

# UN-NECESSARY TREATED VT/VF IN ICD PATIENTS

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# Prognostic Importance of Defibrillator Shocks in Patients with Heart Failure

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## ABSTRACT

### BACKGROUND

Patients with heart failure who receive an implantable cardioverter-defibrillator (ICD) for primary prevention (i.e., prevention of a first life-threatening arrhythmic event) may later receive therapeutic shocks from the ICD. Information about long-term prognosis after ICD therapy in such patients is limited.

### METHODS

Of 129 patients with heart failure who were randomly assigned to ICD therapy, we implanted the ICD in 811. ICD shocks that followed the onset of ventricular tachycardia or ventricular fibrillation were considered to be appropriate. All other ICD shocks were considered to be inappropriate.

### RESULTS

Over a median follow-up period of 45.5 months, 269 patients (33.2%) received at least one ICD shock, with 128 patients receiving only appropriate shocks, 87 receiving only inappropriate shocks, and 54 receiving both types of shock. In a Cox proportional-hazards model adjusted for baseline prognostic factors, an appropriate ICD shock, as compared with no appropriate shock, was associated with a significant increase in the subsequent risk of death from all causes (hazard ratio, 5.68; 95% confidence interval [CI], 3.97 to 8.12;  $P<0.001$ ). An inappropriate ICD shock, as compared with no inappropriate shock, was also associated with a significant increase in the risk of death (hazard ratio, 1.98; 95% CI, 1.29 to 3.05;  $P=0.002$ ). For patients who survived longer than 24 hours after an appropriate ICD shock, the risk of death remained elevated (hazard ratio, 2.99; 95% CI, 2.04 to 4.37;  $P<0.001$ ). The most common cause of death among patients who received any ICD shock was progressive heart failure.

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*N Engl J Med* 2008;359:1009-17.

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## CONCLUSIONS

Among patients with heart failure in whom an ICD is implanted for primary prevention, those who receive shocks for any arrhythmia have a substantially higher risk of death than similar patients who do not receive such shocks.

# PROGNOSTIC IMPACT OF INAPPROPRIATE SHOCKS IN MADIT II AND SCDE-HFT

*Hazard- ratio for all-cause mortality of inappropriate shocks as compared with patients with no shock*

- MADIT II: 2.29,  $p = 0.025$ ).

*Daubert JP et al, JACC 2008;51:1357-1365*

- SCDDeHFT: 1.98,  $p < 0.002$ )

*Poole JE et al, N Engl J Med 2008; 359:1009-1017*

# Long-Term Outcome After ICD and CRT Implantation and Influence of Remote Device Follow-Up: The ALTITUDE Survival Study

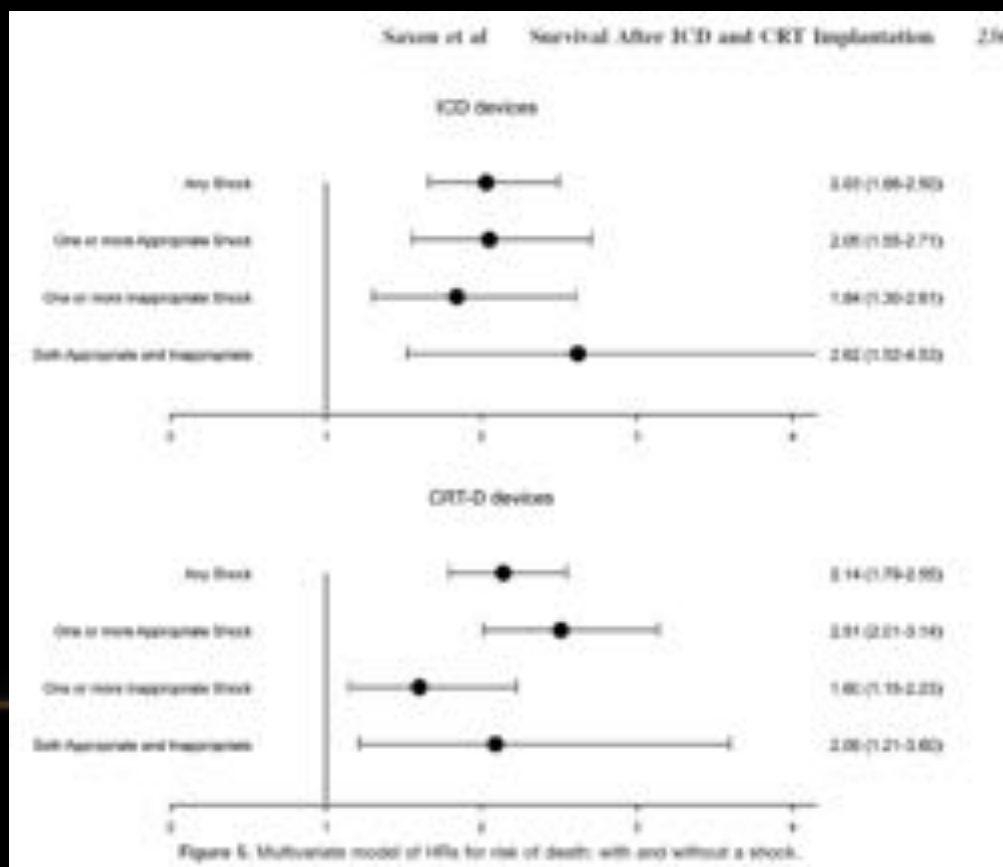
Leslie A. Saxon, David L. Hayes, F. Roosevelt Gilliam, Paul A. Heidenreich, John Day, Milan Seth, Timothy E. Meyer, Paul W. Jones and John P. Boehmer

*Circulation* 2010;122:2359-2367; originally published online Nov 22, 2010;

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2135 pts

Painfree I + II  
Empiric  
Prepare

## Differences in effects of electrical therapy type for ventricular arrhythmias on mortality in implantable cardioverter-defibrillator patients

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**BACKGROUND** Implantable cardioverter-defibrillator (ICD) shocks have been associated with an increased risk of death. It is unknown whether this is due to the ventricular arrhythmia (VA) or shocks and whether antitachycardia pacing (ATP) termination can reduce this risk.

**OBJECTIVE** The purpose of this study was to determine whether mortality in ICD patients is influenced by the type of therapy (shocks of ATP) delivered.

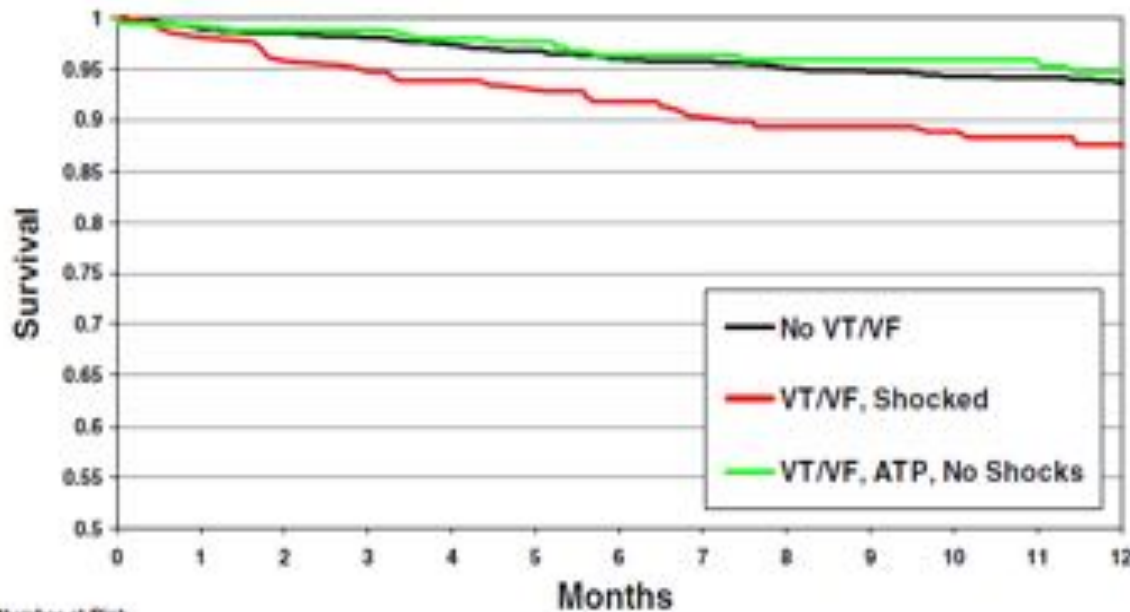
**METHODS** Cox models evaluated effects of baseline characteristics (PVT; 188-nd therapy pts in four

established. For FVT (32% shocked, 68% ATP), episode and therapy effects could be uncoupled: ATP-terminated FVT did not increase episode mortality risk, whereas shocked FVT increased risk by 32%. Survival rates were highest among patients with no VA (93.8%) of ATP-only (94.7%) and lowest for shocked patients (88.4%). Monthly episode rates were 80% higher among shocked versus ATP-only patients.

**CONCLUSIONS** Shocked VA episodes are associated with increased mortality risk. Shocked patients have substantially higher VA episode burden and poorer survival compared with ATP-only-treated patients.

**KEYWORDS** Implantable cardioverter defibrillators; Ventricular tachycardia; Ventricular fibrillation; Shocks; Antitachycardia pacing; Death

**ABBREVIATIONS** ATP = antitachycardia pacing; CAD = coronary disease; CI = confidence interval; CL = cycle length; EF = ejection fraction; EGM = electrogram; HF = heart failure; ICD = implantable cardioverter-defibrillator; FVT = fast ventricular tachycardia; MI = myocardial infarction; NYHA = New York Heart Association; SVT = supraventricular tachycardia; VA = ventricular arrhythmia; VF = ventricular fibrillation; VT = ventricular tachycardia (Heart Rhythm 2010;7:353-360) © 2010 Heart Rhythm Society. All rights reserved.



Shocked VA episodes are associated with increased mortality risk.

Shocked pts have poorer survival as compared with ATP-only treated pts

# BASED ON AVAILABLE DATA IN 2012, SHOCK PREVENTION STRATEGIES WERE NOT ASSOCIATED WITH REDUCTION OF MORTALITY RISK: PREPARE AND RELEVANT INCLUDED IN ANALYSIS

Heart Rhythm. 2012 Dec;9(12):2068-74. doi: 10.1016/j.hrthm.2012.08.032. Epub 2012 Sep 1.

## Implantable cardioverter-defibrillator shock prevention does not reduce mortality: a systemic review.

Hsu AH<sup>1</sup>, Ham L, Nair GM, Connolly SJ, Dorian P, Morillo CA, Healey JS.

### Ⓔ Author information

### Abstract

**BACKGROUND:** Mortality is increased among implantable cardioverter-defibrillator (ICD) recipients who receive shocks; however, whether shocks cause this increase or are simply a marker of risk is unknown. Antiarrhythmic medications, catheter ablation, and enhanced ICD programming all may reduce ICD shocks, but whether shock reduction decreases mortality is unknown.

**OBJECTIVE:** The purpose of this study was to conduct a meta-analysis to estimate the impact of ICD shock reduction on survival.

**METHODS:** Two independent reviewers searched MEDLINE, EMBASE, and clinicaltrials.gov and extracted data from randomized controlled trials assessing the efficacy of interventions to prevent ICD shocks.

**RESULTS:** Seventeen randomized trials were included in this analysis, including 5875 patients. Mean ejection fraction of all trial participants was 32%, and 25% of the patients received ICD therapy for primary prophylaxis. Antiarrhythmic medications (odds ratio [OR] 0.59, 95% confidence interval [CI] 0.36-0.96,  $P = .03$ ) and catheter ablation of ventricular tachycardia (OR 0.36, 95% CI 0.19-0.62,  $P = .0004$ ) significantly reduced the proportion of patients receiving shocks. However, there was no significant reduction in mortality among trials of antiarrhythmic medications (OR 1.07, 95% CI 0.72-1.59,  $P = .73$ ) or catheter ablation (OR 0.72, 95% CI 0.32-1.64,  $P = .44$ ). The 5 ICD programming trials had sufficiently heterogeneous interventions that pooling of their results was not performed. However, only the PAINFREE-III (Pacing Fast Ventricular Tachycardia Reduces Shock Therapies) trial demonstrated a significant reduction in shocks (OR 0.38, 95% CI 0.22-0.65), but this was not associated with any significant reduction in mortality (OR 1.41, 95% CI 0.81-2.45).

**CONCLUSION:** There is no compelling evidence that existing interventions that reduce ICD shocks significantly improve survival.

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### Comment in

There are lots of things about implantable cardioverter-defibrillators that should be eliminated: shocks are a good start. [Heart Rhythm. 2012]

Reply to the Editor--Shocks and mortality versus pacing and mortality. [Heart Rhythm. 2013]

To the Editor--Shocks and mortality versus pacing and mortality. [Heart Rhythm. 2013]

## Strategic Programming of Detection and Therapy Parameters in Implantable Cardioverter-Defibrillators Reduces Shocks in Primary Prevention Patients

Results From the PREPARE  
(Primary Prevention Parameters Evaluation) Study

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*Cleveland and Elyria, Ohio; Troy, Michigan; San Pablo and San Diego, California; Minneapolis, Minnesota;  
Takoma Park, Maryland; Nashville, Tennessee; and Groningen, the Netherlands*

|                    |  |
|--------------------|--|
| <b>Objectives</b>  | Our purpose was to demonstrate that strategically chosen implantable cardioverter-defibrillator (ICD) ventricular tachycardia (VT) or ventricular fibrillation (VF) detection and therapy parameters can reduce the combined incidence of device-delivered shocks, arrhythmic syncope, and untreated sustained symptomatic VT/VF (morbidity index).  |
| <b>Background</b>  | Strategically chosen ICD VT/VF detection and therapy parameters have been shown in previous studies to reduce the number of shocked episodes. In the PREPARE (Primary Prevention Parameters Evaluation) study, these prior strategies were combined with additional strategies specific to primary prevention patients.  |
| <b>Methods</b>     | The PREPARE study was a prospective, cohort-controlled study that analyzed 700 patients (biventricular [Bi-V] ICD and non-Bi-V ICD) with primary prevention indications for an ICD from 38 centers followed for 1 year. VT/VF was detected for rates $\geq 182$ beats/min that were maintained for at least 30 of 40 beats. Antitachycardia pacing was programmed as the first therapy for regular rhythms with rates of 182 to 250 beats/min, and supraventricular tachycardia discriminators were used for rhythms $\leq 200$ beats/min. The control cohort consisted of 689 primary prevention patients from the EMPIRIC (Comparison of Empiric to Physician-Tailored Programming of Implantable Cardioverter Defibrillators Trial) (non-Bi-V ICD, physician arm only) and MIRACLE ICD (Multicenter InSync Implantable Cardioversion Defibrillation Randomized Clinical Evaluation) (Bi-V ICD) trials for whom VT/VF detection and therapy programming were not controlled. |
| <b>Results</b>     | The PREPARE programming significantly reduced the morbidity index incidence density (0.26 events/patient-year for PREPARE study patients vs. 0.69 control cohort, $p = 0.003$ ). The PREPARE study patients were less likely to receive a shock in the first year compared with control patients (9% vs. 17%, $p < 0.01$ ). The incidence of untreated VT and arrhythmic syncope was similar between the PREPARE study patients and the control cohort.  |
| <b>Conclusions</b> | Strategically chosen VT/VF detection and therapy parameters can safely reduce shocks and other morbidities associated with ICD therapy in patients receiving an ICD for primary prevention indications. (PREPARE-Primary Prevention Parameters Evaluation, NCT00279279) (J Am Coll Cardiol 2008;52:541-50) © 2008 by the American College of Cardiology Foundation   |

700 ICD or CRTD  
Medtronic devices

# “STRATEGIC” PROGRAMMING TO REDUCE ICD SHOCK

- Prolonged VF detection time : NID 30 of 40
- At least one ATP attempt for all VT and FVT
- Discrimination algorithms ON up to 200/min VTs
- First VF shock energy > 30 J (maximal energy)



## Strategic Programming of Detection and Therapy

### Param Reduc

### Results (Primary

Bruce L.  
Stephen J.  
Ulrika M.  
Brooke N.  
PREPARE  
Cleveland  
Talima J.

Comparison of Incidence Rates  
 $p = 0.001$

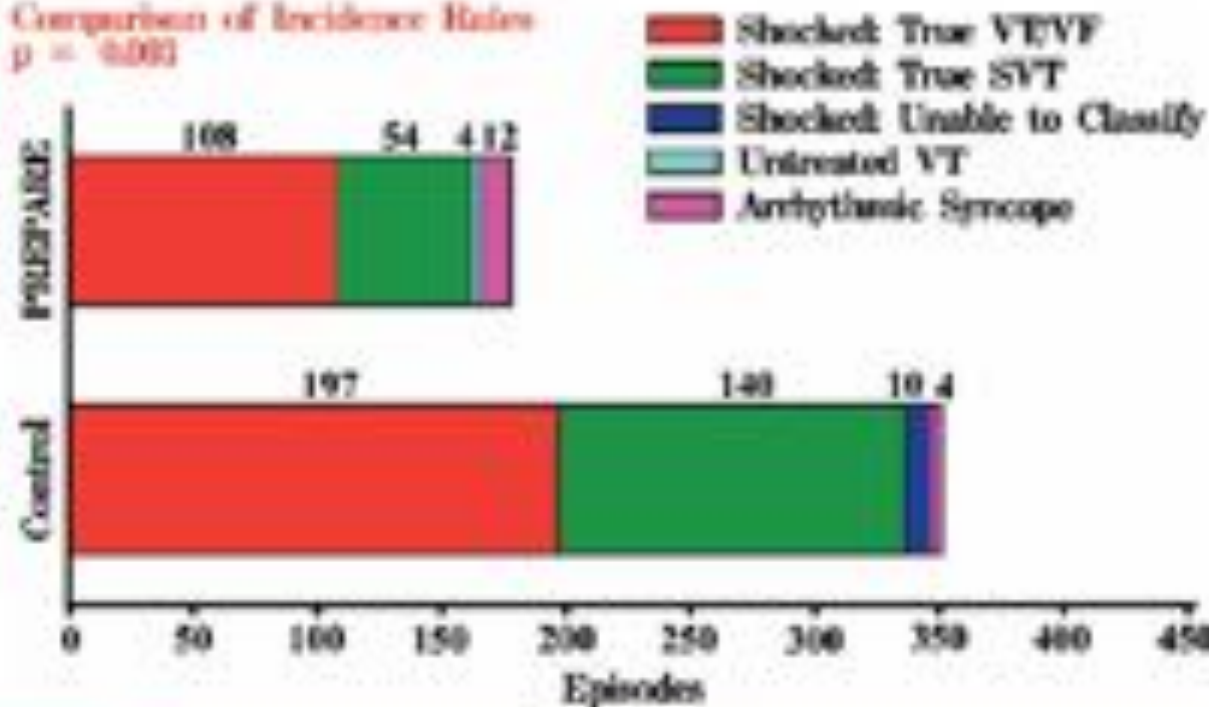


Figure 2

### Morbidity Index for the PREPARE Study Patients Versus the Control Cohort

The PREPARE study patients had fewer morbidity index events (primary end point) as compared with the control cohort. Both appropriate and inappropriate shocks were substantially reduced in the PREPARE study programmed patients.



## A simplified biventricular defibrillator with fixed long detection intervals reduces implantable cardioverter defibrillator (ICD) interventions and heart failure hospitalizations in patients with non-ischaemic cardiomyopathy implanted for primary prevention: the RELEVANT [Role of long dEtection window programming in patients with LEft VentriculAr dysfunction, Non-ischemic eTiology in primary prevention treated with a biventricular ICD] study

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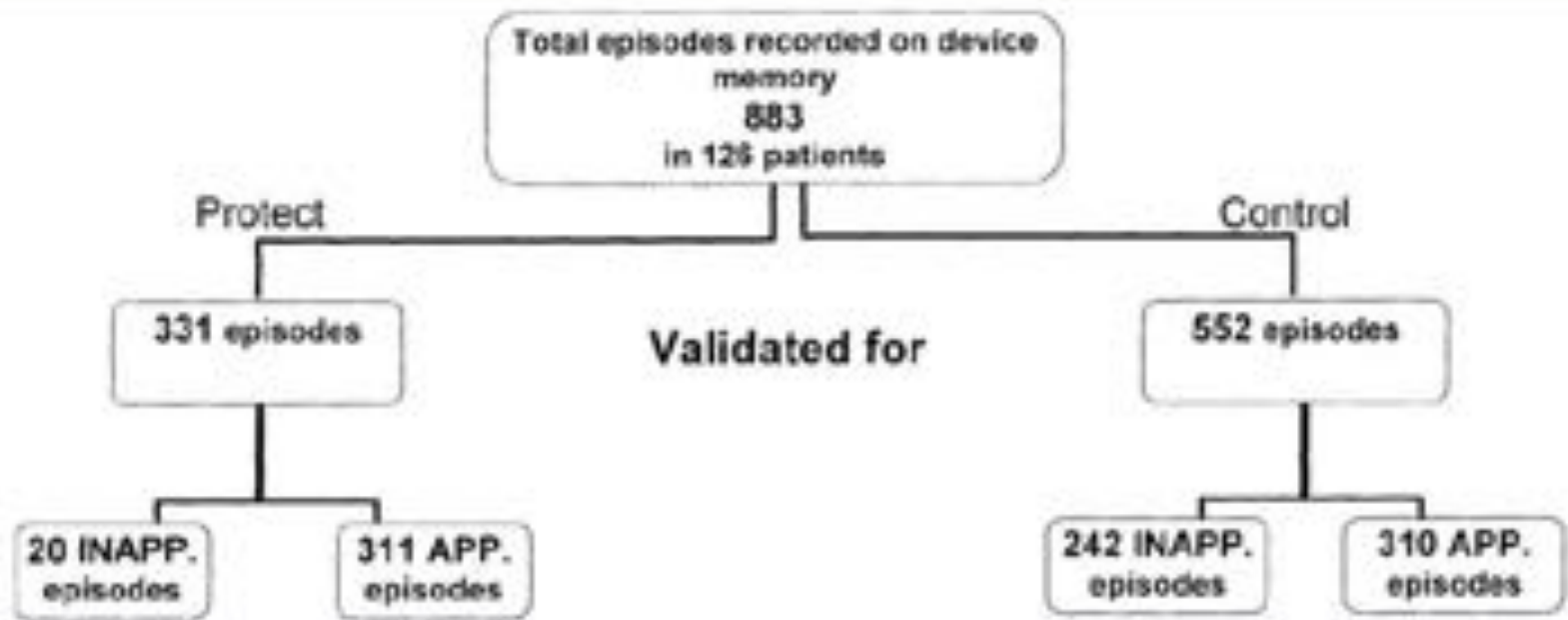
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Received 16 January 2009; revised 10 April 2009; accepted 2 June 2009

**SAME NUMBER OF APPROPRIATE DETECTIONS IN PROTECT  
AND CONTROL ARMS.**

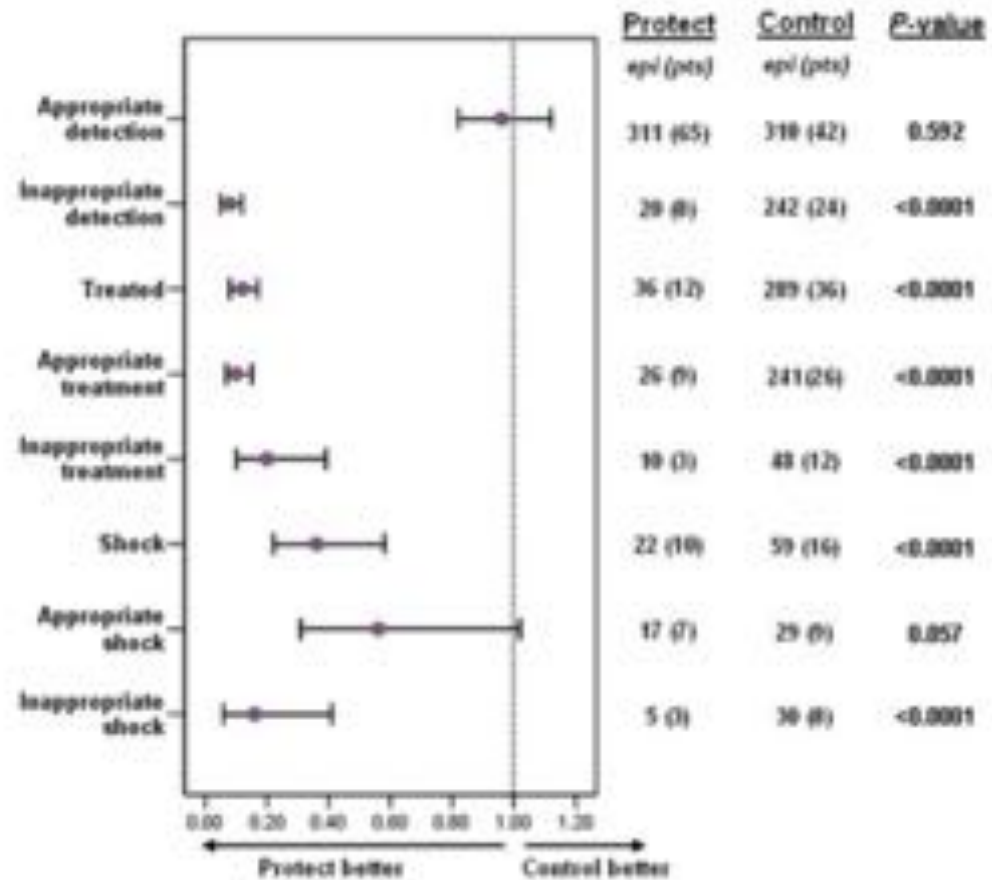
**DRAMATIC REDUCTIONS OF INAPPROPRIATE  
DETECTIONS**

324 pts



**Figure 1** Distribution and numbers of all detected episodes (appropriate and inappropriate) in the two study groups.

# Poisson Regression Estimates of Incidence Rate Ratio Values of ICD Interventions between PROTECY vs CONTROL arms



*RELEVANT Study, Gasparini M et al, Eur Heart J 2009*

2012-2015

3 MAJOR CLINICAL TRIALS COMPARING THE CLINICAL EFFECTS OF STRATEGIES AIMED TO REDUCE ALL NON-ESSENTIAL IDC THERAPIES, MAINLY ICD SHOCKS

**MADIT RIT (Boston Sc)**

*Moss A, New Engl J Med 2012; 367: 2255-2265*

**ADVANCE III (Medtronic)**

*Gasparini M, JAMA 2013; 309 : 1903-1911*

**PROVIDE (S Jude Medical)**

*Saed M, J Cardiovasc Electrophysiol 2014; 25: 52-59*

# Reduction in Inappropriate Therapy and Mortality through ICD Programming

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## ABSTRACT

### BACKGROUND

The implantable cardioverter-defibrillator (ICD) is highly effective in reducing mortality among patients at risk for fatal arrhythmias, but inappropriate ICD activations are frequent, with potential adverse effects.

### METHODS

We randomly assigned 1500 patients with a primary-prevention indication to receive an ICD with one of three programming configurations. The primary objective was to determine whether programmed high-rate therapy (with a 2.5-second delay before the initiation of therapy at a heart rate of  $\geq 200$  beats per minute) or delayed therapy (with a 60-second delay at 170 to 199 beats per minute, a 12-second delay at 200 to 249 beats per minute, and a 2.5-second delay at  $\geq 250$  beats per minute) was associated with a decrease in the number of patients with a first occurrence of inappropriate antitachycardia pacing or shocks, as compared with conventional programming (with a 2.5-second delay at 170 to 199 beats per minute and a 1.0-second delay at  $\geq 200$  beats per minute).

### RESULTS

During an average follow-up of 1.4 years, high-rate therapy and delayed ICD therapy, as compared with conventional device programming, were associated with reductions in a first occurrence of inappropriate therapy (hazard ratio with high-rate therapy vs. conventional therapy, 0.25; 95% confidence interval [CI], 0.17 to 0.34;  $P<0.001$ ; hazard ratio with delayed therapy vs. conventional therapy, 0.24; 95% CI, 0.15 to 0.40;  $P<0.001$ ) and reductions in all-cause mortality (hazard ratio with high-rate therapy vs. conventional therapy, 0.45; 95% CI, 0.24 to 0.85;  $P=0.01$ ; hazard ratio with delayed therapy vs. conventional therapy, 0.56; 95% CI, 0.30 to 1.02;  $P=0.06$ ). There were no significant differences in procedure-related adverse events among the three treatment groups.

### CONCLUSIONS

Programming of ICD therapies for tachyarrhythmias of 200 beats per minute or higher or with a prolonged delay in therapy at 170 beats per minute or higher, as compared with conventional programming, was associated with reductions in inappropriate therapy and all-cause mortality during long-term follow-up. (Funded by Boston Scientific; MADIT-RIT ClinicalTrials.gov number, NCT00947110.)

From the Departments of Medicine (A.J.M., M.W.B., D.T.H., H.K., S.M., W.J.) and Biostatistics and Computational Biology (C.A.B., W.J.H.), University of Rochester Medical Center, Rochester, NY; the Division of Cardiology, Henry Ford Hospital, Detroit (C.S.); the Division of Cardiology, Hospital of the Good Samaritans, Los Angeles (D.S.C.); the Department of Medicine, Duke University Medical Center, Durham, NC (J.P.D.); New England Cardiac Arrhythmia Center, Tufts-New England Medical Center, Boston (N.A.M.E.); St. Luke's and Roosevelt Hospitals, Departments of Medicine and Epidemiology, Columbia University, New York (H.K.); the Cardiology Department, Institute for Clinical and Experimental Medicine, Prague, Czech Republic (J.K.); the Department of Medicine, University of Iowa Health Care, Iowa City (H.O.); the Department of Cardiology, Tokyo Women's Medical University, Tokyo (M.S.); and the Cardiovascular Institute, Lipscia University Medical Center, Chicago (D.W.). Address reprint requests to Dr. Moss at the Heart Research Follow-up Program, University of Rochester Medical Center, 265 Colton Hall, CL 430653, Rochester, NY 14642-0653, or at [heart@pilot.heart.rochester.edu](mailto:heart@pilot.heart.rochester.edu).

\*Deceased.

†The investigators in the Multicenter Automatic Defibrillator Implantation Trial—Reduce Inappropriate Therapy (MADIT-RIT) are listed in the Supplementary Appendix, available at [NEJM.org](http://NEJM.org).

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1500 PTS

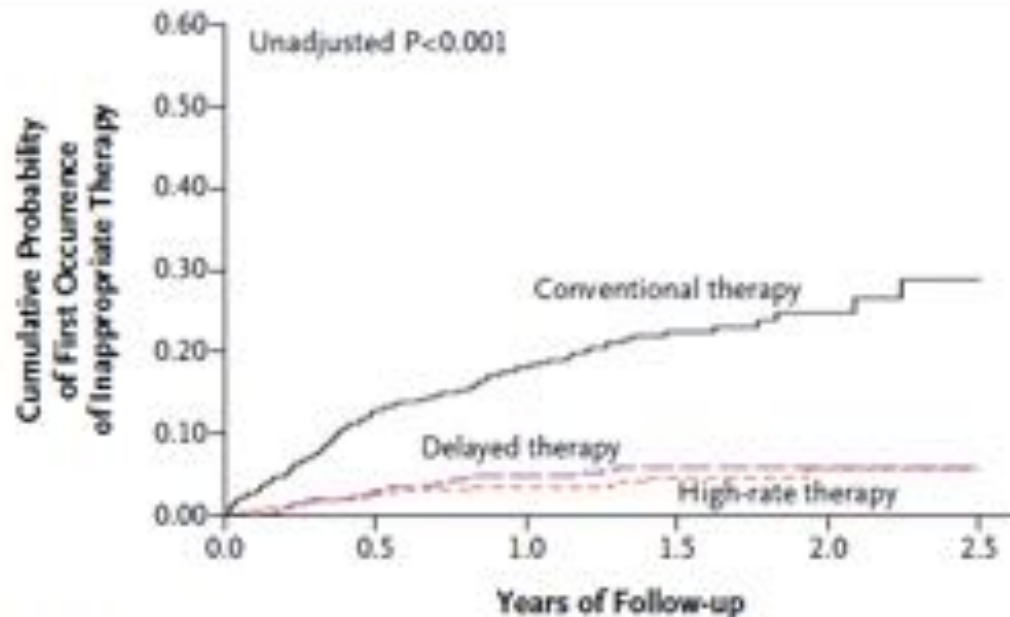
ICD, CRTD

PRIMARY PREVENTION

# MADIT RIT : PROGRAMMATION IN THE DIFFERENT ARMS

| Arm A<br>(Convenzional)  | Arm B<br>(high cut-off)   | Arm C<br>(long duration)   |
|--|---|--|
| <p><u>Zone VT:</u><br/> <b>≥170 bpm, 2.5s duration</b><br/>                     Onset/Stability Detection<br/>                     Enhancements ON</p> <p>ATP + Shock</p> <p>SRD 3 min</p> <p><u>Zone FV:</u><br/> <b>≥200 bpm, 1s duration</b><br/>                     Quick Convert™ ATP<br/>                     Shock</p> | <p><u>Zone VT:</u><br/>                     170 bpm<br/>                     Monitor Only</p> <p><u>Zone FV:</u><br/> <b>≥200 bpm, 2.5s duration</b><br/>                     Quick Convert™ ATP<br/>                     Shock</p> | <p><u>Zone TV-1*:</u><br/> <b>≥170 bpm, 60s duration</b><br/>                     Rhythm ID® Detection<br/>                     Enhancements ON</p> <p>ATP + Shock</p> <p>SRD Off</p> <p><u>Zone TV:</u><br/> <b>≥200 bpm, 12s duration</b><br/>                     Rhythm ID® Detection<br/>                     Enhancements ON</p> <p>ATP + Shock</p> <p>SRD Off</p> <p><u>Zone FV :</u><br/> <b>≥250 bpm, 2.5s duration</b><br/>                     Quick Convert™ ATP + Shock</p> |

\*All programming is within approved labeling. Rhythm ID® and Quick Convert™ are trademarks of Boston Scientific Corporation



**No. at Risk**

|                      |     |            |            |            |           |           |
|----------------------|-----|------------|------------|------------|-----------|-----------|
| Conventional therapy | 514 | 420 (0.13) | 305 (0.18) | 149 (0.22) | 56 (0.25) | 8 (0.29)  |
| High-rate therapy    | 500 | 454 (0.03) | 339 (0.04) | 191 (0.05) | 70 (0.06) | 17 (0.06) |
| Delayed therapy      | 486 | 445 (0.03) | 342 (0.05) | 177 (0.06) | 82 (0.06) | 13 (0.06) |

**Figure 1. Cumulative Probability of First Occurrence of Inappropriate Therapy According to Treatment Group.**

The values in parentheses are Kaplan–Meier estimates of the cumulative probability of a first occurrence of inappropriate device-delivered therapy in patients randomly assigned to therapy programmed for delivery at a heart rate of 170 beats per minute or higher (conventional therapy), at a heart rate of 200 beats per minute or higher (high-rate therapy), or at a heart rate of 170 beats per minute or higher with longer tachyarrhythmia monitoring (delayed therapy).



# PRIMARY ENDPOINT

**Table 2.** First Occurrence, Any Occurrence, and Total Occurrences of Appropriate and Inappropriate Device Therapy According to Treatment Group.\*

| Variable   | Conventional Therapy (N=514) | High-Rate Therapy (N=500) | Delayed Therapy (N=486) | P Value for High-Rate Therapy vs. Conventional Therapy | P Value for Delayed Therapy vs. Conventional Therapy |
|--|------------------------------|---------------------------|-------------------------|--|--|
| <b>First occurrence of therapy — no. of patients (%)</b> |                              |                           |                         |  |  |
| Appropriate therapy                                      | 114 (22)                     | 45 (9)                    | 27 (6)                  | <0.001   | <0.001   |
| Shock  | 20 (4)                       | 22 (4)                    | 17 (3)                  | 0.68   | 0.74   |
| Antitachycardia pacing                                   | 94 (18)                      | 23 (5)                    | 10 (2)                  | <0.001   | <0.001   |
| Inappropriate therapy                                    | 105 (20)                     | 21 (4)                    | 26 (5)                  | <0.001   | <0.001   |
| Shock  | 20 (4)                       | 11 (2)                    | 13 (3)                  | 0.12   | 0.28   |
| Antitachycardia pacing                                   | 85 (17)                      | 10 (2)                    | 13 (3)                  | <0.001   | <0.001   |
| <b>Any occurrence of therapy — no. of patients (%)</b>   |                              |                           |                         |  |  |
| Appropriate therapy                                      |                              |                           |                         |  |  |
| Shock  | 28 (5)                       | 26 (5)                    | 19 (4)                  | 0.86   | 0.25   |
| Antitachycardia pacing                                   | 111 (22)                     | 38 (8)                    | 20 (4)                  | <0.001   | <0.001   |
| Inappropriate therapy                                    |                              |                           |                         |  |  |
| Shock  | 31 (6)                       | 14 (3)                    | 15 (3)                  | 0.01   | 0.03   |
| Antitachycardia pacing                                   | 104 (20)                     | 20 (4)                    | 25 (5)                  | <0.001   | <0.001   |
| <b>Total occurrences of therapy — no. of occurrences</b> |                              |                           |                         |  |  |
| Appropriate therapy                                      | 517                          | 185                       | 196                     | <0.001   | <0.001   |
| Shock  | 71                           | 72                        | 53                      | 0.35   | 0.15   |
| Antitachycardia pacing                                   | 446                          | 113                       | 143                     | <0.001   | <0.001   |
| Inappropriate therapy                                    | 998                          | 75                        | 264                     | <0.001   | <0.001   |
| Shock  | 105                          | 25                        | 49                      | 0.001  | 0.16   |
| Antitachycardia pacing                                   | 893                          | 50                        | 215                     | <0.001   | <0.001   |

\* Crude rates of the first occurrence of therapy and any occurrence of therapy were compared with the use of chi-square tests, and mean counts of total occurrences of therapy were compared with the use of negative binomial regression models.



#### No. at Risk

|                      |     |            |            |            |           |           |
|----------------------|-----|------------|------------|------------|-----------|-----------|
| Conventional therapy | 514 | 490 (0.02) | 392 (0.03) | 219 (0.07) | 89 (0.10) | 14 (0.12) |
| High-rate therapy    | 500 | 478 (0.01) | 372 (0.02) | 221 (0.03) | 90 (0.05) | 21 (0.05) |
| Delayed therapy      | 486 | 471 (0.01) | 375 (0.02) | 205 (0.04) | 99 (0.07) | 14 (0.09) |

#### Figure 2. Cumulative Probability of Death According to Treatment Group.

The values in parentheses are Kaplan–Meier estimates of the cumulative probability of death.

# RISK REDUCTION FOR DEATH FROM 44 TO 55%

THE NEW ENGLAND JOURNAL of MEDICINE

**Table 3.** Hazard Ratios for a First Occurrence of Inappropriate Therapy, Death, and a First Episode of Syncope According to Treatment Group.

| Variable                                  | Conventional Therapy (N=514) | High-Rate Therapy (N=500) | Delayed Therapy (N=486) | High-Rate Therapy vs. Conventional Therapy |         | Delayed Therapy vs. Conventional Therapy |         |
|---|------------------------------|---------------------------|-------------------------|--|---------|--|---------|
|   | no. of patients              |                           |                         | Hazard Ratio (95% CI)                      | P Value | Hazard Ratio (95% CI)                    | P Value |
| First occurrence of inappropriate therapy | 105                          | 21                        | 26                      | 0.21 (0.13–0.34)                           | <0.001  | 0.24 (0.15–0.40)                         | <0.001  |
| Death                                     | 34                           | 16                        | 21                      | 0.45 (0.24–0.85)                           | 0.01    | 0.56 (0.30–1.02)                         | 0.06    |
| First episode of syncope                  | 23                           | 22                        | 22                      | 1.32 (0.71–2.47)                           | 0.39    | 1.09 (0.58–2.05)                         | 0.80    |

# MADIT- RIT conclusions

## CONCLUSIONS

Programming of ICD therapies for tachyarrhythmias of 200 beats per minute or higher or with a prolonged delay in therapy at 170 beats per minute or higher, as compared with conventional programming, was associated with reductions in inappropriate therapy and all-cause mortality during long-term follow-up. (Funded by Boston Scientific; MADIT-RIT ClinicalTrials.gov number, NCT00947310.)

# Effect of Long-Detection Interval vs Standard-Detection Interval for Implantable Cardioverter-Defibrillators on Antitachycardia Pacing and Shock Delivery

## The ADVANCE III Randomized Clinical Trial

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**T**HERAPY WITH IMPLANTABLE cardioverter-defibrillators (ICDs) is now the standard of care in primary<sup>1,2</sup> and secondary prevention.<sup>3</sup> As indications for implantation have expanded, concern about possible adverse effects of ICD therapies on prognosis and quality of life has arisen. Several authors have reported that ICD therapies, both appropriate and inappropriate, are associated with an increased risk of death and worsening of heart failure.<sup>4,5</sup> To reduce these unfavorable outcomes, several studies have focused on identifying the best device programming strategies, either by targeting the antitachycardia pacing (ATP) algorithms for interrupting fast ventricular tachyarrhythmias or by investigating the use of prolonged arrhythmia detection intervals.<sup>6,7</sup> Increasing the

**Importance** Using more intervals to detect ventricular tachyarrhythmias has been associated with reducing unnecessary implantable cardioverter-defibrillator (ICD) therapies.

**Objective** To determine whether using 30 of 40 intervals to detect ventricular arrhythmias (VT) (long-detection) during spontaneous fast VT episodes reduces antitachycardia pacing (ATP) and shock delivery more than 18 of 24 intervals (standard detection).

**Design, Setting, and Participants** Randomized, single-blind, parallel-group trial that enrolled 1502 primary and secondary prevention patients (mean [SD] age, 65 [11] years; 84% men; 75% primary prevention ICD) with ischemic and nonischemic etiology undergoing first ICD implant at 1 of 94 international centers (March 2008–December 2010).

**Interventions** Patients were randomized 1:1 to programming with long- (n=948) or standard-detection (n=954) intervals.

**Main Outcomes and Measures** Total number of ATPs and shocks delivered for all episodes (primary outcomes) and inappropriate shocks, mortality, and syncope rate (secondary outcomes).

**Results** During a median follow-up of 12 months (interquartile range, 11–13), long-detection group had 346 delivered therapies (42 therapies per 100 person-years [95% CI, 38–47]) vs 557 in the standard-detection group (67 therapies per 100 person-years [95% CI, 62–72]; incident rate ratio [IRR], 0.62 [95% CI, 0.51–0.78];  $P < .001$ ). The long- vs the standard-detection group experienced 23 ATPs per 100 person-years (95% CI, 20–27) vs 37 ATPs per 100 person-years (95% CI, 33–41; IRR, 0.58 [95% CI, 0.47–0.72];  $P < .001$ ); 19 shocks per 100 person-years (95% CI, 16–22) vs 30 shocks per 100 person-years (95% CI, 26–34; IRR, 0.77 [95% CI, 0.59–1.01];  $P = .06$ ), with a significant difference in the probability of therapy occurrence ( $P < .001$ ); and a reduction in first occurrence of inappropriate shock (5.1 per 100 patient-years [95% CI, 3.7–6.3] vs 11.6 [95% CI, 9.4–14.1]; IRR, 0.55 [95% CI, 0.36–0.85];  $P = .008$ ). Mortality (5.5 [95% CI, 4.0–7.2] vs 6.3 [95% CI, 4.8–8.2] per 100 patient-years; HR, 0.87;  $P = .50$ ) and arrhythmic syncope rates (3.1 [95% CI, 2.6–4.6] vs 1.9 [95% CI, 1.1–3.1] per 100 patient-years; IRR, 1.60 [95% CI, 0.76–3.41];  $P = .22$ ) did not differ significantly between groups.

**Conclusions and Relevance** Among patients receiving an ICD, the use of a long- vs standard-detection interval resulted in a lower rate of ATP and shocks, and inappropriate shocks. This programming strategy may be an appropriate alternative.

**Trial Registration** clinicaltrials.gov Identifier: NCT00617175

JAMA. 2012;308(26):3363–3371

www.jama.com

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number of intervals to detect arrhythmias has been shown to safely permit fast ventricular tachyarrhythmias will-

1902 pts  
ICD and CRTD , Medtronic

Primary and secondary  
prevention

Standard arm  
18/24 VF NID

Long Detection arm:  
30/40 VF NID

**Table 2.** Primary End Point Results of Delivered ICD Therapies According to Intention-to-Treat and On-Treatment Analyses

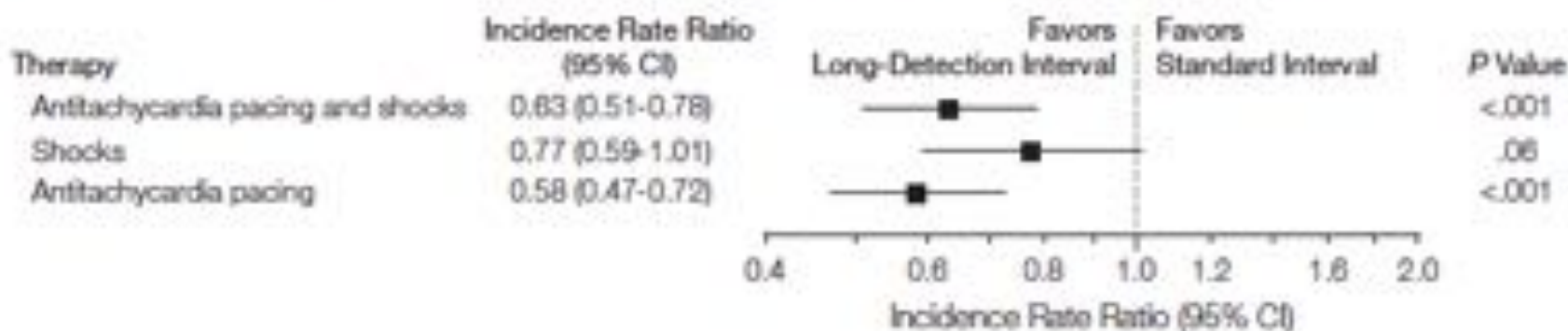
|   | Exposure, per Patient-Year <sup>a</sup> | No. of Detected Arrhythmias | No. of Therapies Delivered | No. of Patients | Therapy Rate per 100 Patient-Year (95% CI) <sup>b</sup> | IRR (95% CI) <sup>c</sup> | P Value |
|---|---|-----------------------------|----------------------------|-----------------|---|---------------------------|---------|
| <b>Intention to Treat—Therapies (ATP + Shock)</b> |   |                             |                            |                 |   |                           |         |
| Standard-interval detection                       | 830                                     | 321                         | 557 Therapies              | 149             | 67 (62-73)  | 1 [Reference]             | <.001   |
| Long detection                                    | 826                                     | 209                         | 346 Therapies              | 97              | 42 (38-47)  | 0.63 (0.51-0.78)          |         |
| <b>Intention to Treat—ATP Only</b>                |   |                             |                            |                 |   |                           |         |
| Standard-interval detection                       | 830                                     | 321                         | 308 ATP                    | 192             | 37 (33-41)  | 1 [Reference]             | <.001   |
| Long detection                                    | 826                                     | 209                         | 142 ATP                    | 85              | 23 (20-26)  | 0.58 (0.47-0.72)          |         |
| <b>Intention to Treat—Shock Only</b>              |   |                             |                            |                 |   |                           |         |
| Standard-interval detection                       | 830                                     | 321                         | 249 Shocks                 | 95              | 30 (26-34)  | 1 [Reference]             | .06     |
| Long detection                                    | 826                                     | 209                         | 154 Shocks                 | 75              | 19 (16-22)  | 0.77 (0.59-1.01)          |         |
| <b>On-Treatment—Therapies (ATP + Shock)</b>       |   |                             |                            |                 |   |                           |         |
| Standard-interval detection                       | 822                                     | 313                         | 542 Therapies              | 147             | 66 (61-72)  | 1 [Reference]             | <.001   |
| Long Detection                                    | 817                                     | 181                         | 310 Therapies              | 91              | 38 (33-42)  | 0.60 (0.49-0.74)          |         |

Abbreviations: ATP, antitachycardia pacing; IQR, interquartile range.

<sup>a</sup>Exposure time is measured as the number of patients per year.

<sup>b</sup>Therapy rate is expressed as the number of events per 100 patient-years.

<sup>c</sup>The incident rate ratios (IRRs) and 95% CIs are reported as a measure of efficacy (IRR = rate long-detection group/rate standard-interval detection group) and were tested by means of a negative binomial regression model.

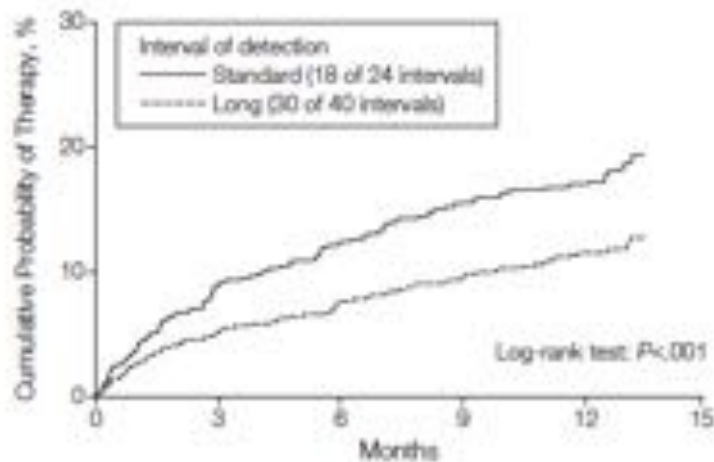
**Figure 2.** Treatment Effect Regarding the Primary End Point and Its Components

# THE TIME TO THE FIRST INAPPROPRIATE THERAPY OR SHOCK WAS PROLONGED IN LONG-DETECTION ARM

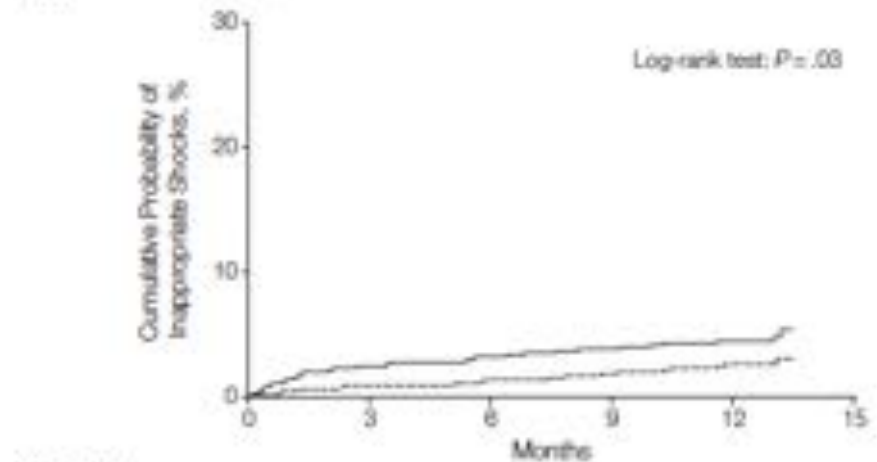
## LONG- AND STANDARD-DETECTION INTERVALS FOR ICDS

**Figure 3.** Kaplan-Meier Estimates of Time to the First Implantable Cardioverter-Defibrillator Therapy and to the First Inappropriate Shock in Each Group

**A** Time to first therapy



**B** Time to first inappropriate shock



No. at risk  
Interval of detection

|          |     |     |     |     |     |
|----------|-----|-----|-----|-----|-----|
| Standard | 891 | 777 | 707 | 639 | 438 |
| Long     | 878 | 812 | 752 | 686 | 492 |

No. at risk  
Interval of detection

|          |     |     |     |     |     |
|----------|-----|-----|-----|-----|-----|
| Standard | 891 | 801 | 781 | 728 | 496 |
| Long     | 878 | 848 | 798 | 741 | 501 |

The analysis population included patients for whom device memory data were available for at least 1 follow-up visit.

# PROVIDE, SAINT JUDE MEDICAL ICD-/CRTDS

## Programming Implantable Cardioverter-Defibrillators in Patients with Primary Prevention Indication to Prolong Time to First Shock: Results from the PROVIDE Study

MOHAMMAD SAEED, M.D., F.A.C.C.,\* IBRAHIM HANNA, M.D.,† DIONYSSIOS ROBOTIS, M.D.,‡ ROBERT STYPEREK, M.D.,§ LEO POLOSADIAN, M.D.,¶ AHMED KHAN, M.D.,# JOSEPH ALONSO, M.D.,\*\* YELENA NABUTOVSKY, M.S.,†† and CURTIS NEASON, B.S.,††

From the \*Texas Heart Institute-St. Luke's Episcopal Hospital, Houston, Texas; †Cardiology, P.C., Birmingham, Alabama; ‡University of Massachusetts Medical Center, Worcester, MA; §Harbin Clinic Southeastern Cardiovascular Institute, Rome, Georgia; ¶Cardiac Rhythm Specialists, Northridge, California; #Cardiology Consultants, Johnson City, Tennessee; \*\*Central Florida Heart Center, Ocala, Florida; and ††St. Jude Medical, Sylmar, California, USA

**ICD Programming for Shock Reduction.** *Background:* Shock therapy delivery by implantable cardioverter-defibrillators (ICD) can be painful and may have adverse consequences. Reducing shock burden for patients with ICDs would be beneficial.

*Methods:* PROVIDE was a prospective, randomized study of primary prevention ICD patients. Patients in the experimental group received a combination of programmed parameters with higher detection rates, longer detection intervals, empiric antitachycardia pacing (ATP), and optimized supraventricular tachycardia (SVT) discriminators, while those in the control group were programmed with conventional parameters. Shock therapy and arrhythmic syncope were compared.

*Results:* Of 1,670 patients enrolled (846 in the experimental group, 824 in the control group) and monitored over a follow-up of  $530 \pm 241$  days, 202 patients received shock therapy for any cause (82 in the experimental group and 120 in the control group). The median time to first shock was significantly prolonged (13.1 vs 7.8 months, hazard ratio [HR]: 0.62, 95% confidence interval [CI]: 0.47 to 0.82,  $P = 0.0005$ ) and the 2-year shock rate significantly reduced (12.4% vs 19.4%,  $P < 0.001$ ) in the experimental group compared to the control group. There was no increase in arrhythmic syncope (HR: 1.64, 95% CI: 0.69 to 3.90,  $P = 0.26$ ), while the overall mortality was reduced (HR: 0.7, 95% CI: 0.50 to 0.98,  $P = 0.036$ ) in the experimental group compared to the control group.

*Conclusion:* A combination of programmed parameters utilizing higher detection rate, longer detection intervals, empiric ATP, and optimized SVT discriminators reduced ICD therapies without increasing arrhythmic syncope and was associated with reduction in all-cause mortality among ICD patients. (*Journal of Cardiovascular Electrophysiology*, Vol. 25, pp. 52-59, January 2014)

implantable cardioverter defibrillator, antitachycardia pacing, ventricular tachycardia, ventricular fibrillation, sudden cardiac death, shock reduction, PROVIDE study

1670 pts

Primary prevention

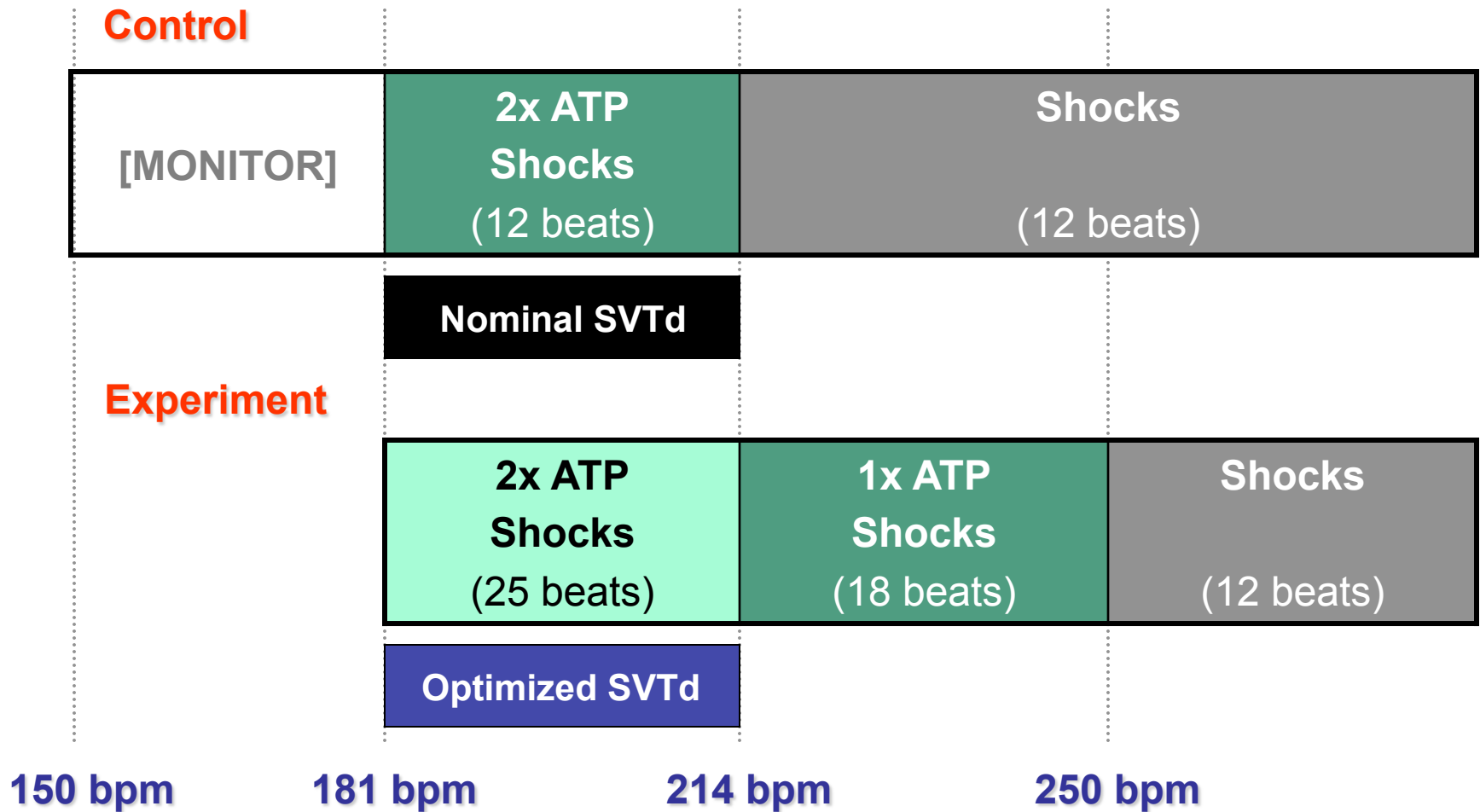
Endpoints

Shock rates and mortality



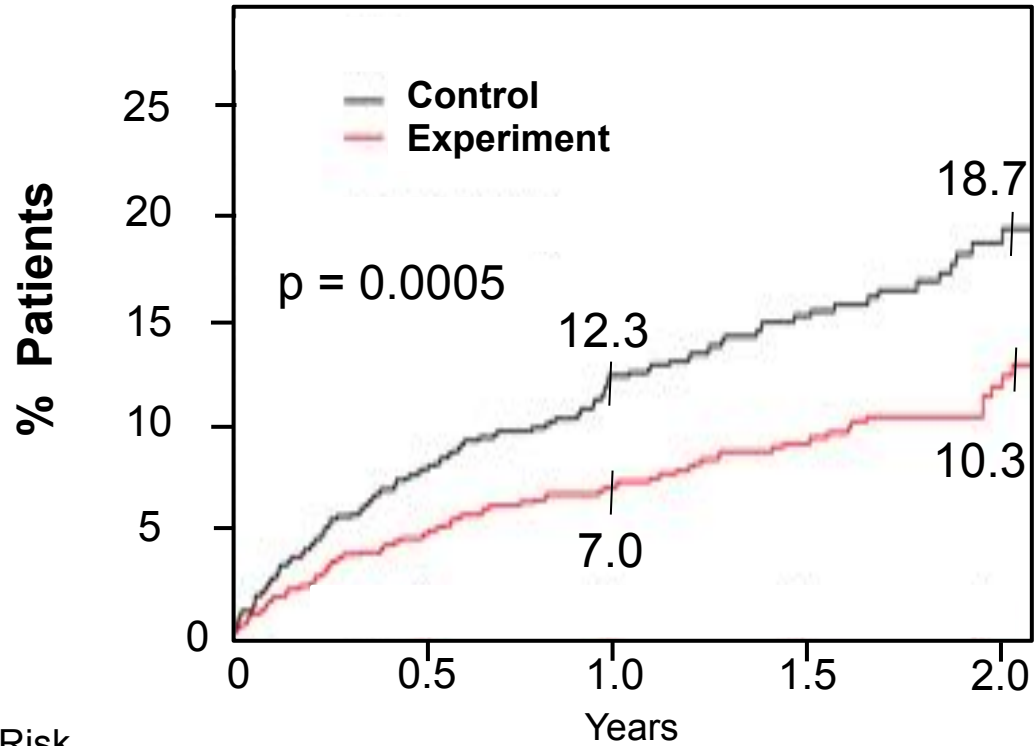
# Device Programming

Presented at HRS 2012



# Results: Primary Endpoint

**Time to First Shock : All-Cause**

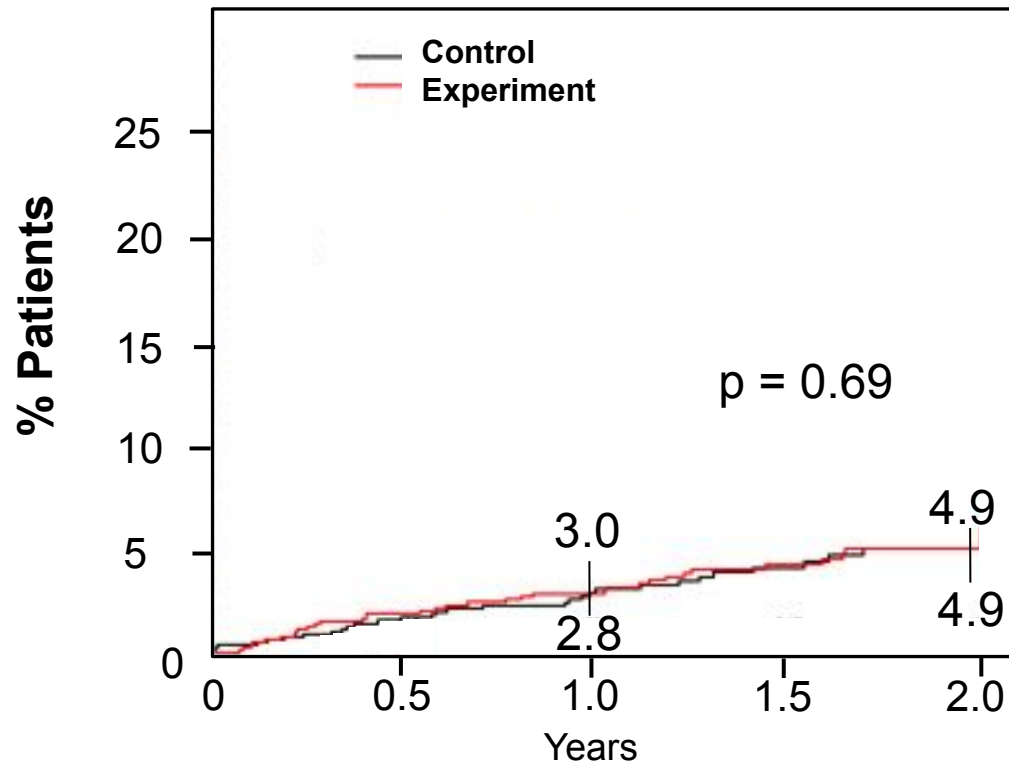


N at Risk

|            |     |     |     |     |     |
|------------|-----|-----|-----|-----|-----|
| Control    | 824 | 671 | 542 | 313 | 141 |
| Experiment | 846 | 729 | 599 | 392 | 190 |

# Results: Primary Endpoint

## Time to First Shock - Appropriate

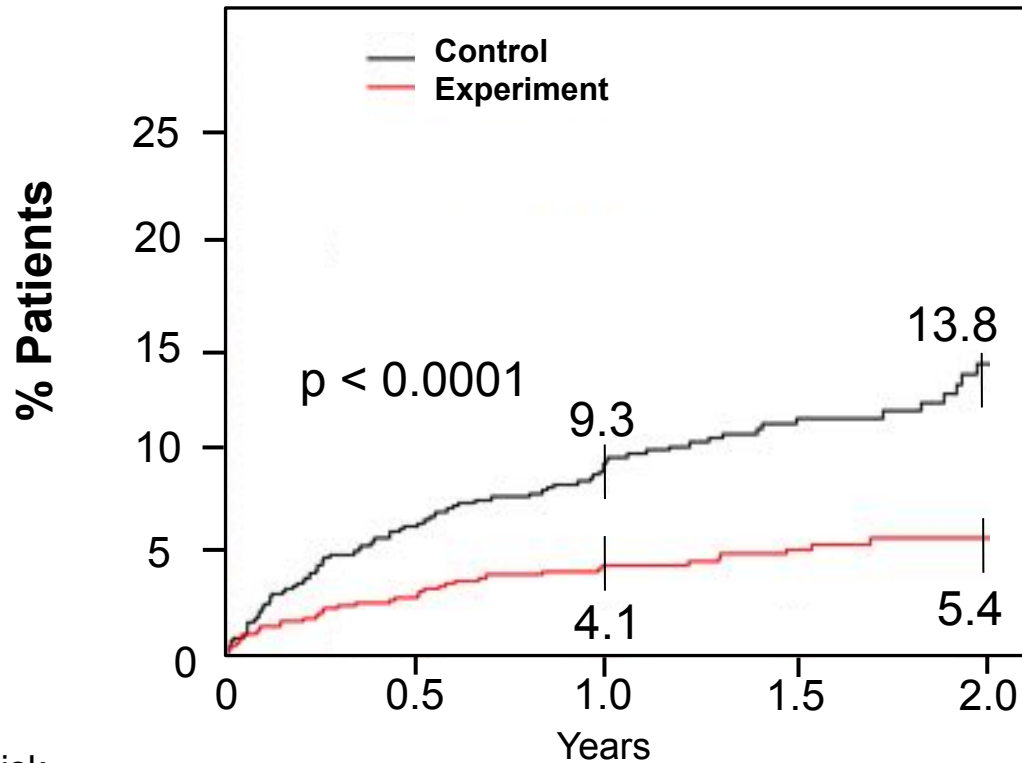


### N at Risk

|            |     |     |     |     |     |
|------------|-----|-----|-----|-----|-----|
| Control    | 824 | 716 | 592 | 347 | 160 |
| Experiment | 846 | 749 | 625 | 406 | 196 |

# Results: Primary Endpoint

## Time to First Shock - Inappropriate



N at Risk

|            |     |     |     |     |     |
|------------|-----|-----|-----|-----|-----|
| Control    | 824 | 683 | 559 | 331 | 153 |
| Experiment | 846 | 743 | 616 | 411 | 199 |

## PROVIDE : CONCLUSIONS

OVERALL MORTALITY REDUCED

HR 0.7, 95% CI:0.50 to 0.98, P= 0.036

*Conclusion: A combination of programmed parameters utilizing higher detection rate, longer detection intervals, empiric ATP, and optimized SVT discriminators reduced ICD therapies without increasing arrhythmic syncope and was associated with reduction in all-cause mortality among ICD patients. (Journal of Cardiovascular Electrophysiology, Vol. 25, pp. 52-59, January 2014)*

# Impact of Programming Strategies Aimed at Reducing Nonessential Implantable Cardioverter Defibrillator Therapies on Mortality

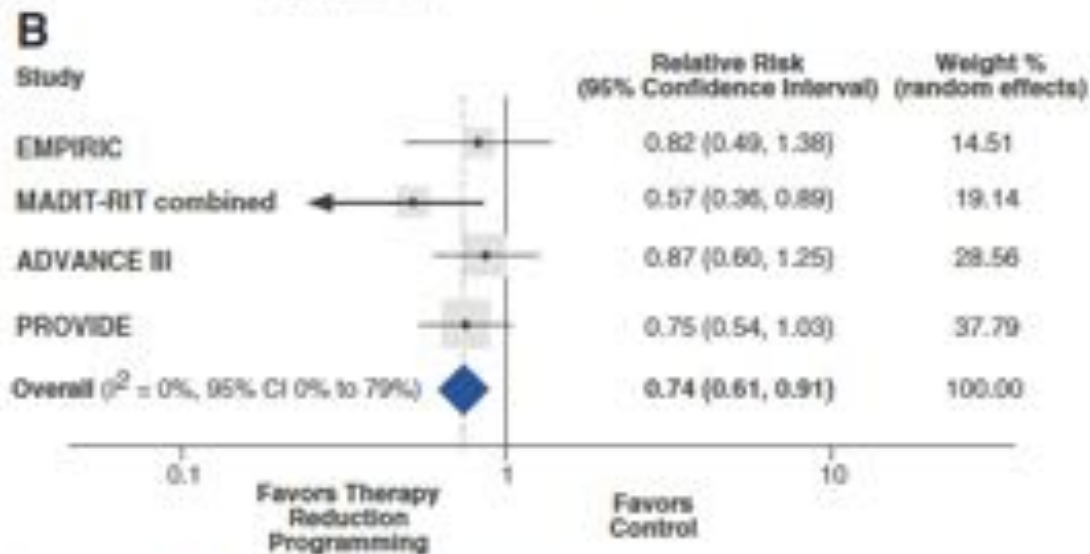
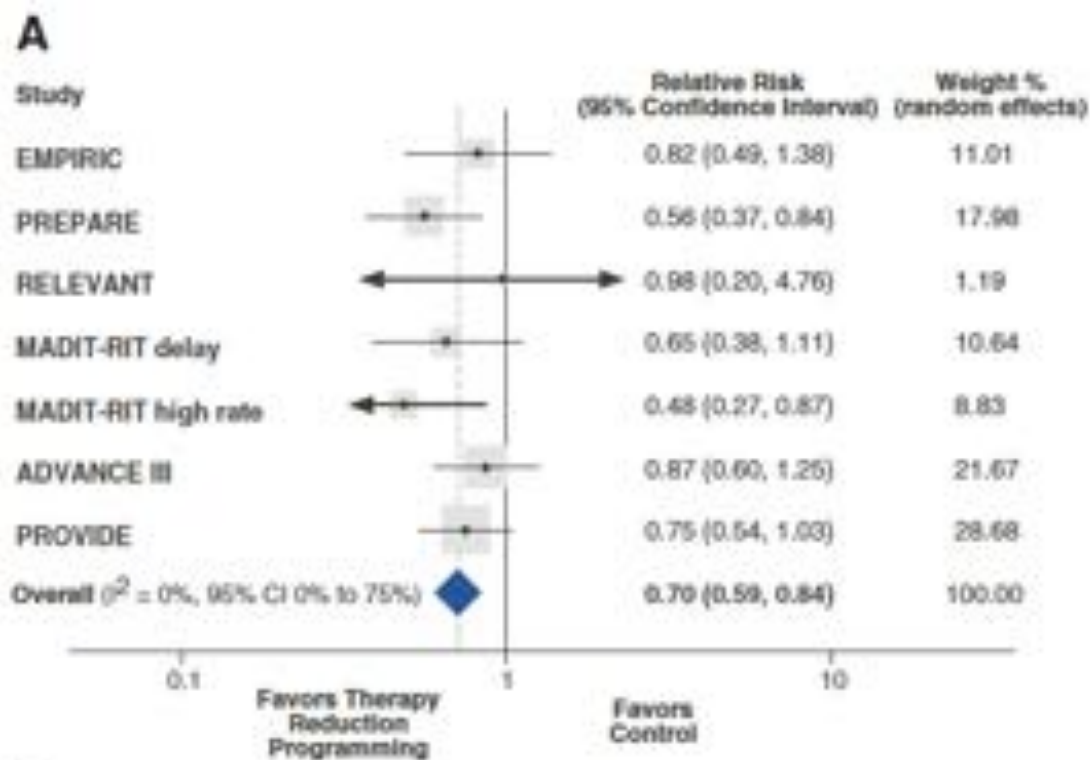
## A Systematic Review and Meta-Analysis

Vern Hsen Tan, MBBS, MRCP; Stephen B. Wilton, MD, MSc; Vikas Kuriachan, MD, FHRS; Glen L. Sumner, MD; Derek V. Exner, MD, MPH, FHRS

*Conclusions*—Therapy reduction programming results in a large, significant, and consistent reduction in mortality, with no apparent increase in the risk of syncope. (*Circ Arrhythm Electrophysiol.* 2014;7:164-170.)

(*Circ Arrhythm Electrophysiol.* 2014;7:164-170.)

Randomized +  
non-randomized studies



Randomized trials

Figure 2. A, Therapy reduction vs convention programming and risk of death, randomized and nonrandomized studies. Random



# A randomized study of remote follow-up of implantable cardioverter defibrillators: safety and efficacy report of the ECOST trial

**Laurence Guédon-Moreau<sup>1\*</sup>, Dominique Lacroix<sup>1</sup>, Nicolas Sadoul<sup>2</sup>, Jacques Clémenty<sup>3</sup>, Claude Kouakam<sup>1</sup>, Jean-Sylvain Hermida<sup>4</sup>, Etienne Aliot<sup>2</sup>, Michel Boursier<sup>5</sup>, Olivier Bizeau<sup>6</sup>, and Salem Kacet<sup>1</sup>, for the ECOST trial Investigators**

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Received 19 July 2012; revised 16 October 2012; accepted 15 November 2012



**Table 4** All shocks, inappropriate shocks, and capacitor charges observed in the intention-to-treat population

|  | Study groups        |                      | P    |
|--|---------------------|----------------------|------|
|  | Active<br>(n = 221) | Control<br>(n = 212) |      |
| Appropriate and inappropriate shocks delivered | 193 [0–33]          | 657 [0–116]          |      |
| Patients with $\geq 1$ delivered shock         | 47 (21.3)           | 56 (26.4)            | 0.21 |
| Mean per patient-month                         | 0.04 $\pm$ 0.27     | 0.20 $\pm$ 1.13      | 0.02 |
| Inappropriate shocks delivered                 | 28 [1–8]            | 283 [1–82]           |      |
| Patients with $\geq 1$ inappropriate shock     | 11 (5.0)            | 22 (10.4)            | 0.03 |
| Mean per patient-month                         | 0.13 $\pm$ 0.15     | 0.83 $\pm$ 1.86      | 0.28 |
| Capacitor charges                              | 499 [0–58]          | 2081 [0–760]         |      |
| Patients with $\geq 1$ capacitor charge        | 69 (31.2)           | 72 (34.0)            | 0.54 |
| Mean per patient-month                         | 0.11 $\pm$ 0.38     | 1.65 $\pm$ 18.81     | 0.11 |

Values are number of observations [ranges], numbers (%) of observations, or means  $\pm$  SD.

Early AF detection

Early noise and lead –related problems detection

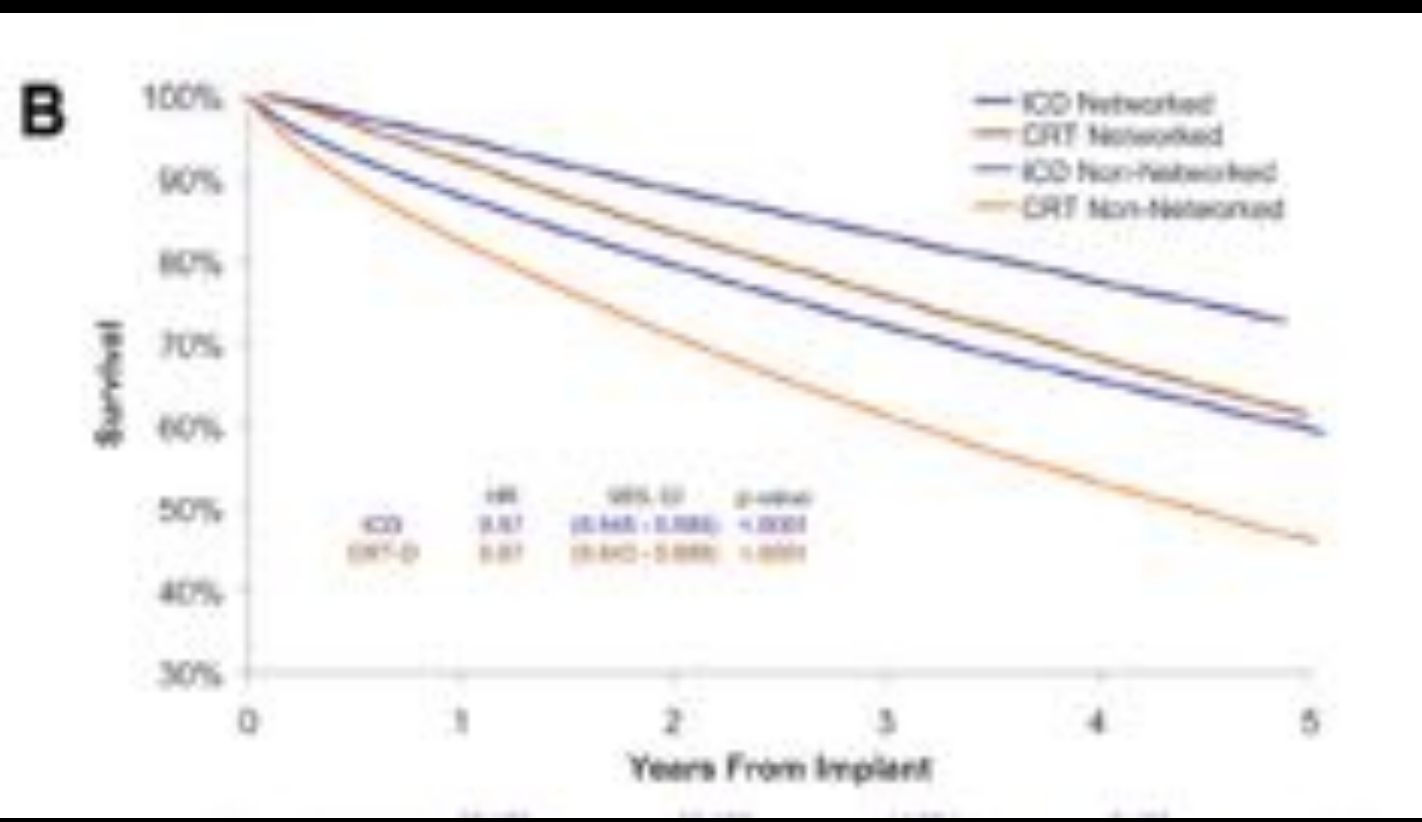
Early T-wave oversensing detection

Early HF and its related VA and SVA detection

# Long-Term Outcome After ICD and CRT Implantation and Influence of Remote Device Follow-Up

## The ALTITUDE Survival Study

Leslie A. Saxon, MD; David L. Hayes, MD; F. Roosevelt Gilliam, MD; Paul A. Heidenreich, MD; John Day, MD; Milan Seth, MS; Timothy E. Meyer, PhD; Paul W. Jones, MS; John P. Boehmer, MD



50% mortality reduction in networked pts with either ICD or CRTD

# Implant-based multiparameter telemonitoring of patients with heart failure (IN-TIME): a randomised controlled trial



Gerhard Hindricks, Milos Taborsky, Michael Glikson, Ullus Heinrich, Bernhard Schumacher, Arnes Ketz, Johannes Brachmann, Thorsten Lewalter, Andreas Goette, Michael Block, Josef Kautzner, Stefan Sack, Daniela Hruska, Christopher Florkowski, Peter Søgaard, for the IN-TIME study group\*

## Summary

**Background** An increasing number of patients with heart failure receive implantable cardioverter-defibrillators (ICDs) or cardiac resynchronisation defibrillators (CRT-Ds) with telemonitoring function. Early detection of worsening heart failure, or upstream factors predisposing to worsening heart failure, by implant-based telemonitoring might enable pre-emptive intervention and improve outcomes, but the evidence is weak. We investigated this possibility in IN-TIME, a clinical trial.

**Methods** We did this randomised, controlled trial at 36 tertiary clinical centres and hospitals in Australia, Europe, and Israel. We enrolled patients with chronic heart failure, NYHA class II–III symptoms, ejection fraction of no more than 35%, optimal drug treatment, no permanent atrial fibrillation, and a recent dual-chamber ICD or CRT-D implantation. After a 1 month run-in phase, patients were randomly assigned (1:1) to either automatic, daily, implant-based, multiparameter telemonitoring in addition to standard care or standard care without telemonitoring. Investigators were not masked to treatment allocation. Patients were masked to allocation unless they were contacted because of telemonitoring findings. Follow-up was 1 year. The primary outcome measure was a composite clinical score combining all-cause death, overnight hospital admission for heart failure, change in NYHA class, and change in patient global self-assessment, for the intention-to-treat population. The trial is registered with ClinicalTrials.gov, number NCT00538356.

**Findings** We enrolled 716 patients, of whom 664 were randomly assigned (333 to telemonitoring, 331 to control). Mean age was 65.5 years and mean ejection fraction was 26%. 285 (43%) of patients had NYHA functional class II and 378 (57%) had NYHA class III. Most patients received CRT-Ds (390; 58.7%). At 1 year, 63 (18.9%) of 333 patients in the telemonitoring group versus 90 (27.2%) of 331 in the control group ( $p=0.013$ ) had worsened composite score (odds ratio 0.63, 95% CI 0.43–0.90). Ten versus 27 patients died during follow-up.

**Interpretation** Automatic, daily, implant-based, multiparameter telemonitoring can significantly improve clinical outcomes for patients with heart failure. Such telemonitoring is feasible and should be used in clinical practice.

**Funding** Biotronik SE & Co. KG.

Lancet 2024; 384: 583–90

See Comment page 560

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Medicine, Prague, Czech Republic (Prof J Kautzner MD); Klinikum Schwabing, Munich,

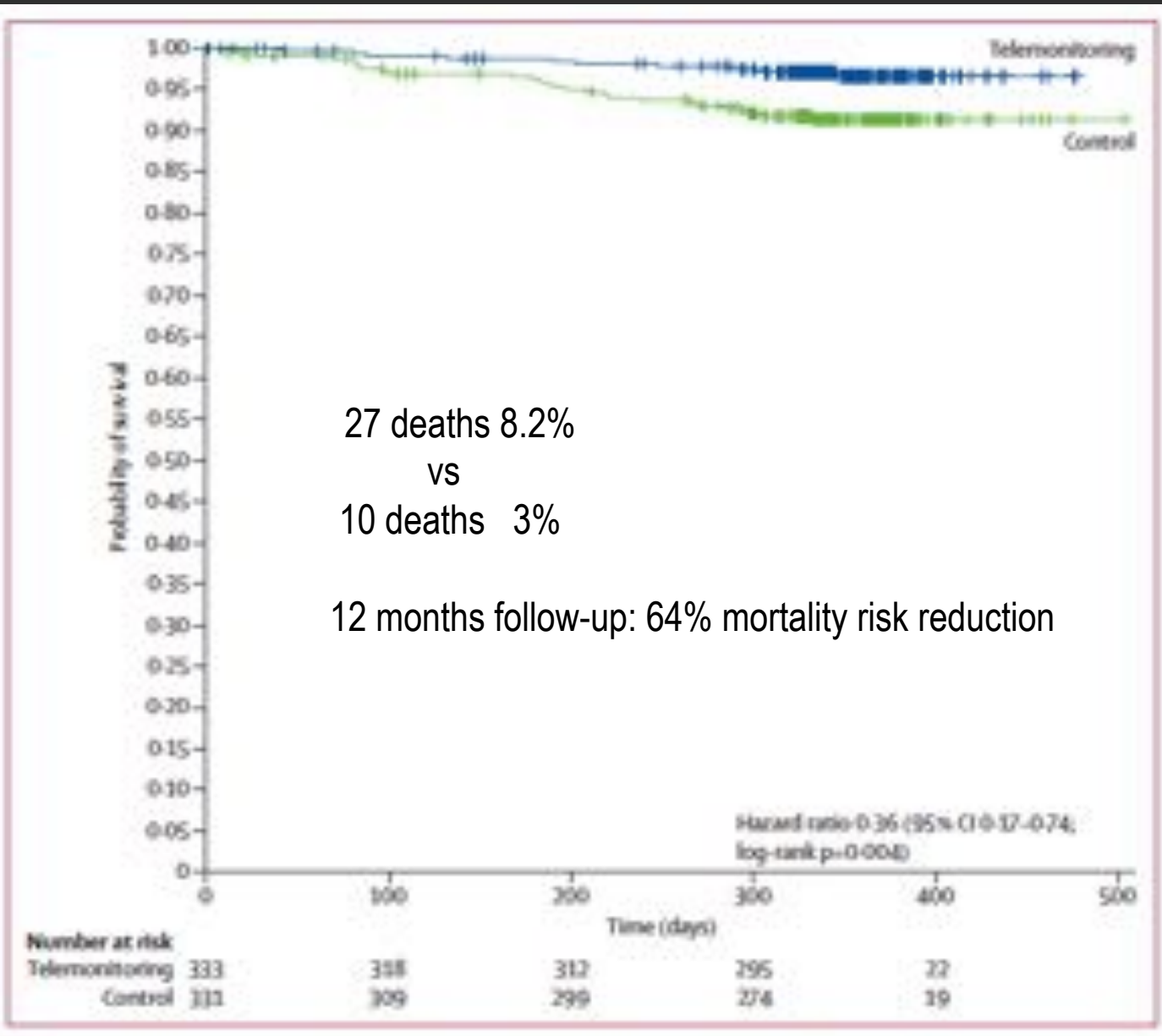
# HOME MONITORING REDUCES DEATH AND A COMPOSITE CLINICAL ENDPOINT IN CRTD/ICD WITH NYHA II-III HF: 64% REDUCTION OF MORTALITY RISK

|  | Telemonitoring group (n=333) | Control group (n=331) | p value |
|--|------------------------------|-----------------------|---------|
| Worsened   | 63 (18.9%)                   | 90 (27.2%)            | 0.013*  |
| Death  | 10 (3.0%)                    | 27 (8.2%)             | 0.004*  |
| Overnight admission to hospital for worsening heart failure† | 23 (6.9%)                    | 27 (8.2%)             | --      |
| Worsened NYHA functional class and global self-assessment    | 0 (0.0%)                     | 1 (0.3%)              | --      |
| Worsened NYHA functional class only                          | 23 (6.9%)                    | 31 (9.4%)             | --      |
| Worsened global self-assessment only                         | 7 (2.1%)                     | 4 (1.2%)              | --      |
| Improved‡  | 111 (33.3%)                  | 105 (31.7%)           | --      |
| Unchanged  | 159 (47.8%)                  | 136 (41.1%)           | --      |

Data are n (%). Patients are included only once, in the topmost subcategory. \*Also statistically significant difference in a post-hoc multivariable logistic regression model after adjustment for use of angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers (the only substantial imbalance between groups at randomisation; data not shown). †Adjudicated by an endpoint committee masked to patients' treatment assignment (appendix). ‡Improved NYHA class or moderately to markedly improved self-assessed condition. NYHA=New York Heart Association.

Table 2: Results for composite clinical score

Hindricks G et al, Lancet 2014;384:583-90



# HRS Expert Consensus Statement on remote interrogation and monitoring for cardiovascular implantable electronic devices



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Heart Rhythm, Vol 12, No 7, July 2015

## HRS Remote Monitoring Consensus Statement Recommendations

|  | Class of                | Level of          |
|--|-------------------------|-------------------|
| Device and Disease Management  | Class of Recommendation | Level of Evidence |
| RM should be performed for surveillance of lead function and battery conservation.   | I                       | A                 |
| Patients with a CIED component that has been recalled or is on advisory should be enrolled in RM to enable early detection of actionable events.   | I                       | E                 |
| RM is useful to reduce the incidence of inappropriate ICD shocks.  | I                       | B-R               |
| RM is useful for the early detection and quantification of atrial fibrillation.  | I                       | A                 |
| The effectiveness of RM for thoracic impedance alone or combined with other diagnostics to manage congestive heart failure is currently uncertain. | IIb                     | C                 |

B-R = level of evidence B indicates a moderate level from randomized trials; CIED = cardiac implantable electronic device; ICD = implantable cardioverter-defibrillator; RM = remote monitoring.

# HOW TO REDUCE UN-NECESSARY ICD SHOCKS (AND REDUCE MORTALITY)

- ANTI-TACHYCARDIA PACING
  - DISCRIMINATION ALGORITHMS AND DISCRIMINATOR TIME-OUT (OFF)
  - EXTEND DETECTION TIME / INCREASE DETECTION INTERVALS
  - INCREASE VENTRICULAR FIBRILLATION CUT-OFF RATE
  - USE REMOTE PATIENT MONITORING (Wireless)
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