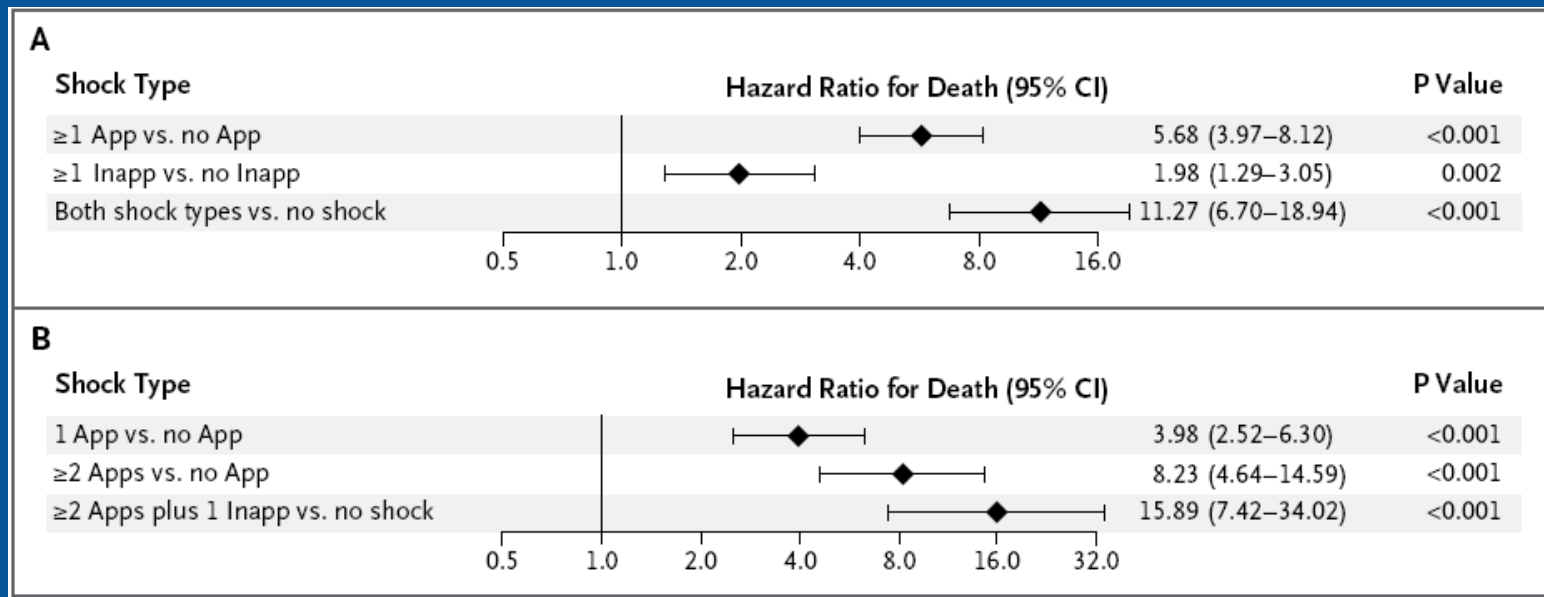
- **Meta Analysis of inappropriate shocks in 1,544 ICD pts.:**
 - Incidence: 7% at 1 y, 13% at 3 y, 18% at 5 years
 - Causes: SVT (76% of pts.)
 - Outcome: Associated with higher mortality

Predictors of all-cause mortality

	Univariate			Multivariate		
	HR	95% CI	p Value	HR	95% CI	p Value
Baseline variables						
History of atrial fibrillation*	1.3	1.0-1.7	0.11	1.4	1.0-1.7	<0.01
Age >70 yrs*	2.7	2.2-3.4	<0.01	1.9	1.5-2.5	<0.01
NYHA functional class >II*	2.0	1.6-1.5	<0.01	1.5	1.1-1.9	0.03
Renal clearance <90 ml/min*	2.7	2.0-3.7	<0.01	1.7	1.2-2.4	0.02
QRS duration >120 ms*	2.0	1.6-2.5	<0.01	1.4	1.1-1.8	0.02
No use of beta-blockers*	1.3	1.0-1.7	0.01			
Interim events						
Inappropriate shock	1.4	1.0-2.0	0.07	1.6	1.1-2.3	0.01
Per inappropriate shocks (≤5)†	1.3	1.1-1.6	<0.01	1.4	1.2-1.7	<0.01
Interim appropriate shocks*	2.5	1.9-3.3	<0.01	1.6	1.2-2.1	<0.01

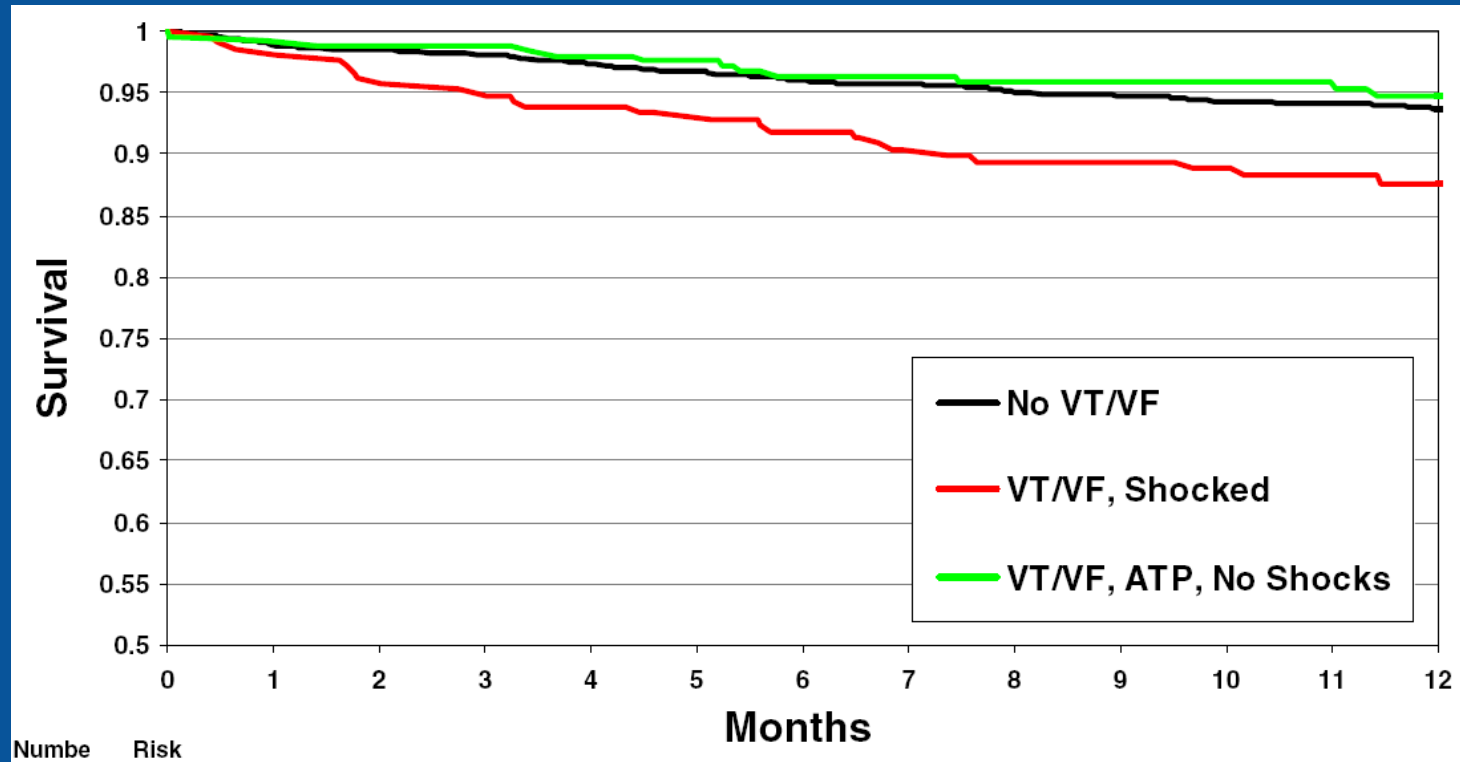
Prognostic Importance of ICD Shocks

- SCD-HeFT patients who received and ICD (n=811)
- 33.2% received shocks: 15.8% only appropriate, 10.7% only inappropriate and 6.7% both
- Patients who receive shocks for any arrhythmia have a higher risk of death than those who do not receive such shocks



Appropriate shocks but not ATP are associated with Higher Mortality

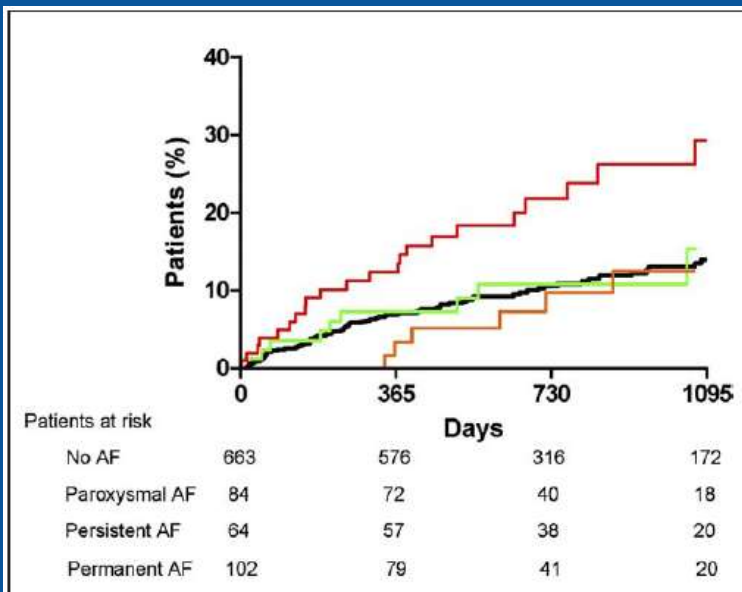
- Retrospective analysis of pooled data
 - PainFREE I and II, EMPIRIC and PREPARE
 - 2,135 pts, EF 31%, 87% CAD, 55% NYHA II/III, 42% NYHA I/ no CHF



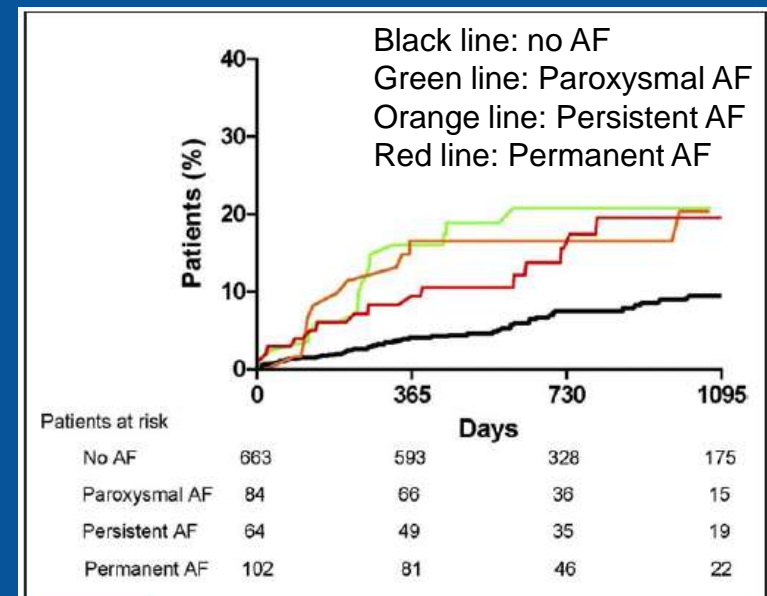
ICD Shocks in Atrial Fibrillation

- 913 consecutive ICD pts: 73% had no AF, 9% paroxysmal AF, 7% persistent AF, 11% permanent AF
- Permanent AF: mortality risk doubled, higher risk any therapy
- Paroxysmal/persistent AF: 3 times higher risk of inappropriate shocks

Appropriate device shock



Inappropriate device shock



Potential Benefits of Shock Reduction

- Improved patient quality of life
- Increased ICD therapy acceptance
- Extended ICD longevity
- Less demand for post-shock care
- May improve survival benefits of ICDs
- Reduced healthcare spending

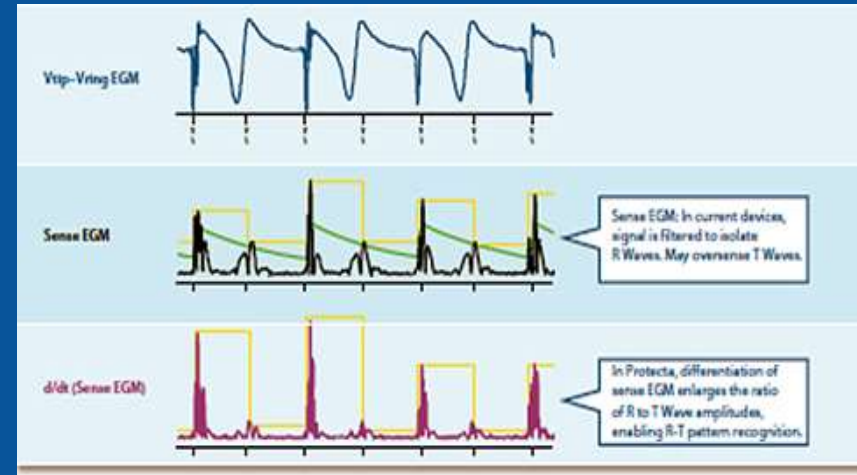
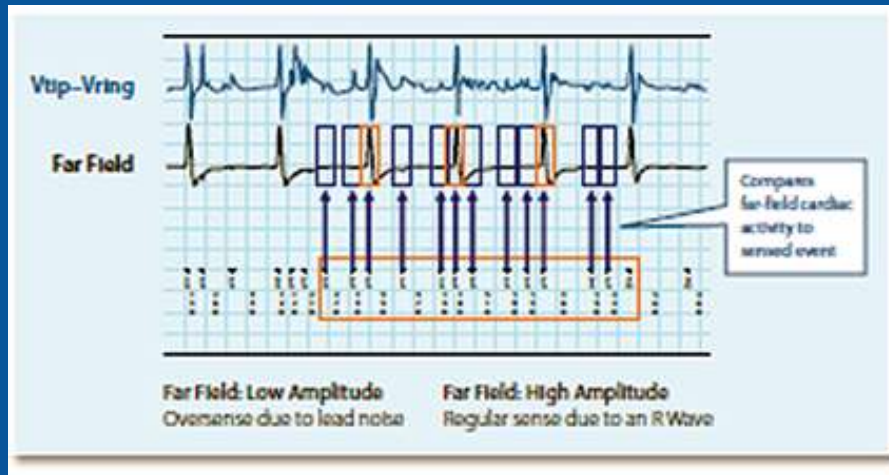
Reducing inappropriate and unnecessary Shocks

Identify patients at high risk to tailor drug + device therapy

- Medical Therapy - esp. antiarrhythmic/AV nodal blocking
- Ablation - SVT, AV node, VT
- Device programming - increase use of generic strategies & specific algorithms



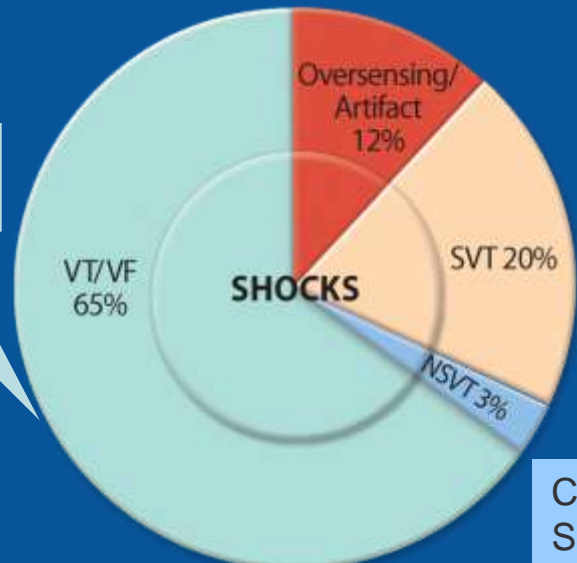
Strategies to Safely Reduce Shocks



Noise
active discriminator & alerts

T wave
specific algorithm

ATP Before and During Charging



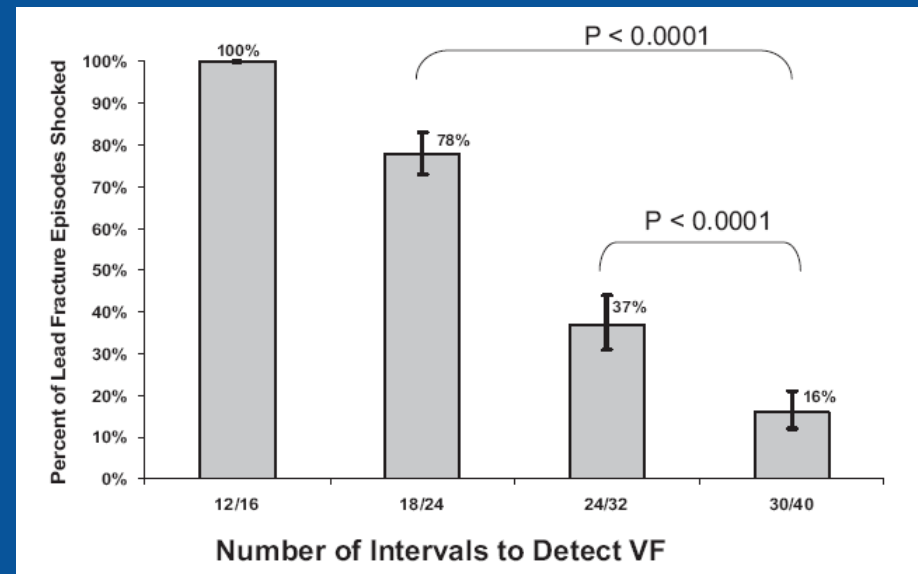
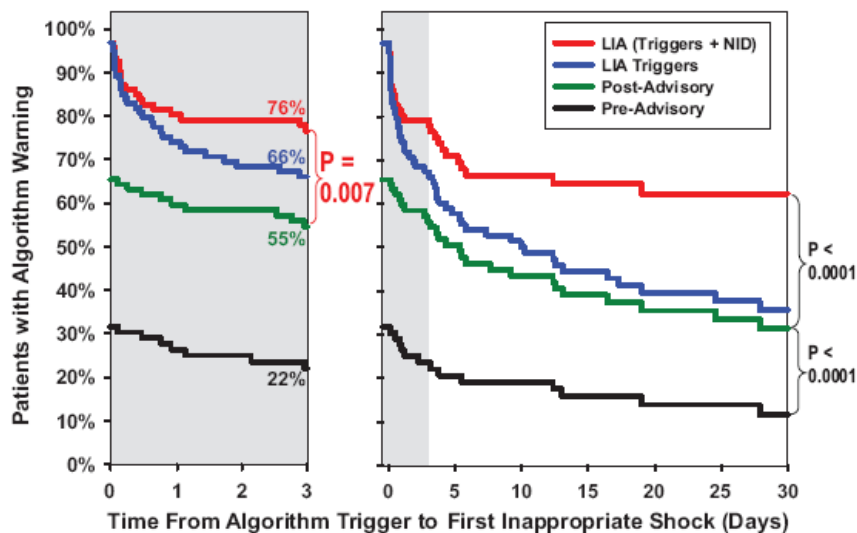
PR logic AND wavelet analysis; discriminate into VF zone

Confirmation Plus; Short charge time

SCDHeFT data

Lead Integrity Alert Avoids Inappropriate Shocks in Lead Failure

- Fractures in pace-sense electrodes of ICDs often lead to inappropriate shocks due to oversensing
- LIA is based on lead impedance and an oversensing trigger
- When triggered it extends the NID to 30 out of 40
- LIA provided at least 3-day warning of inappropriate shocks in 76% of pts.



Lead Integrity Alert Reduces Inappropriate Shocks in Lead Failure

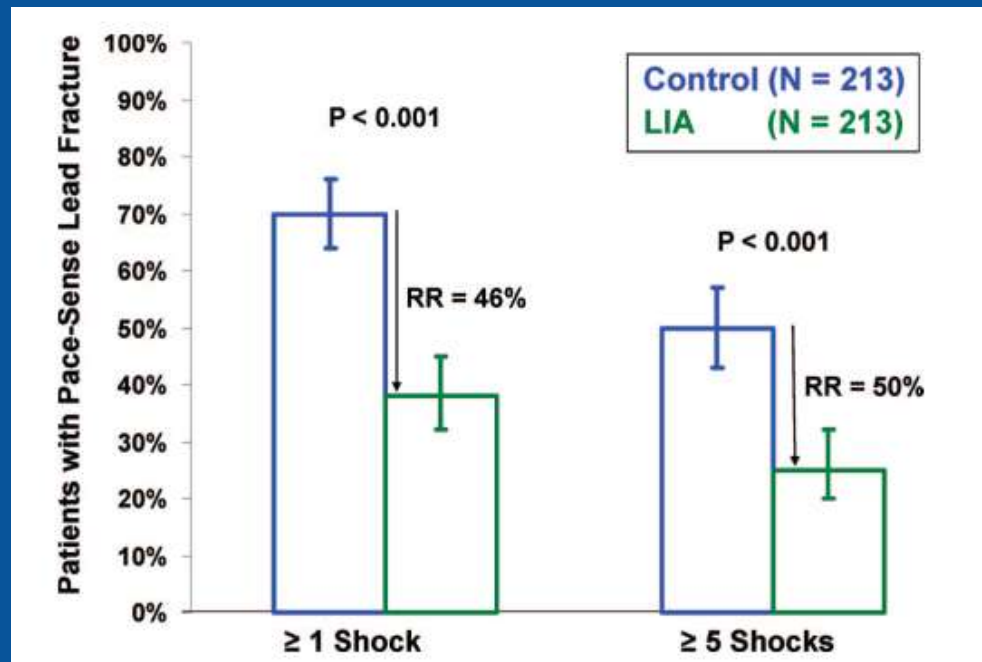
- Evaluation of LIA algorithm by comparing pts. with Sprint Fidelis lead failure without versus with LIA
- Pts. with LIA had:
 - Less often inappropriate shocks as first sign of failure ($p=0.0006$)
 - Less inappropriate shocks ($p=0.017$)

Table 4 First sign of Sprint Fidelis lead failure

	No.	Average no. inappropriate shocks \pm SD		
		No. (%)	Patients with inappropriate shocks (range)	All patients (total no. inappropriate shocks)
Patients without LIA	26	18 (69%)	13.2 \pm 13.6 (2–54)	9.2 \pm 12.8 (238)
Patients with LIA	23	4 (17%)	3.0 \pm 2.0 (2–6)	0.5 \pm 1.4 (12)

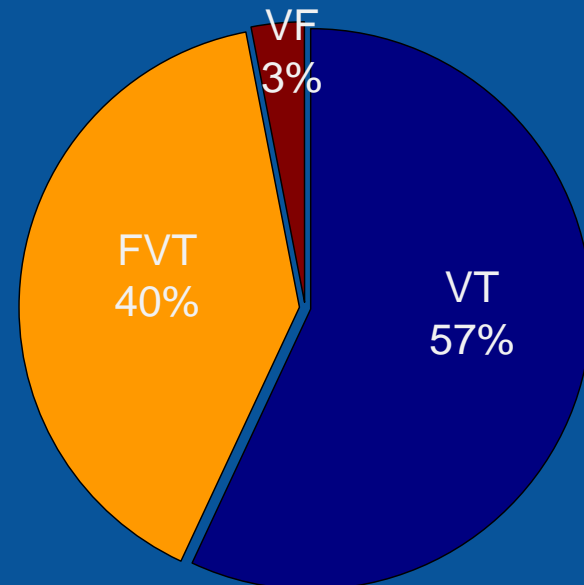
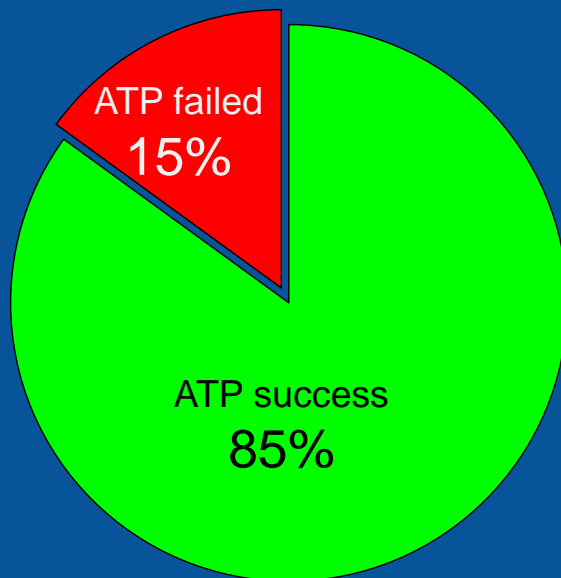
LIA Reduces Inappropriate Shocks

- 213 pts. with lead fracture and LIA were compared to 213 pts. with lead fracture but without LIA
- LIA group had 46% reduction in percentage of pts. receiving inappropriate shocks



ATP for Fast VTs Reduces Shocks

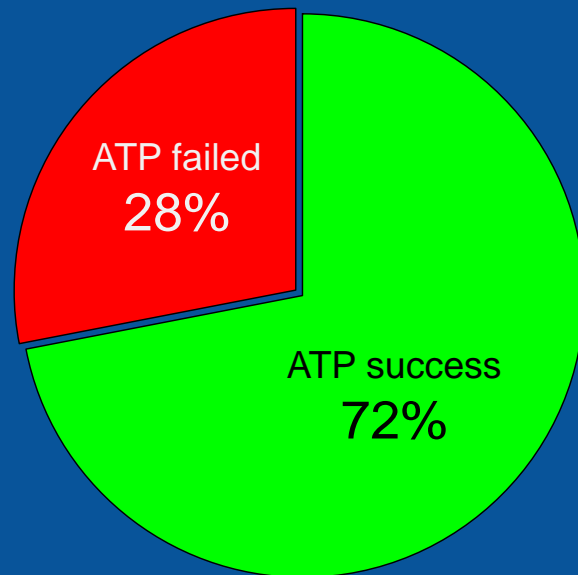
- PainFREE Rx I: 220 ICD pts. with CAD received empirical ATP (up to 2) for fast VTs (188-250 bpm), NID 12/16
- ATP terminated 396 out of 446 FVT episodes (89%)
- VT acceleration and FVT syncope were rare (4 and 2% resp.)



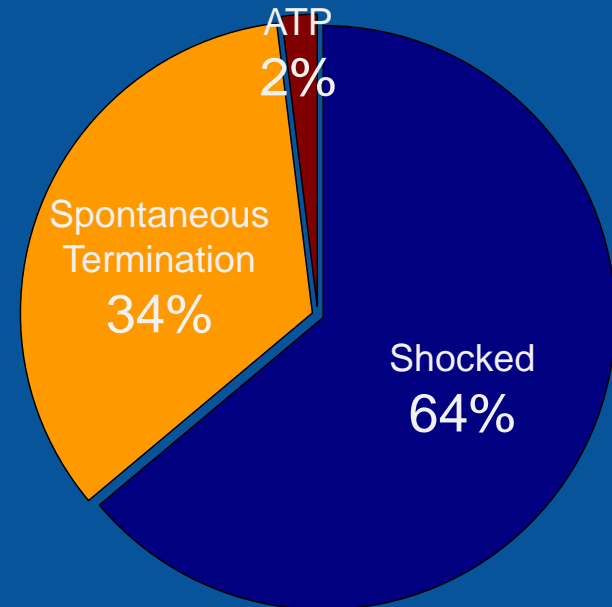
Note: ATP success was 89% with 3 ATP; 85% with up to 2 ATP (protocol), 77% adjusted efficacy rate

ATP for Fast VTs Reduces Shocks

- PainFREE Rx II: 634 prim./sec. prevention ICD pts. randomized to empirical ATP or shock for fast VTs (188-250 bpm), NID 18/24
- ATP is highly effective, equally safe and improves QoL



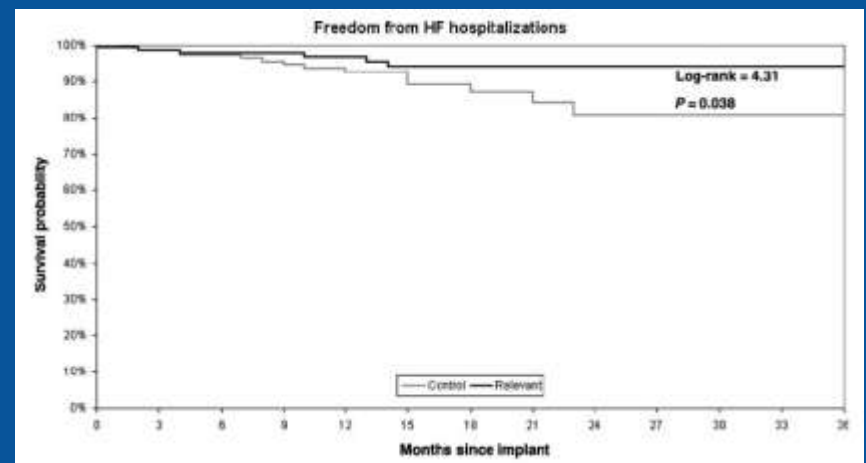
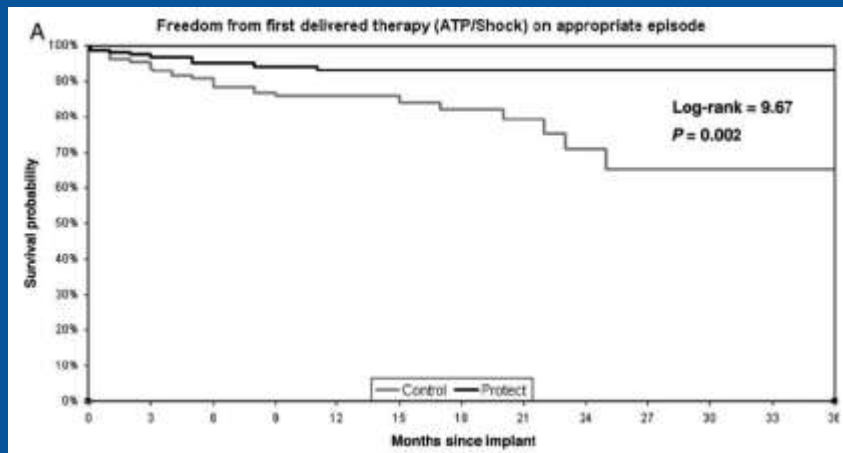
ATP Arm
n=284 episodes



Shock Arm
n=147 episodes

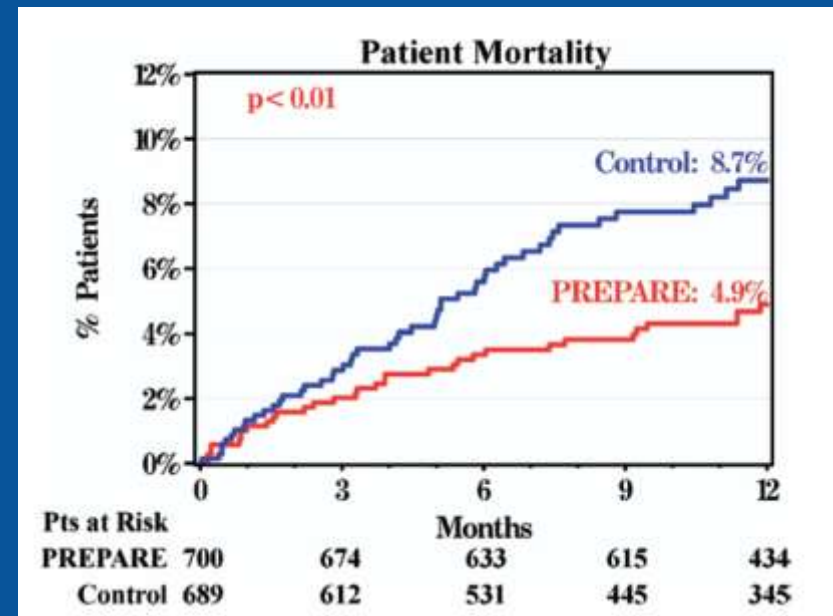
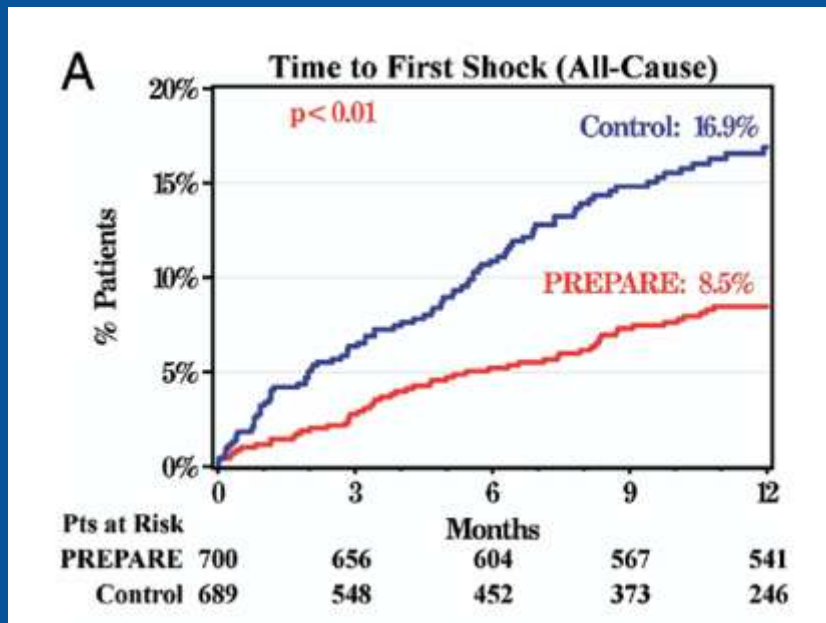
CRT-D with NID programmed to 30/40

- **RELEVANT: 324 primary prevention pts. with non-ischemic etiology with CRT-D programmed to: NID 30/40 or 12/16 (control)**
- **Study arm showed:**
 - Better event-free survival to first delivered therapy for total, appropriate and inappropriate episodes
 - Lower total number of delivered shocks
 - Reduced HF hospitalization

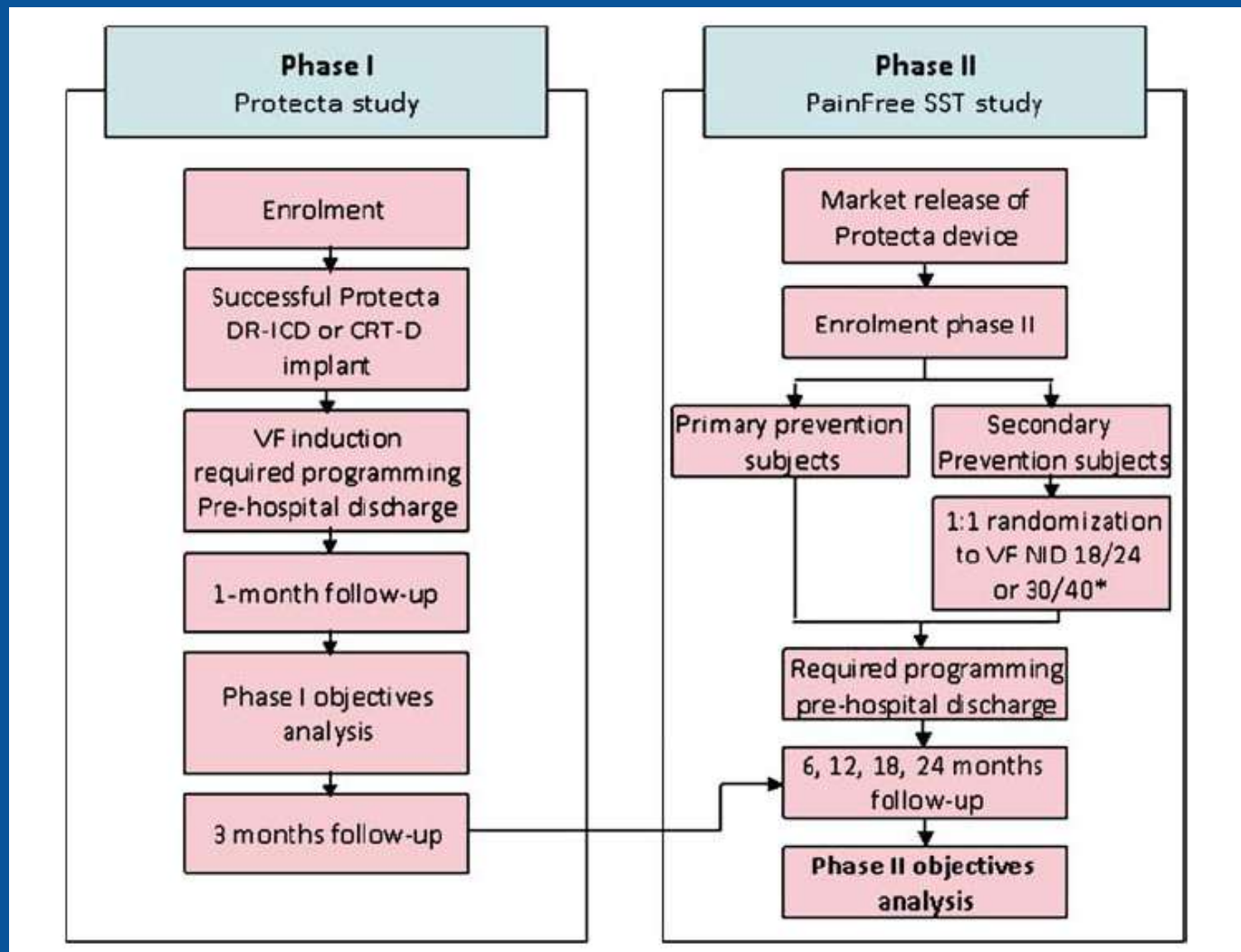


Strategic Programming Reduces Shocks

- PREPARE: Prospective, cohort controlled study
- 700 primary prevention ICD or CRT-D patients programmed to ATP for fast VT (182-250 bpm), NID 30/40, VT monitor (<182 bpm)
- Reduction of unnecessary and inappropriate shocks, improved survival



PainFree SST Study



PainFree SST Study Phase 1: Results

- 100% appropriate detection of VF episodes

Device type	Number of episodes (% of total implant per type)	Time to detection in ms (mean \pm SD)	Median (Range) in ms	Appropriate VF arrhythmia* with features ON (% of total episodes)
ICD	94 (82)	3168.40 \pm 924.67	3150 (1830-6320)	100
CRT-D	102 (76)	3250.49 \pm 924.67	3160 (2010-5990)	100
Total	196 (79)	3211.12 \pm 867.45	3150 (1830-6320)	100

**Appropriate VF arrhythmia is no delay in detection time longer than 2 seconds.*

PainFree SST Study Phase 2

- **Objective:**

- Evaluate percentage of pts. inappropriate shock free at 1 year
- Compare safety of VF NID 30/40 and 18/24 in 2-ary prevention

- **Design**

- Up to 2,000 patients will be included
- CRT-D, DR and VR
- Randomization of 2-ary prevention pts. to VF NID 18/24 or 30/40
- At least 1 year follow-up

- **Status**

- Enrolment complete except for VR devices

Simulating Clinical Experience: Virtual ICD

- **Computer modeling addresses some of the limitations of randomized controlled trials:**
 - Fast and early results
 - Individual algorithms can be tested separately
 - Possibility to repeat the test many times
 - Cost-saving
- **Virtual ICD study predicts shock reduction results for a combination of strategies/features using a computer model and ICD episode data from a long-term clinical study**

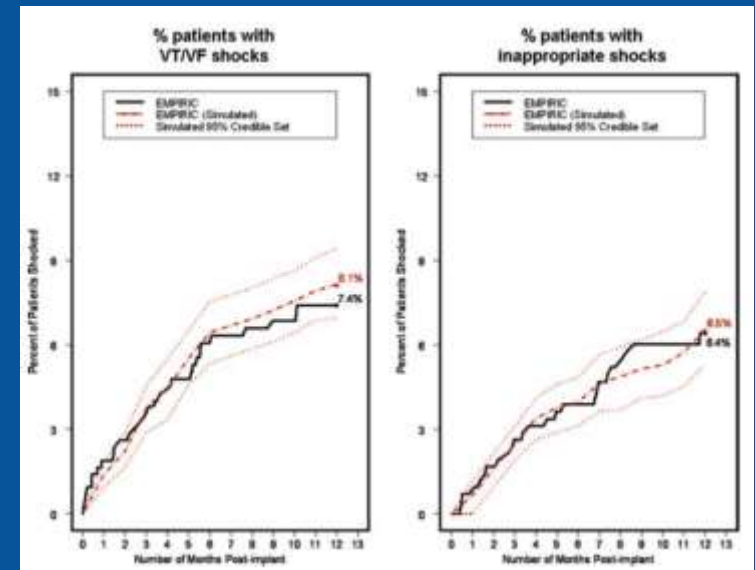
Virtual ICD - Approach

- **Build the model - Virtual ICD**

- Based on data from prior studies (PainFree II, WAVE, ENTRUST)

- **Validate the model**

- Adjudicated episodes from the EMPIRIC trial (ATP, PR-Logic)

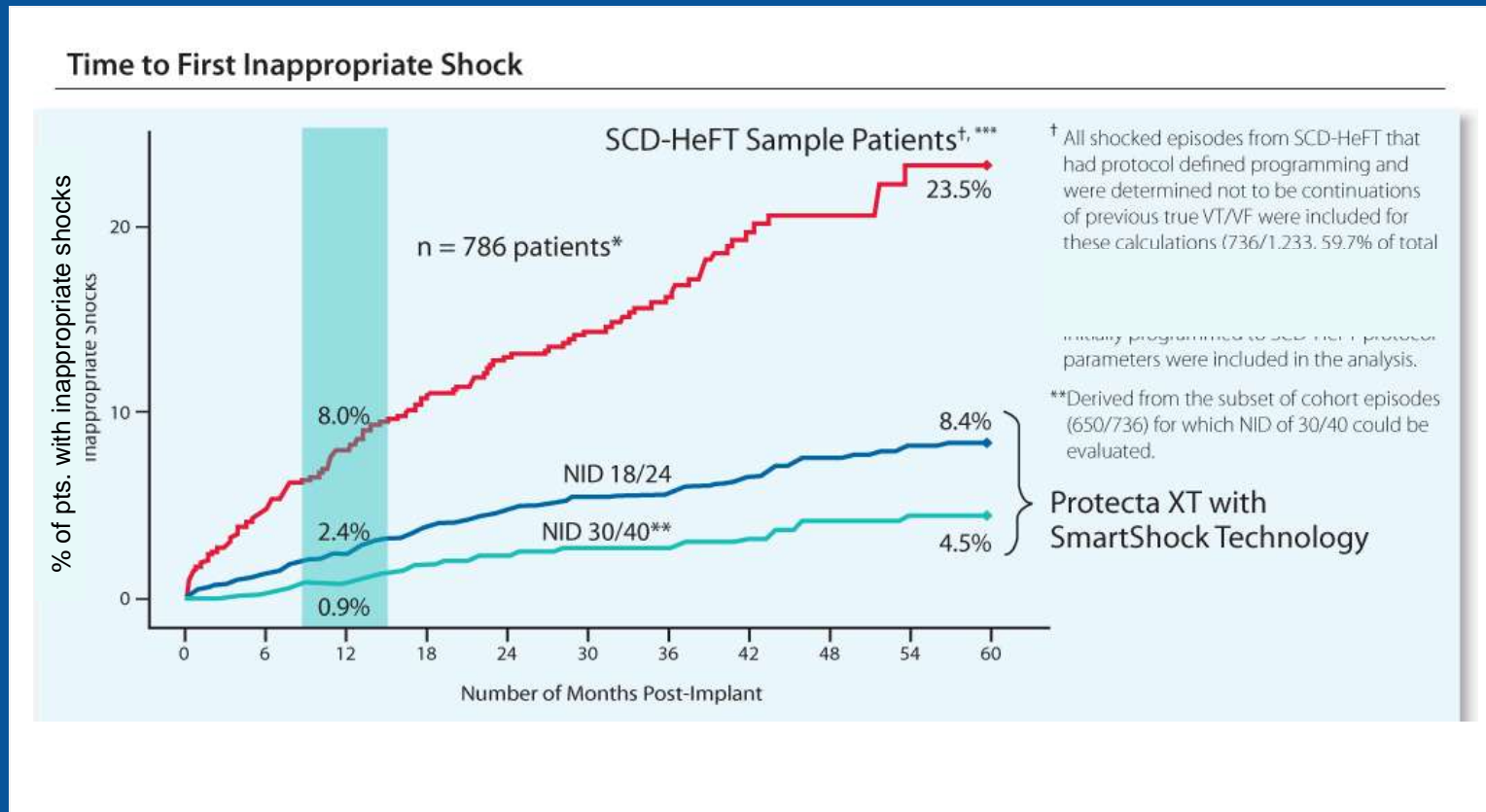


- **Apply the model**

- Adjudicated SCD-HeFT episodes were used to establish clinically understandable performance predictions

Virtual ICD - Results of New Algorithms

98% of patients free of inappropriate shocks at 1 year



Conclusion

- **Inappropriate shocks decrease quality of life and device acceptance while increasing morbidity and potentially mortality**
- **Newer ICD programming and specific algorithms help address the various causes of inappropriate shocks**
- **First indications suggest that up to 98% of pts. May be free of inappropriate shocks 1 year post-implant, while sensitivity for VT/VF detection is ensured**