*Programming ICDs to **Safely** Minimize Shocks*

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I am a consultant, receive research support and/or have lectured on behalf of: Medtronic, Boston Scientific, St. Jude Medical, Biotronik, Sorin, Spectranetics, Inner Pulse, Cook, Lifewatch

EMPIRIC - DESIGN

- Prospective, single blind, parallel, non-inferiority
- 1:1 randomized:
  - Empiric vs. Physician Tailored Programming for VT/VF
    - Stratified by 1º and 2º ICD indication
- 1 year follow-up
- Medtronic Marquis DR ICDs and approved leads
- Episodes adjudicated by at least two reviewers

Main ICD Indication

	Empiric (N=445)	Tailored (N=455)
Secondary Prevention:	**51.7%**	**55.8%**
VT (spontaneous, sustained)	26.7%	25.7%
VF (spontaneous, sustained)	10.6%	13.0%
Syncope	14.4%	17.1%
Primary Prevention:	**48.3%**	**44.2%**
CAD, LV Dysfunction, EPS+	23.8%	22.2%
CAD, LV Dysf., EPS-/not done	17.5%	16.0%
Other	7.0%	5.9%

No significant differences

Baseline Characteristics

	Empiric	Tailored
Age: Mean ± Std	65.1 ± 12.4	64.8 ± 12.7
Male	82.7%	79.8%
EF Mean ± Std	31.9% ± 13.1	32.1% ± 12.3
Myocardial Infarction	71.2%	67.7%
Hypertension	57.5%	49.5%
NYHA Class I	11.5%	12.1%
Class II	35.7%	34.3%
Class III-IV	14.9%	14.1%
Hx of AF/Afl/AT	24.7%	26.4%

All ns, except hypertension: p = 0.02

Empiric Arm Strategies to ↓ Shocks

- Avoid detecting non-sustained tachycardias
- Avoid detecting SVTs as VT
- Empirical ATP for slow and fast VTs
- High Output 1st Shock

Morgan JM, et al. Current Controlled Trials in Cardiovascular Medicine 2004, 5:12

Empiric Arm Programming

Zone	Rate	# beats	Therapies
VF	> 250 **bpm**	18 of 24	30J x 6
FVT	201 - 250	"	Burst(1), 30J x 6
VT	≤ **150 - 200**	16	Burst(2), Ramp(1), 20J, 30J x 3

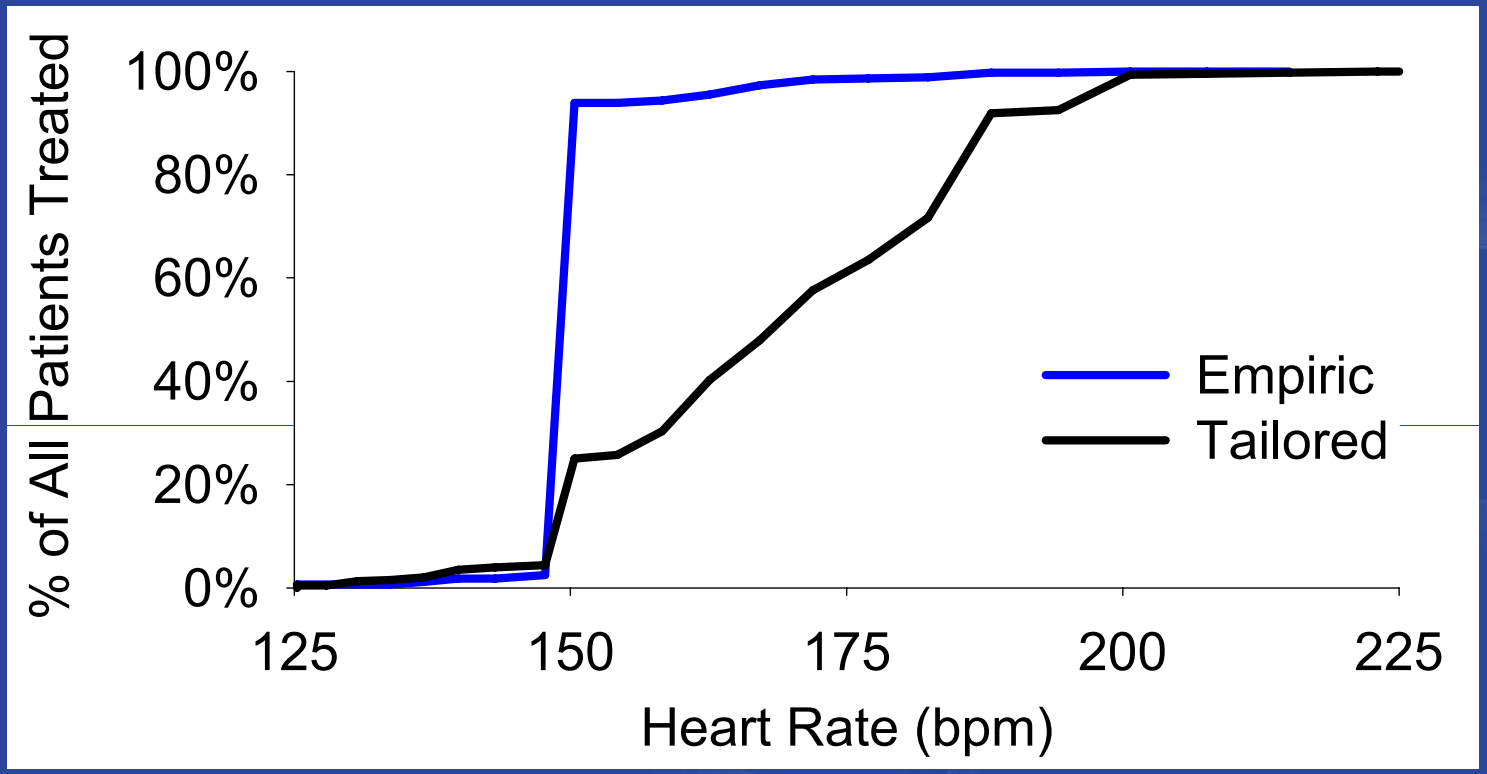
PR Logic On: AF/Afl, Sinus Tach (**1:1 VT-ST = 66%**)
SVT Limit = 200 bpm

Physician Tailored Arm Programming

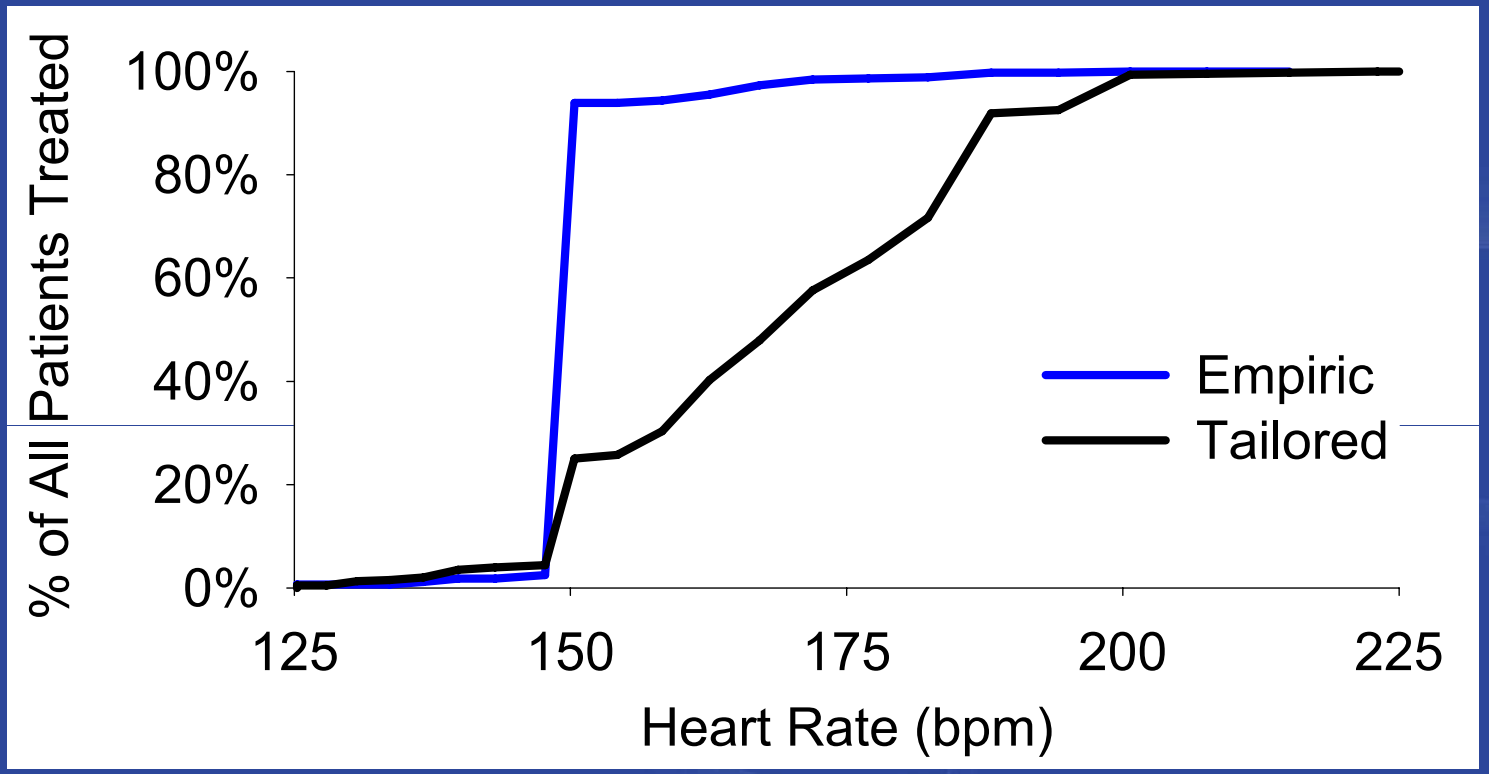
- Physician discretion

Both Arms: Changes during follow-up ok if medically justified

VT Therapy “ON” by Heart Rate

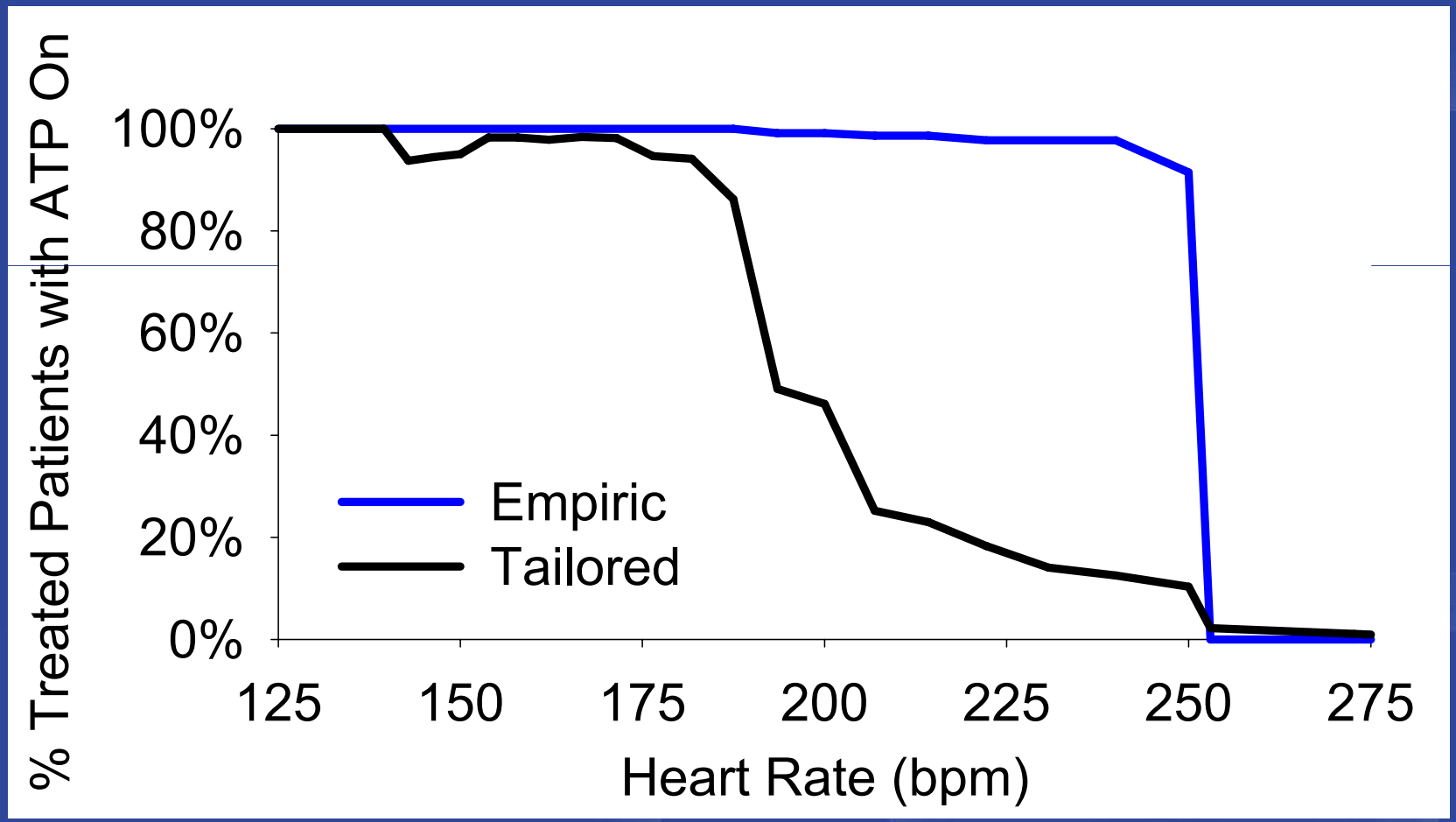


VT Therapy “ON” by Heart Rate



Median Rate Threshold	Empiric	Tailored	P-value
All Patients	150 bpm	**171** bpm	< .001
Only Spont. Sust. MVT	150	**162**	< .001
All Others	150	**176**	< .001

ATP Therapy “ON” by Heart Rate

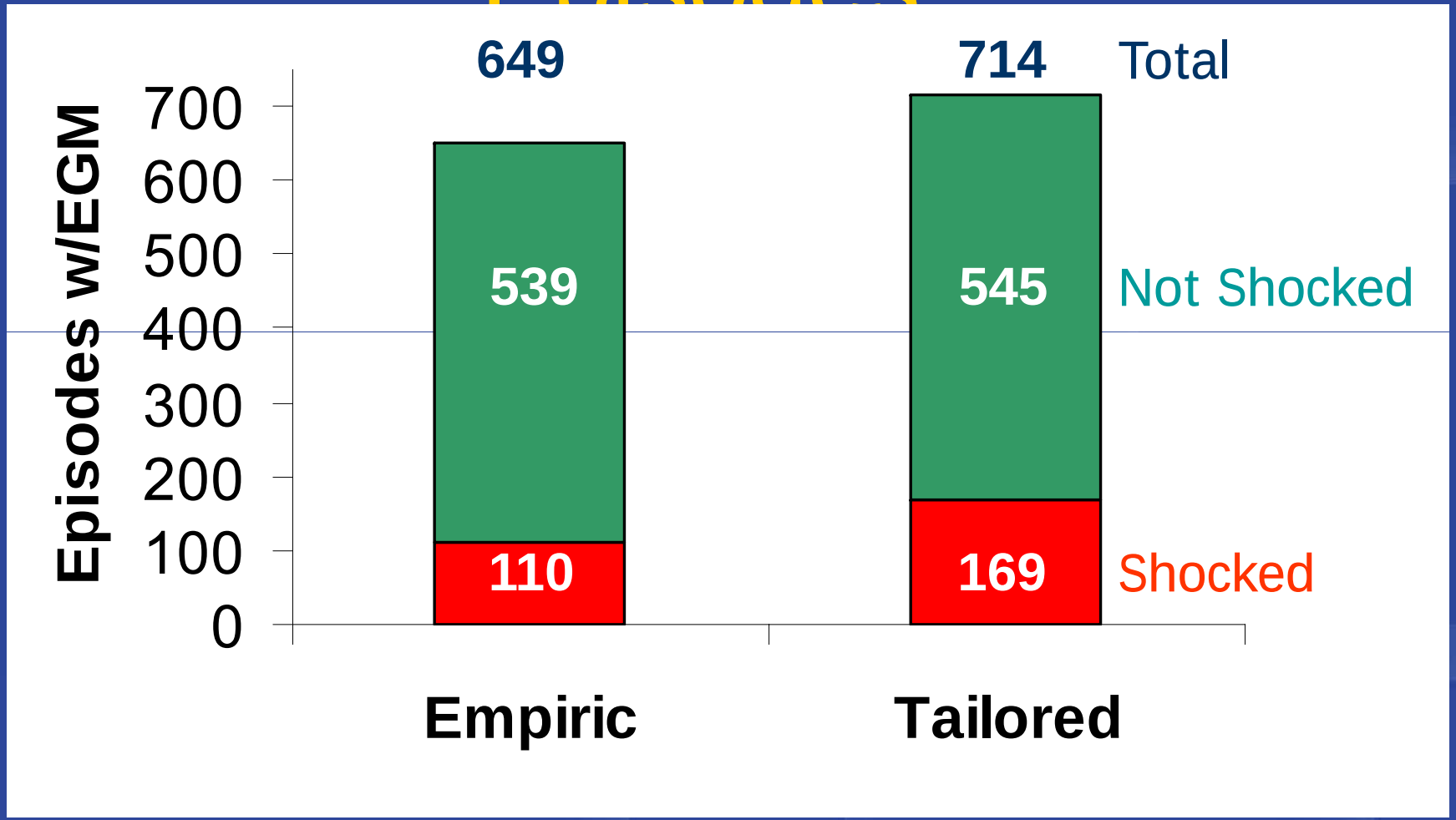


Other Baseline VT/VF Programming

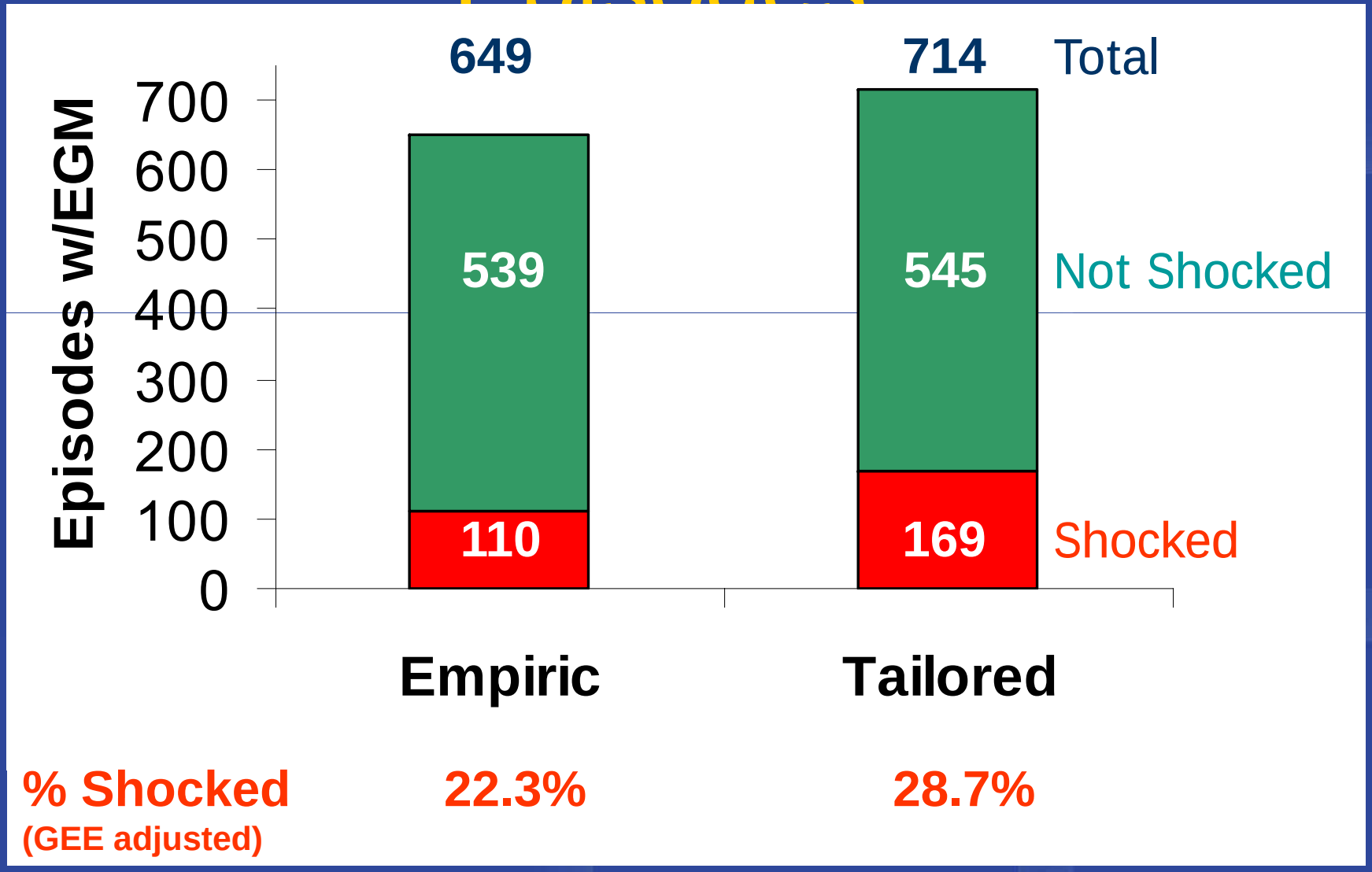
	Empiric	Tailored
VF # beats ≥ 18 of 24	94%	50%
VT Detection and Rx = On	100%	60%
SVT Discriminators = On	100%	76%
1:1 VT-ST Boundary ≥ 66%	98%	18%
First VF Rx = Max. Output Shock	96%	56%

P < 0.001 for ALL

Results: True VT/VF Episodes

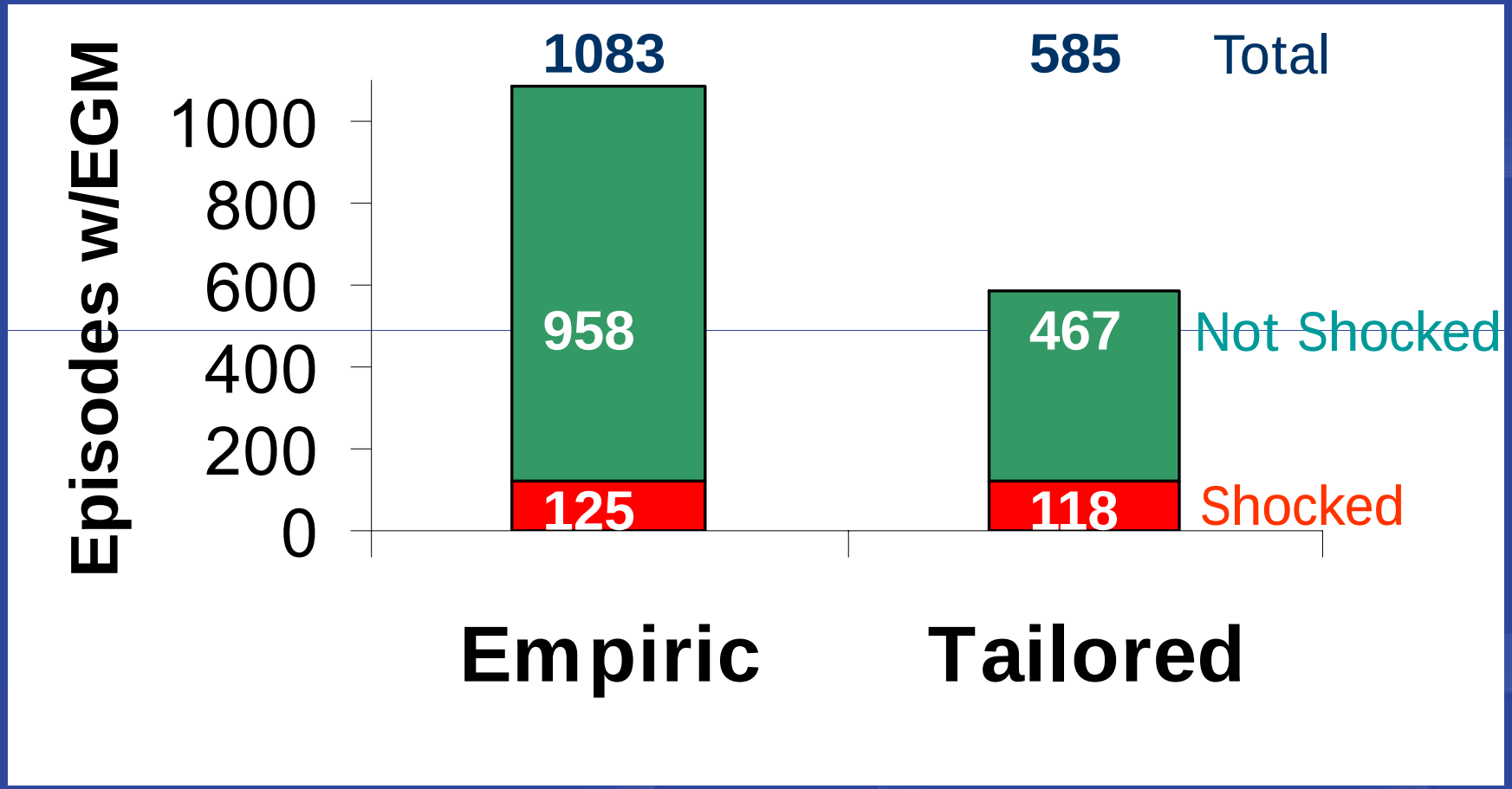


Results: True VT/VF Episodes

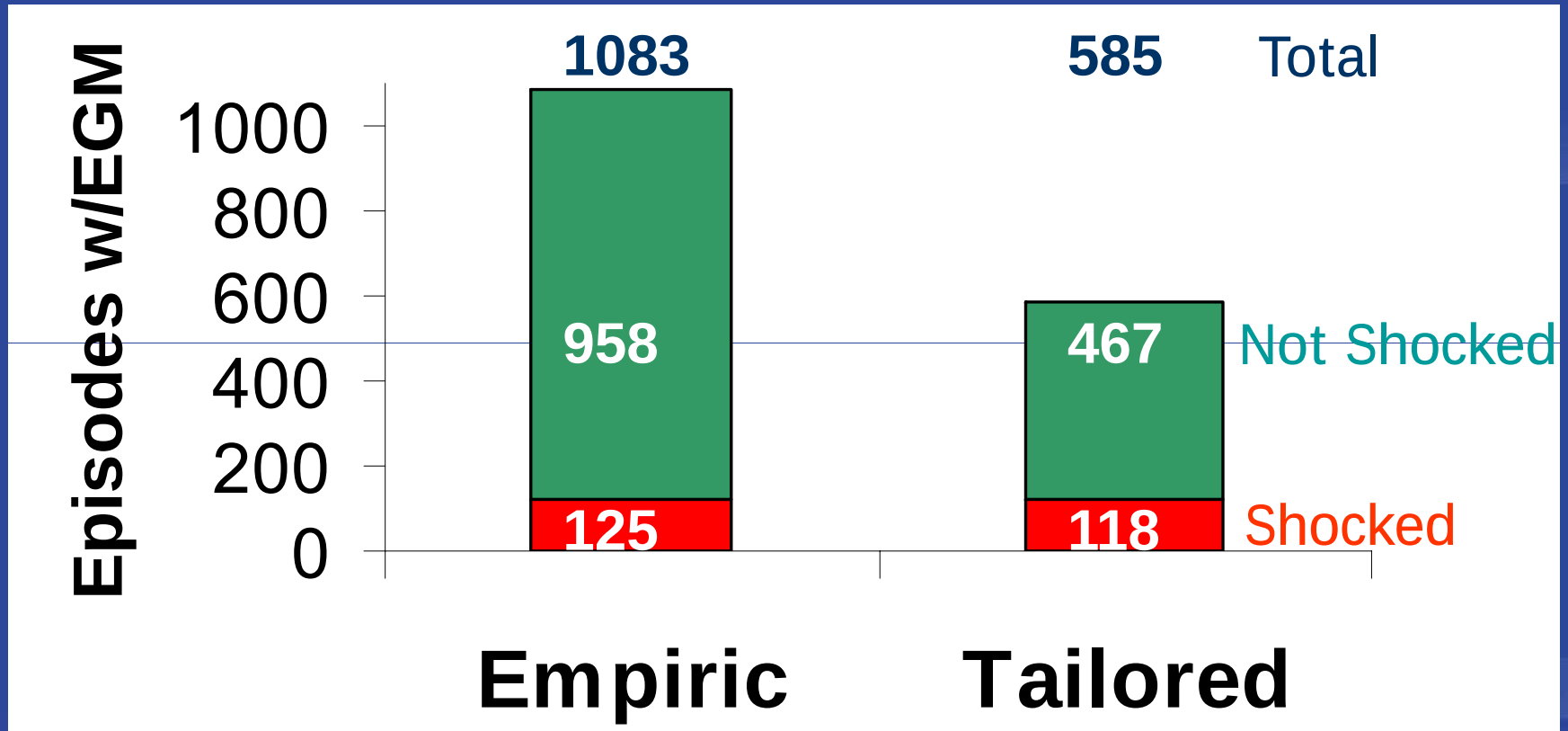


	Empiric	Tailored
% Shocked (GEE adjusted)	22.3%	28.7%

Results: True SVT Episodes



Results: True SVT Episodes



	Empiric	Tailored
% Shocked	11.9%	26.1%

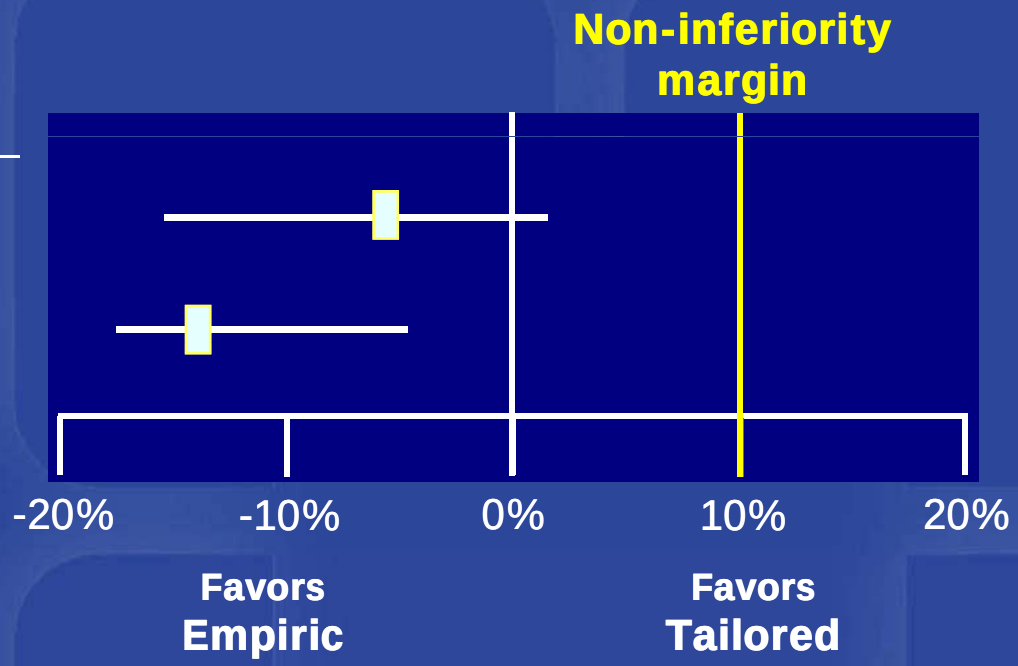
GEE adjusted

Results: % Episodes Shocked

% Episodes Shocked

Rhythm	Empiric	Tailored
VT/VF	22.3%	28.7%
SVT	11.9%	26.1%

Difference of % Shocked



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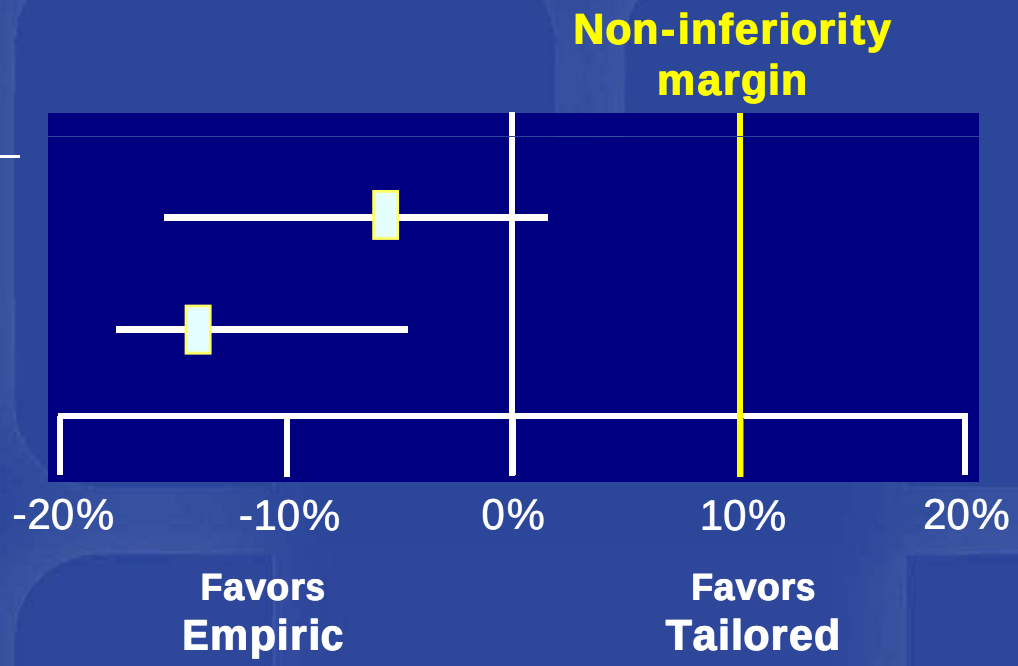
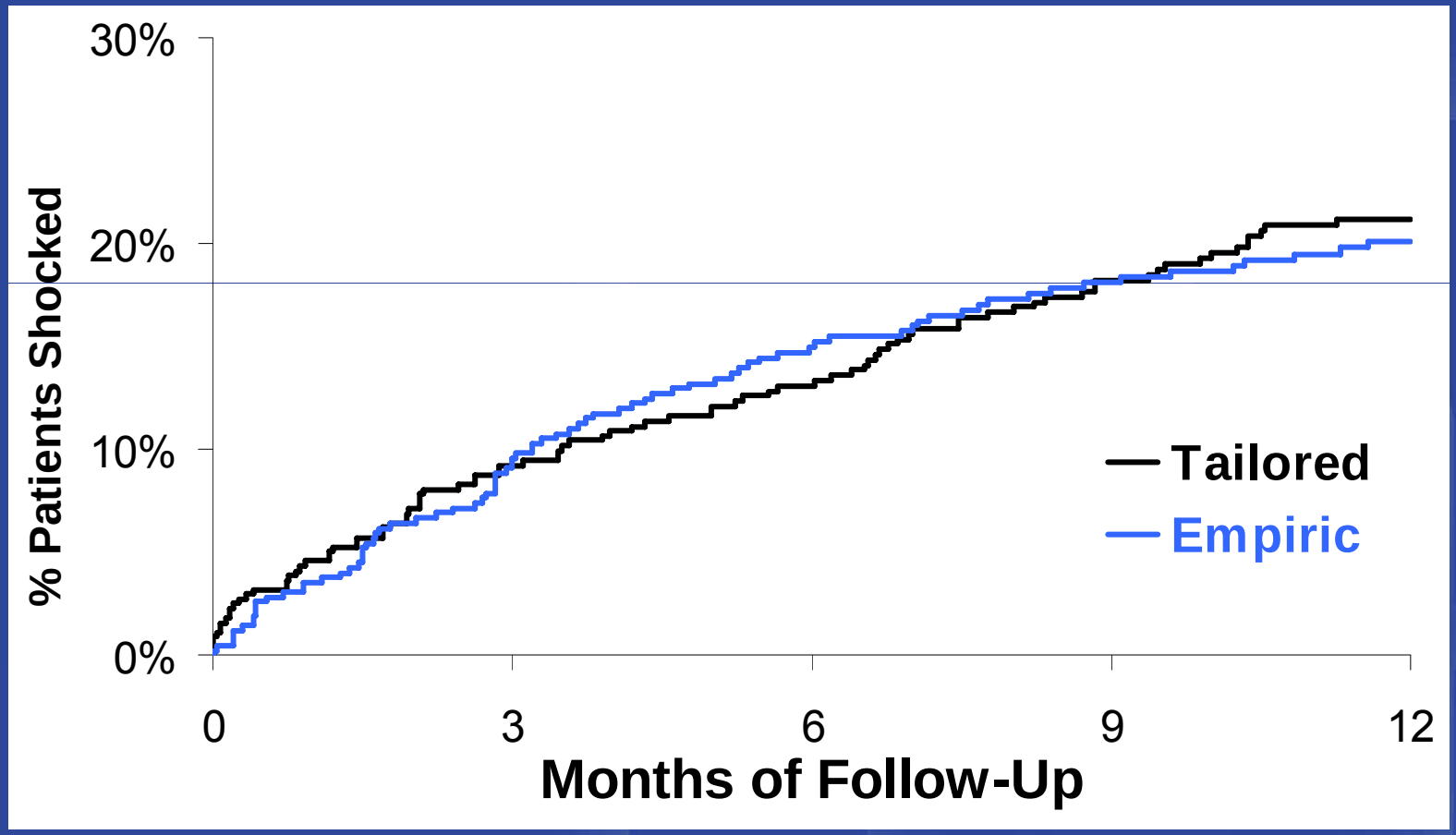
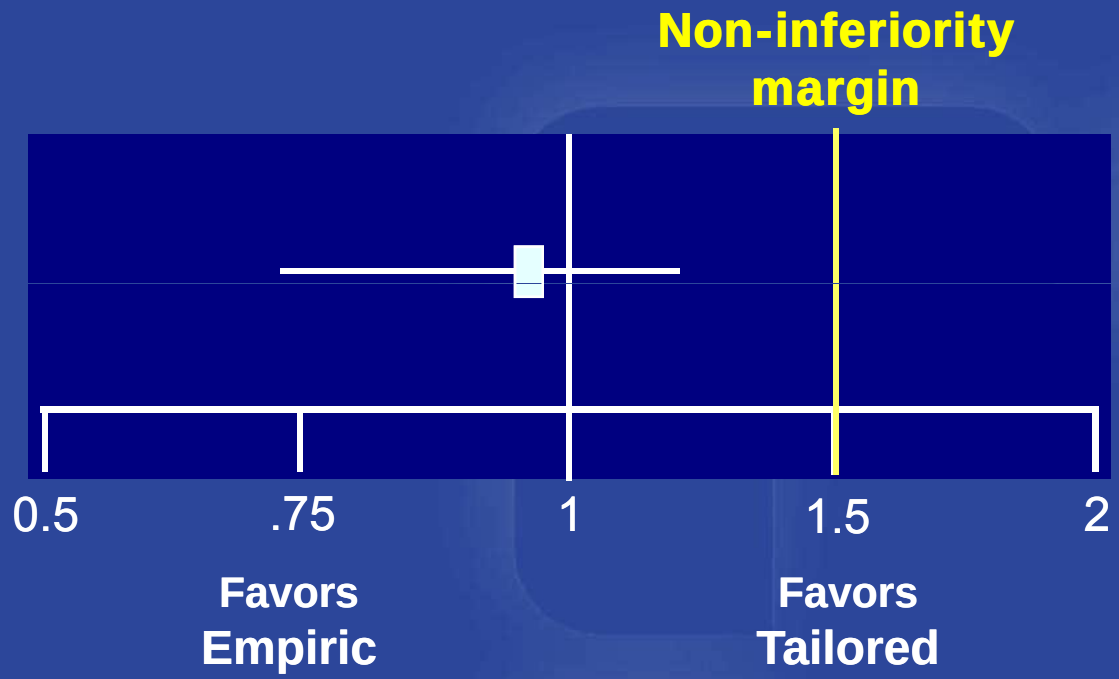


Empiric statistically non-inferior for both VT/VF and SVTs

Time to First **All-Cause** Shock

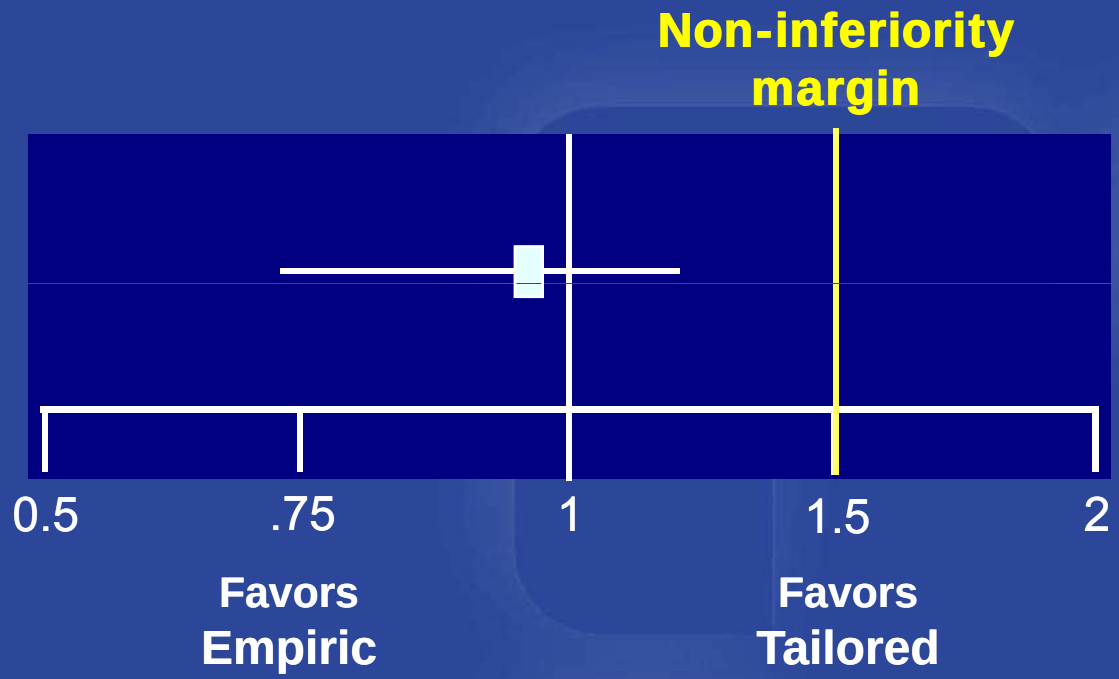


Hazard Ratio
Time to First **All-Cause** Shock



Hazard Ratio (90% CI): 0.95 (0.74 - 1.23)
Non-inferiority p = 0.0016

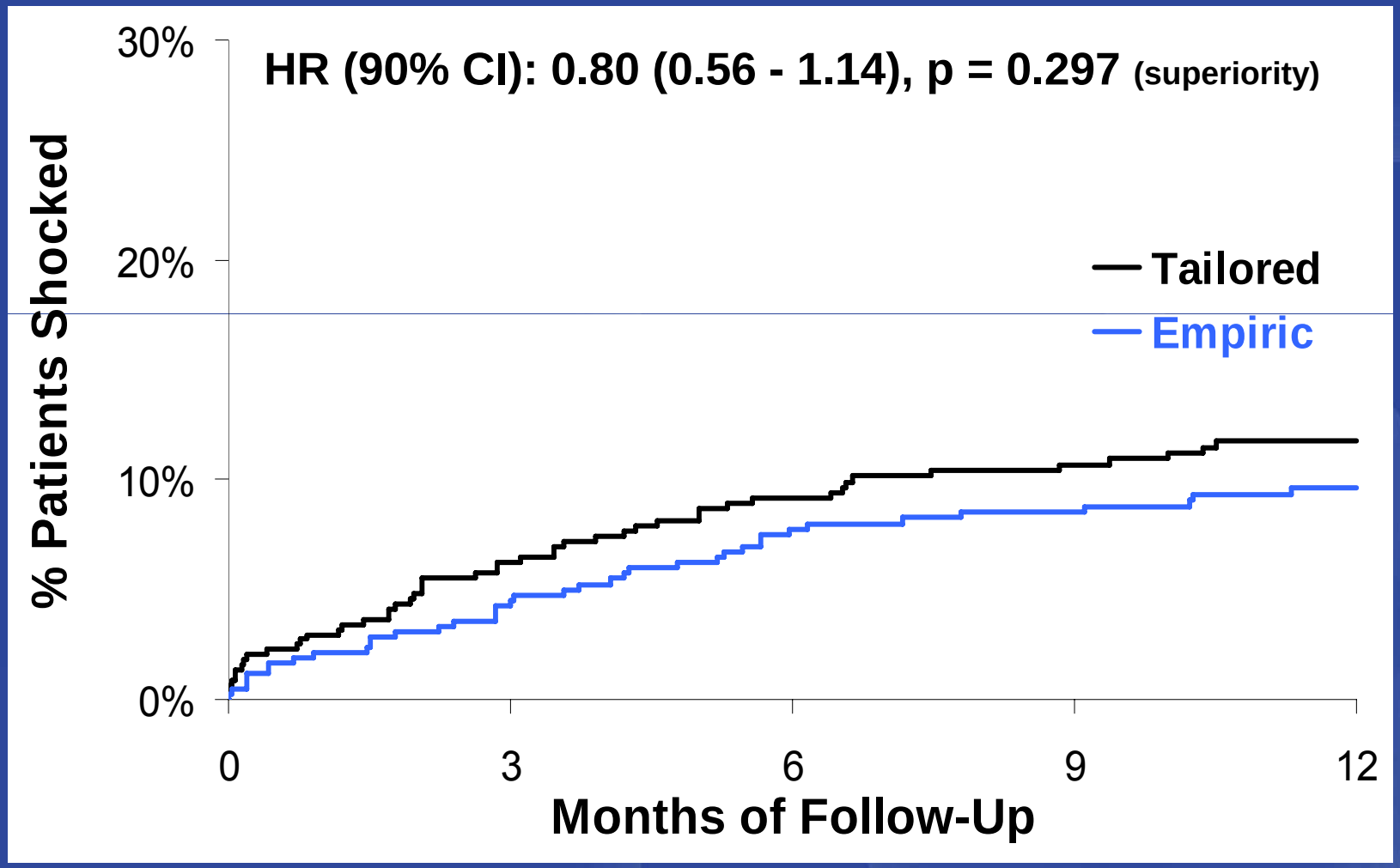
Hazard Ratio
Time to First **All-Cause** Shock



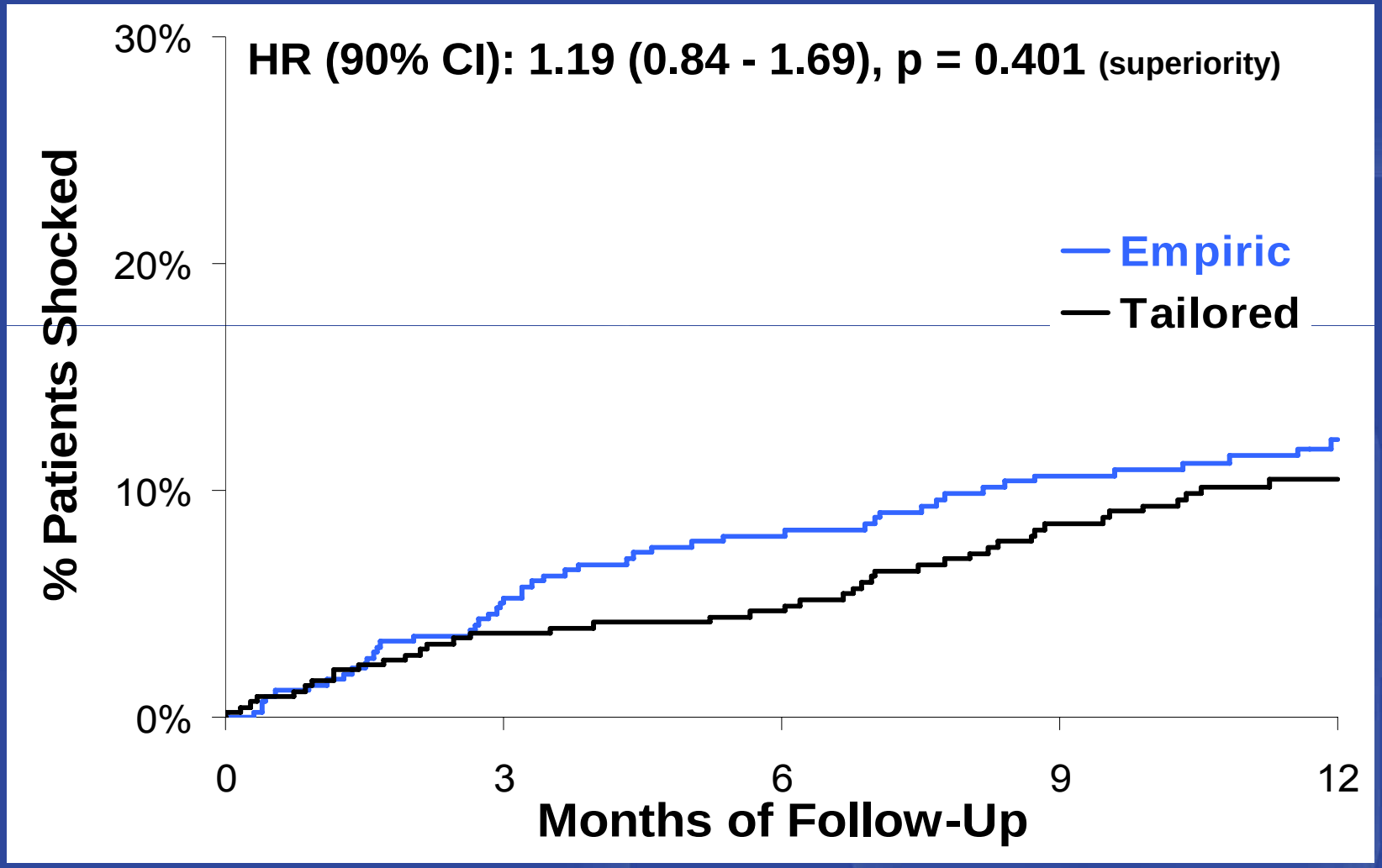
Hazard Ratio (90% CI): 0.95 (0.74 - 1.23)
Non-inferiority p = 0.0016

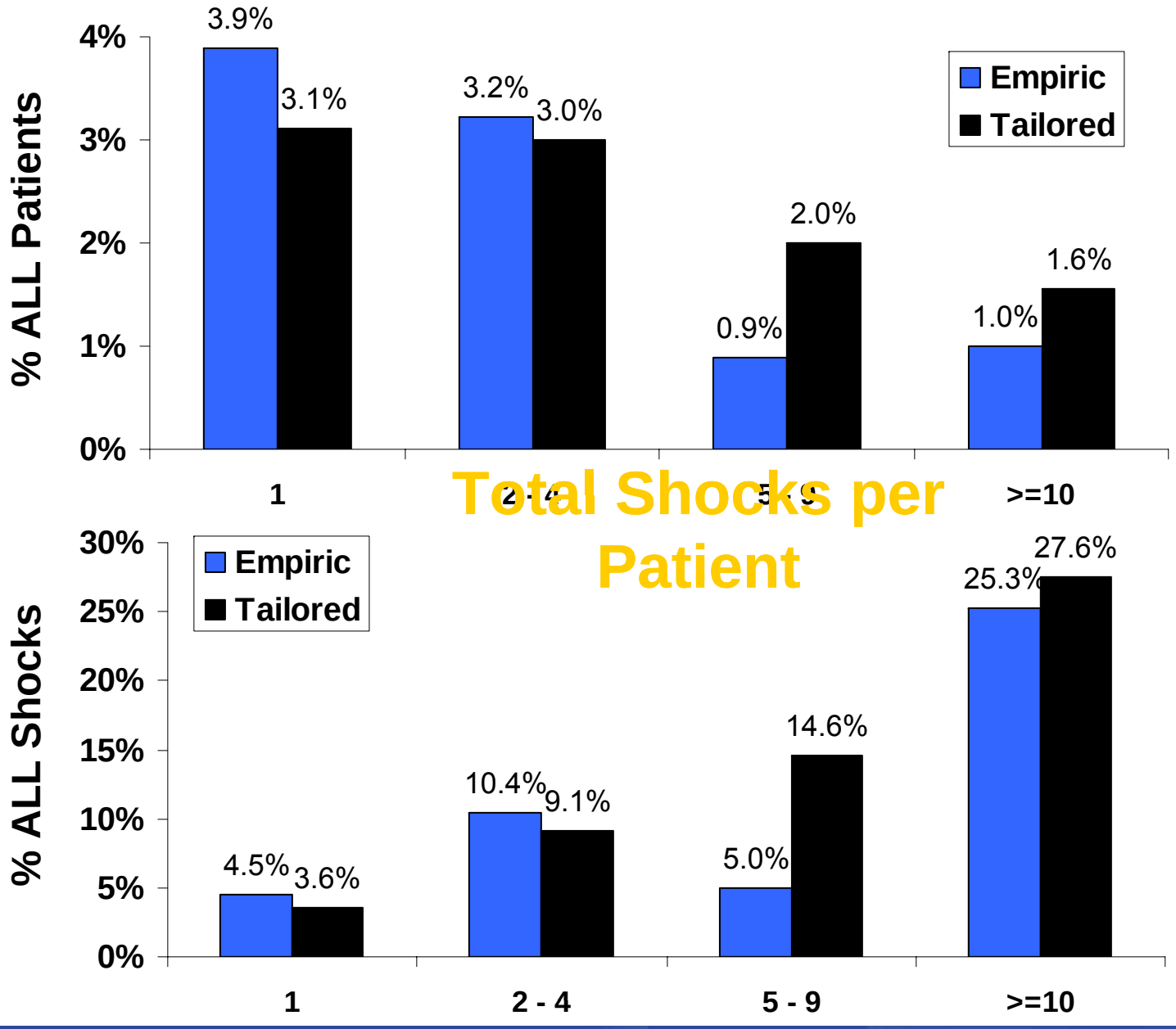
Empiric non-inferior for time to 1st all-cause shock

Time to First VT/VF Shock



Time to First SVT Shock





Pts with

≥10 Shocks

2.6% Pts

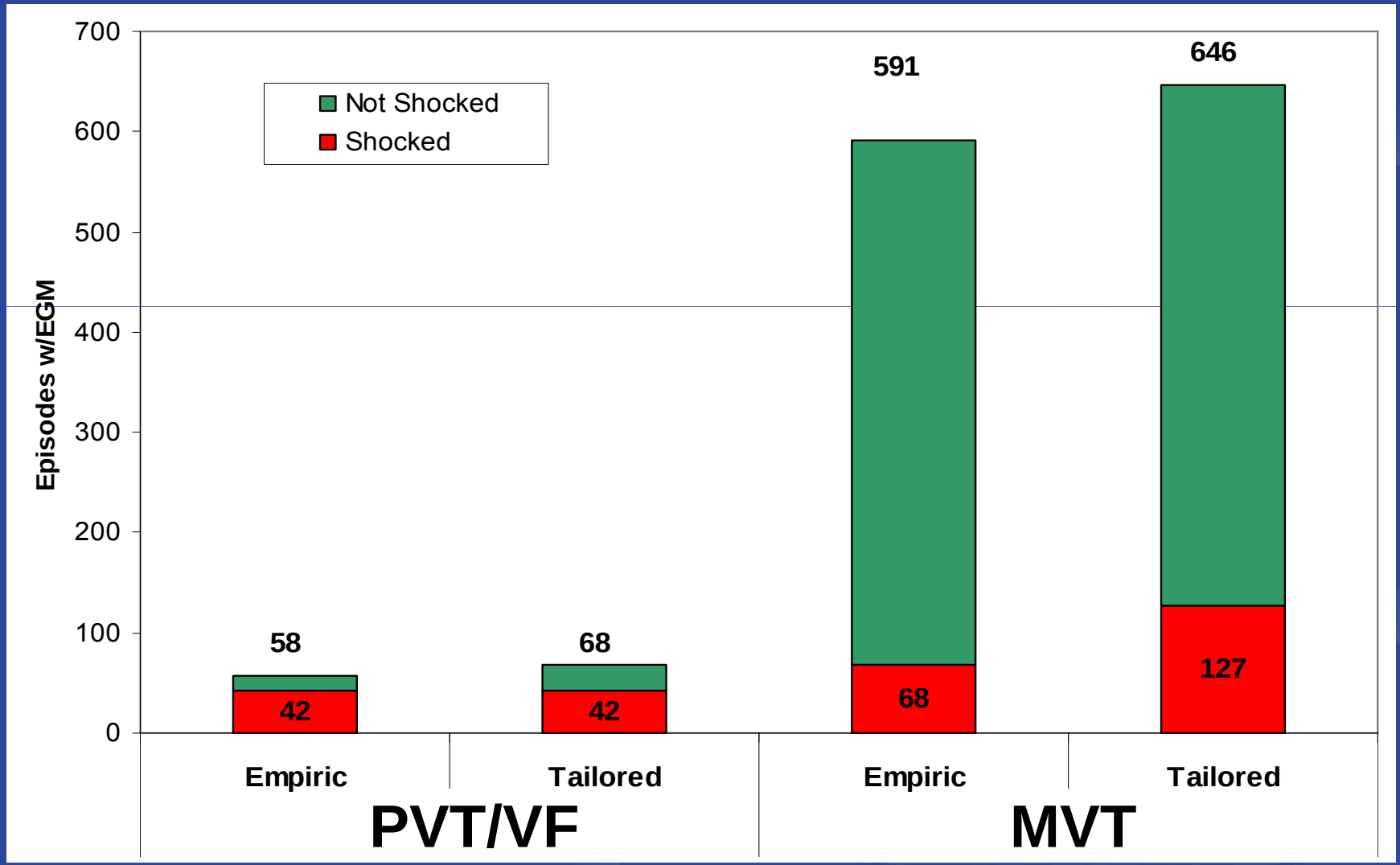
53% Shocks

≥5 Shocks

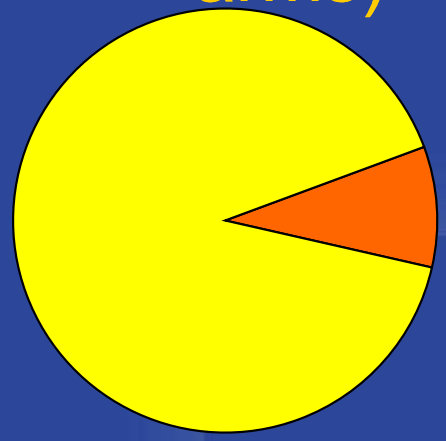
5.5% Pts

72% Shocks

Type of True VT/VF



True VT/VF Detected Episodes (both arms)



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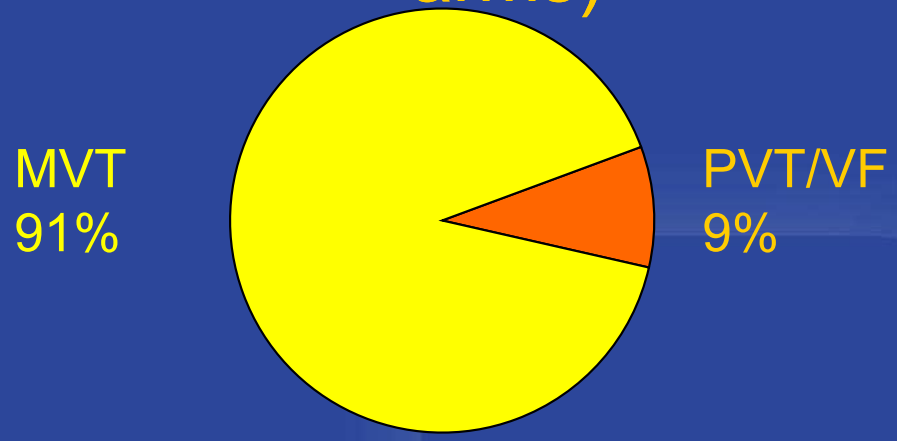
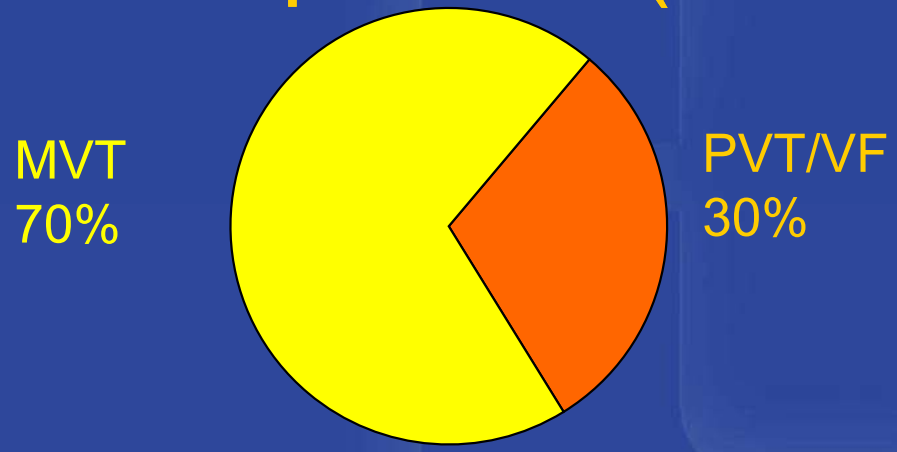
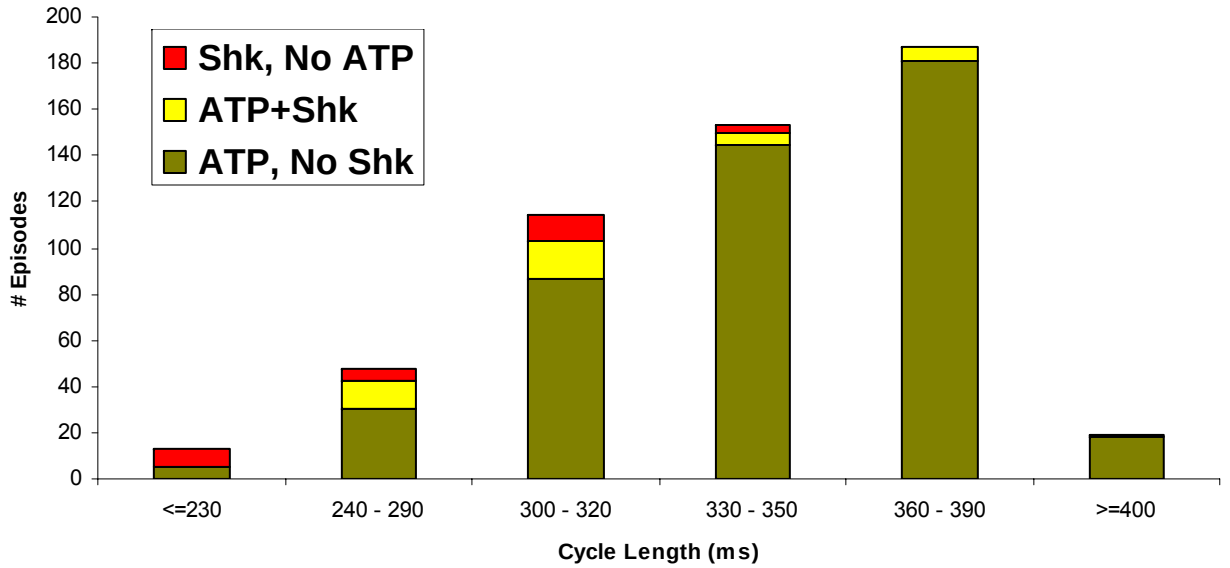


Shocked Episodes (True VT/VF)

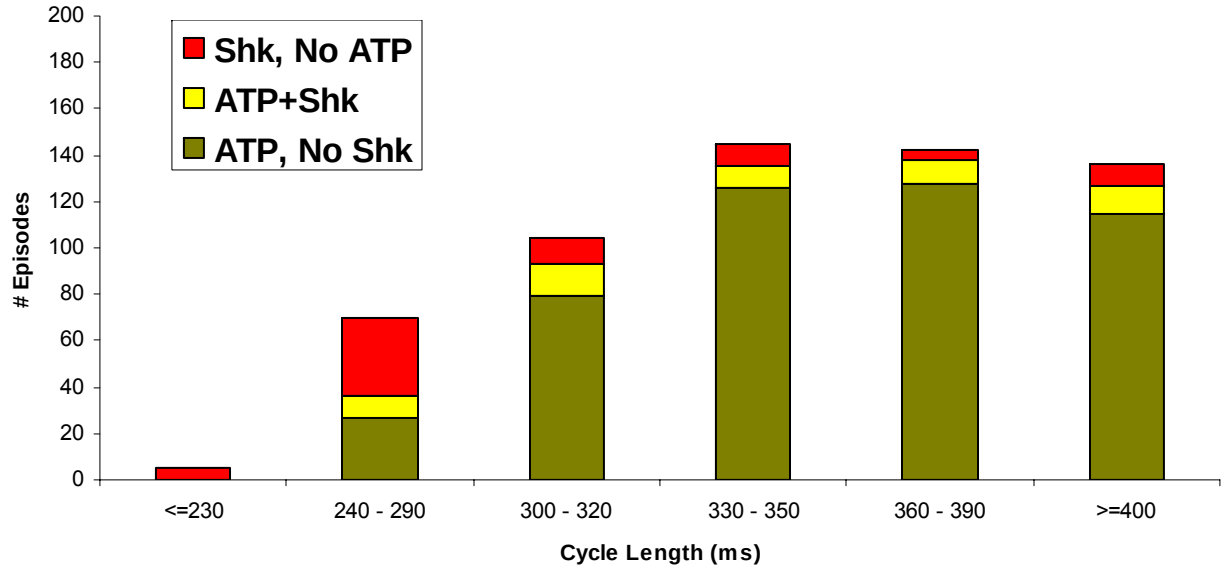


MVT Episodes vs. Cycle Length

Empiric



Tailored



Summary of ATP

	Empiric	Tailored
ATP Efficacy: <300 ms	74%	75%
≥ 300 ms	94%	91%
MVT Episodes Shocked **Without** ATP attempt	28	73
% of MVT Episodes Shocked	11.5%	19.7%
Accelerations of VT (ATP 1st Rx)	2.4% 9 pts	7.8% 14 pts

Is a faster treated cutoff ok? Risk of Slow VTs in Empiric Arm

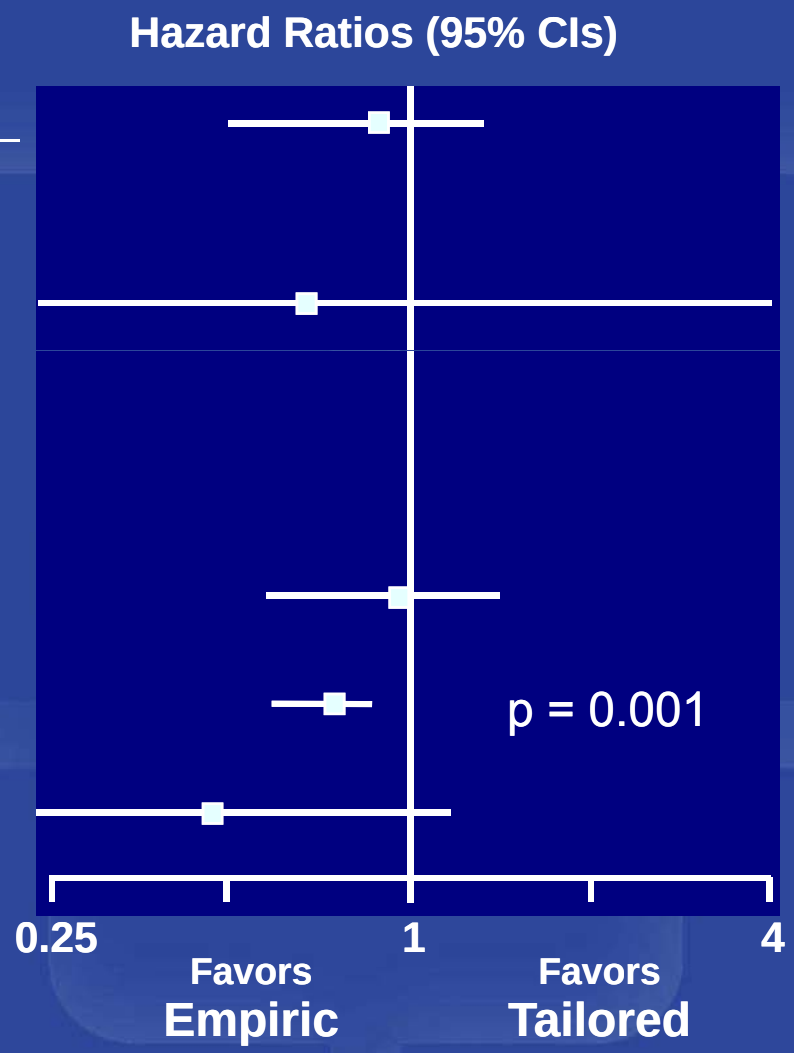
Main ICD Indication	% Patients w/ slow VT
Spontaneous Sustained MVT	12.6%
VF/Syncope	3.6%
Primary Prevention	5.6%

Slow VT: ≤167 bpm (≥ 360 ms)

Are these clinically significant if untreated ?

Safety Endpoints

	Empiric	Tailored
Mortality (all-cause)	24	30
Adverse Events		
Syncope	2	3
Untreated VTs	0	2
Unscheduled Visits:		
ER	44	46
Hospital	163	216
ATP Accelerated VTs	2.4%	7.8%



Conclusion: Strategies to ↓ Shocks

Empiric Arm

- ✓ Avoid detecting non-sustained tachycardias
- ✓ Avoid detecting SVTs as VT
- ✓ Empirical ATP for slow and fast VTs
- ✓ High Output 1st Shock

Other Opportunities

- ❑ 2nd attempt for fast VTs
- ❑ Faster Treated Cutoff in pts w/o hx of slow VT
- ❑ Meds: V. rate control during AF, frequent shocks

PREPARE - DESIGN

- Prospective, historic cohort controlled study
- Primary prevention ICD indications
- 700 pts
  - 38 Centers, US & Europe
  - October 2003 – May 2005
- 1 year follow-up
- Medtronic Marquis-based ICDs and leads
- Single, dual and Bi-V patients

Bi-V & Non Bi-V Controls

- MIRACLE ICD trial
  - 978 Bi-V patients
  - VT/VF programmed – physician-tailored
  - 415 primary prevention patients
- EMPIRIC trial - 900 patients
  - Primary and Secondary Prevention
  - VT/VF detection parameters randomized
  - Physician-tailored and primary prevention
  - 276 patients
- Total Control Cohort
  - 691 primary prevention, Bi-V and Non Bi-V

PREPARE Strategies to ↓ Shocks

- Avoid detecting slower tachycardia
- Avoid detecting non-sustained tachycardia
- Avoid detecting SVT as VT/VF
- ATP therapy for fast VT
- High output 1st shock

Wilkoff BL, Stern R, Williamson B, et al. Design of the Primary Prevention Parameters Evaluation (PREPARE) trial of implantable cardioverter defibrillators to reduce patient morbidity. Trials 2006; 7:18.

Prepare VT/VF Detection

Detection	Heart Rate	Beats to Detect	Therapies
VF ON	> 250 bpm	30 of 40	30-35 J
FVT Via VF	182-250 bpm	(30 of 40)	1 seq ATP, 30-35J
VT Monitor	167-181 bpm	32	None

PR Logic ON: AF/Afl, Sinus Tach (**1:1 VT-ST = 66%**) or **Wavelet ON**; SVT Limit = 200 bpm

Prepare Primary Endpoint

- Morbidity Index
  - Spontaneous episodes treated with shocks
  - Arrhythmic syncope
  - Untreated sustained symptomatic VT/VF episodes

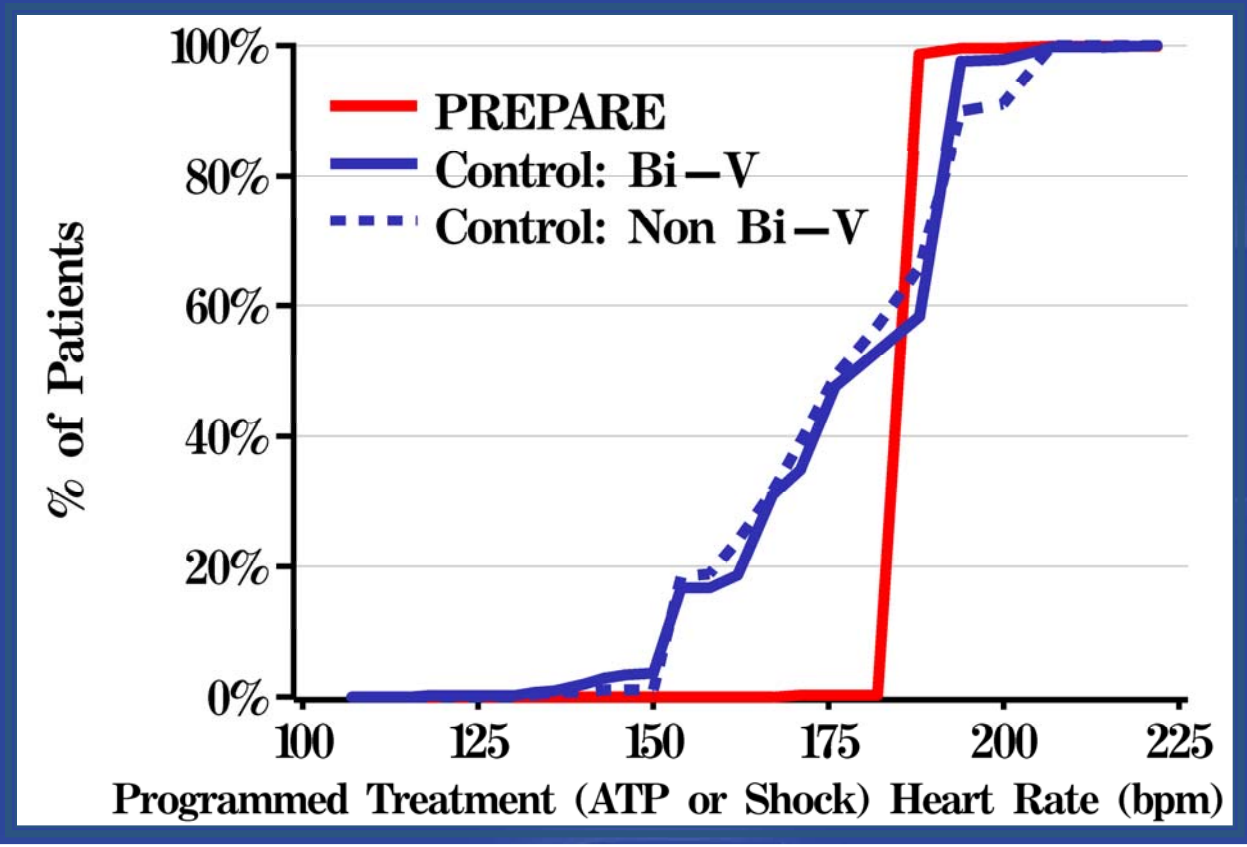
Baseline Characteristics

	PREPARE (n=700)	Control (n=691)	P-value
Age, Mean ± SD	67.4 ± 12.2	65.5 ± 11.7	0.003
Male	79%	77%	0.3
EF Mean ± SD	27.6 ± 10.4	24.7 ± 9.8	<0.001
Ischemic CM	70%	57%	<0.001
Hypertension	57%	48%	<0.001
NYHA			0.06
Class 0/I/II	59%	54%	
Class III-IV	41%	46%	
Hx of AF/Afl/AT	33%	20%	<0.001

Implant and Device Type

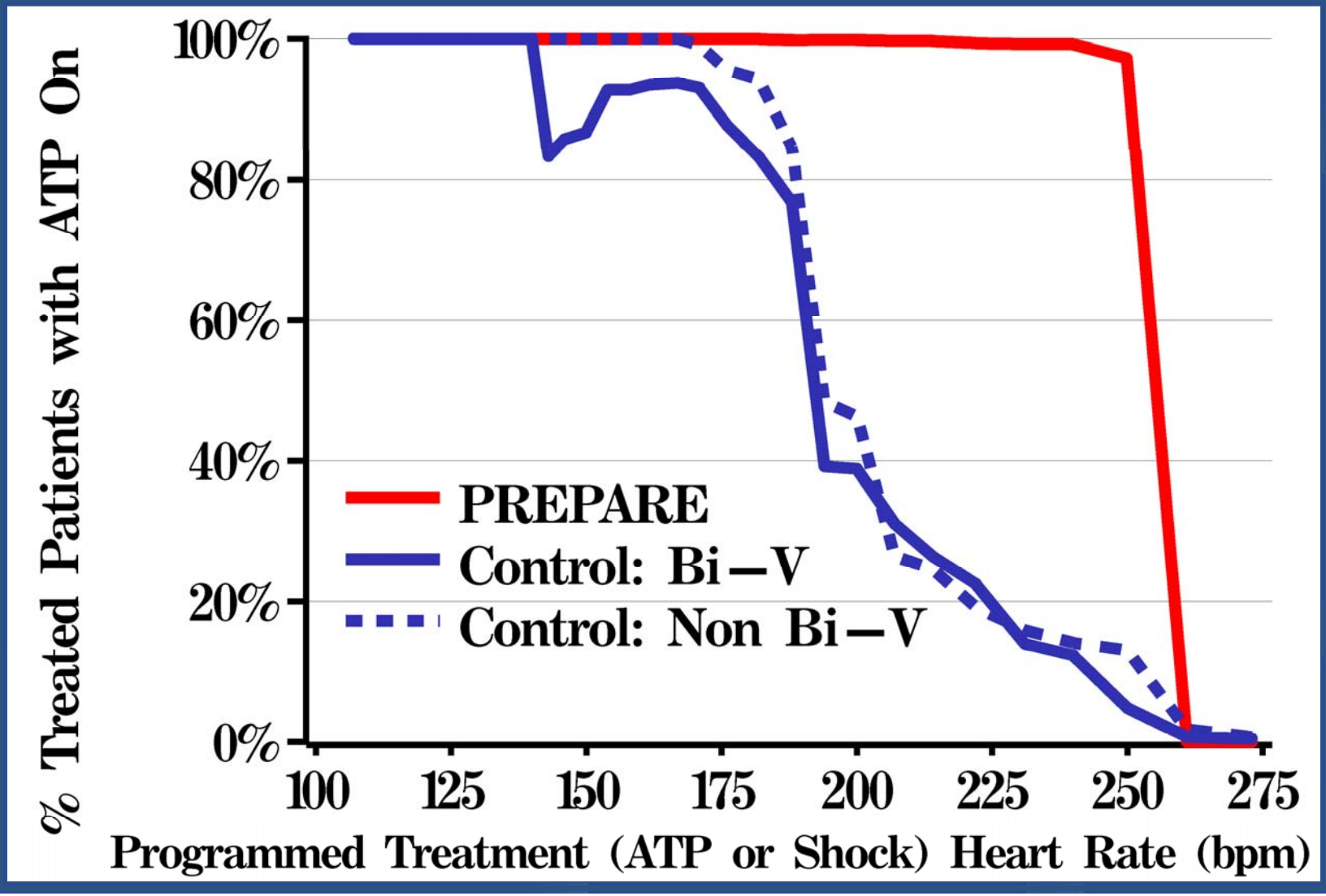
	PREPARE (n=700)	Control (n=691)
Device Type		
Non Bi-Ventricular	452 (65%)	276 (40%)
Single chamber	110 (16%)	0
Dual Chamber	342 (49%)	276 (40%)
Bi-Ventricular	247 (35%)	415 (60%)
Unsuccessful implant	1 (<1%)	N/A

Therapy Rate Threshold

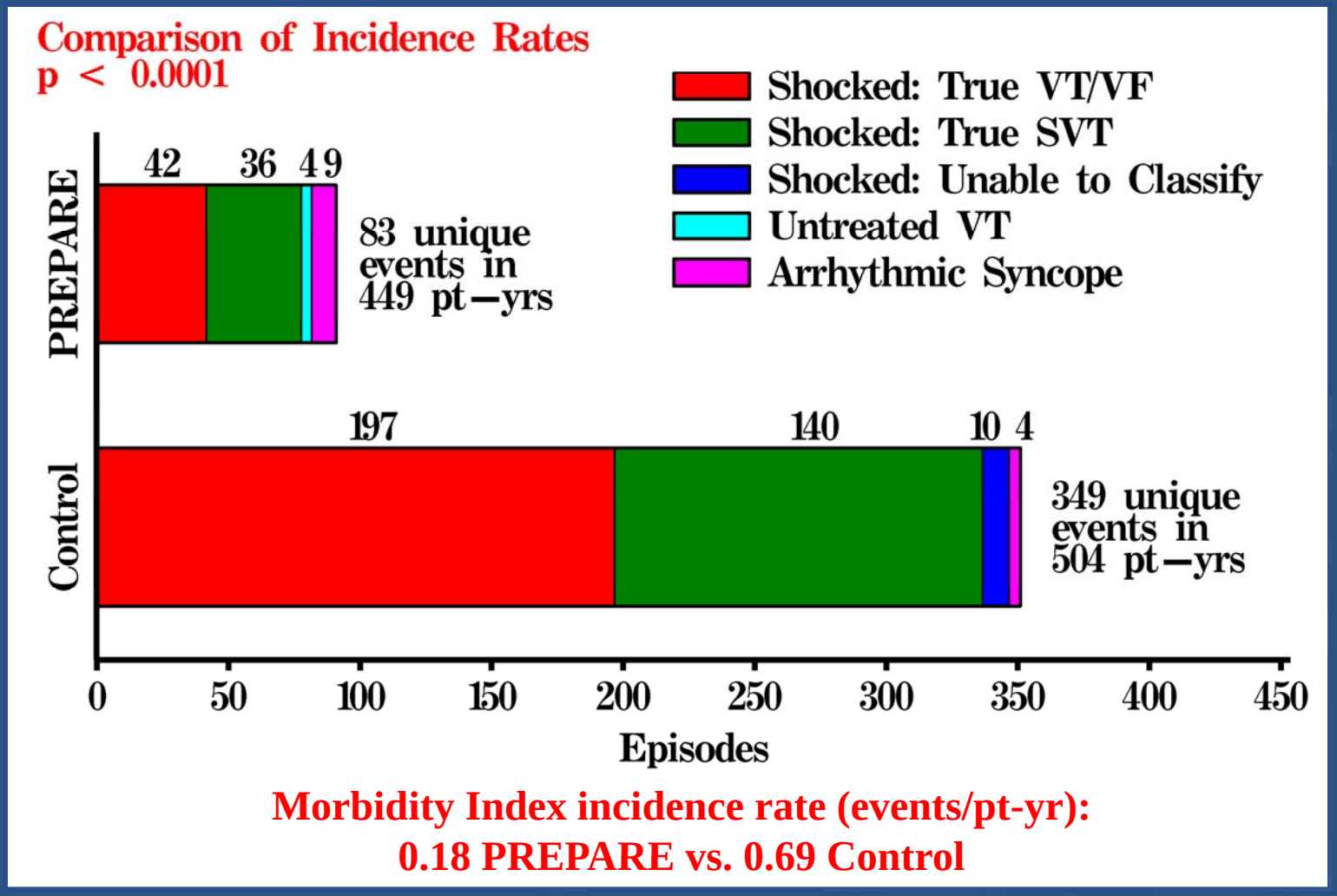


	PREPARE	Control	P-value
Rate Threshold, Median (25%, 75%)	182 bpm (182, 182)	176 bpm (162, 188)	< 0.001

ATP Programming

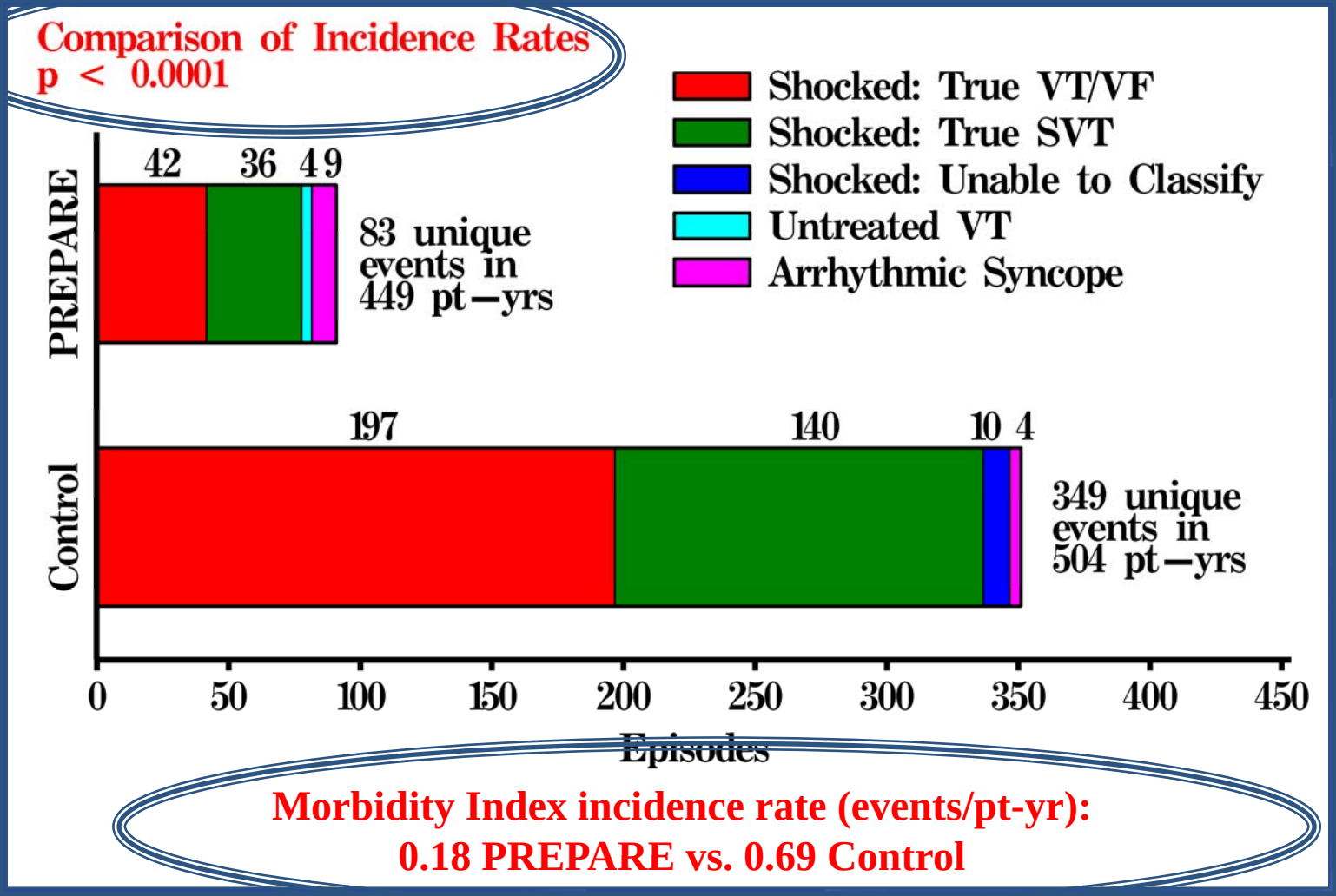


Morbidity Index



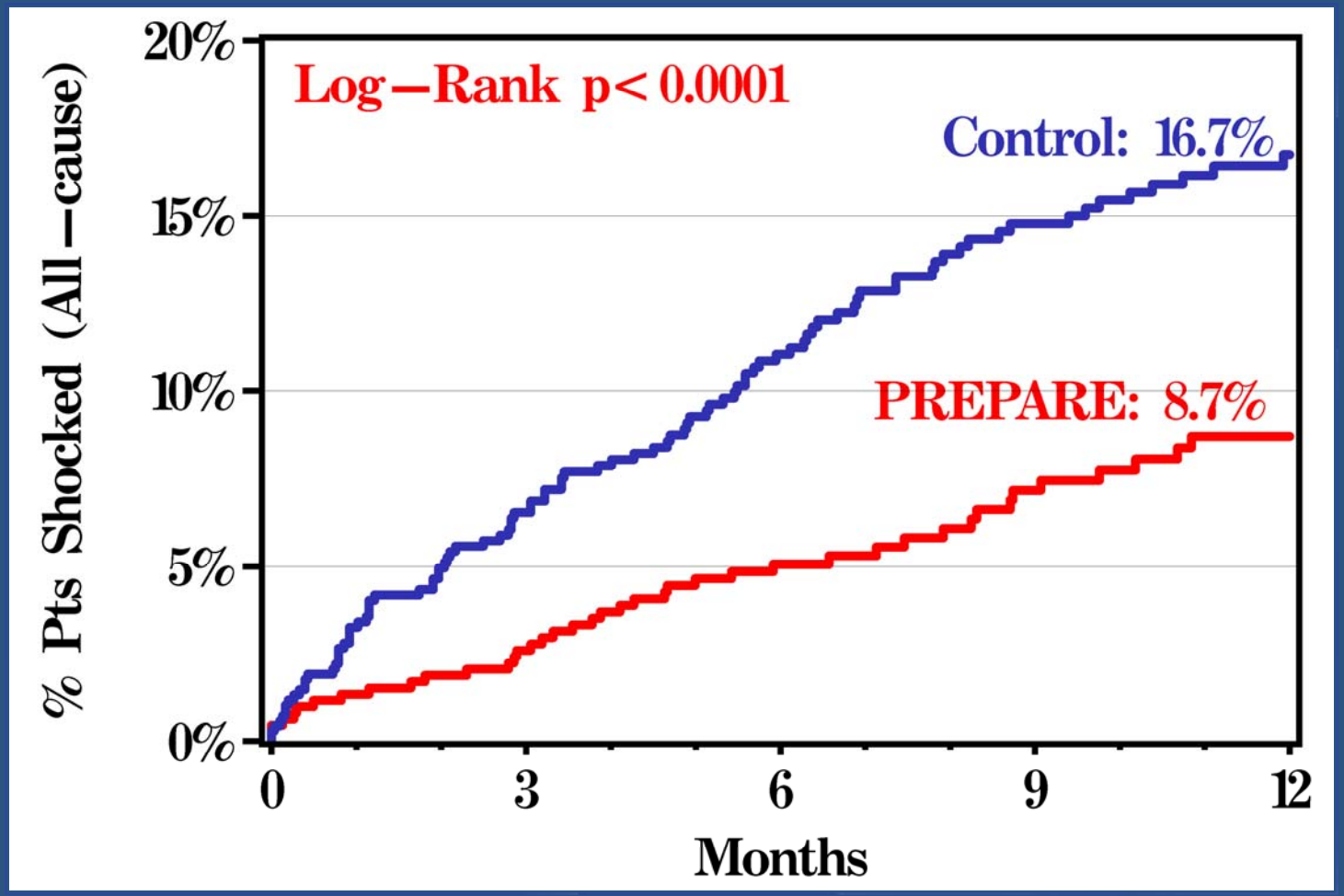
Morbidity Index incidence rate (events/pt-yr):
0.18 PREPARE vs. 0.69 Control

Morbidity Index

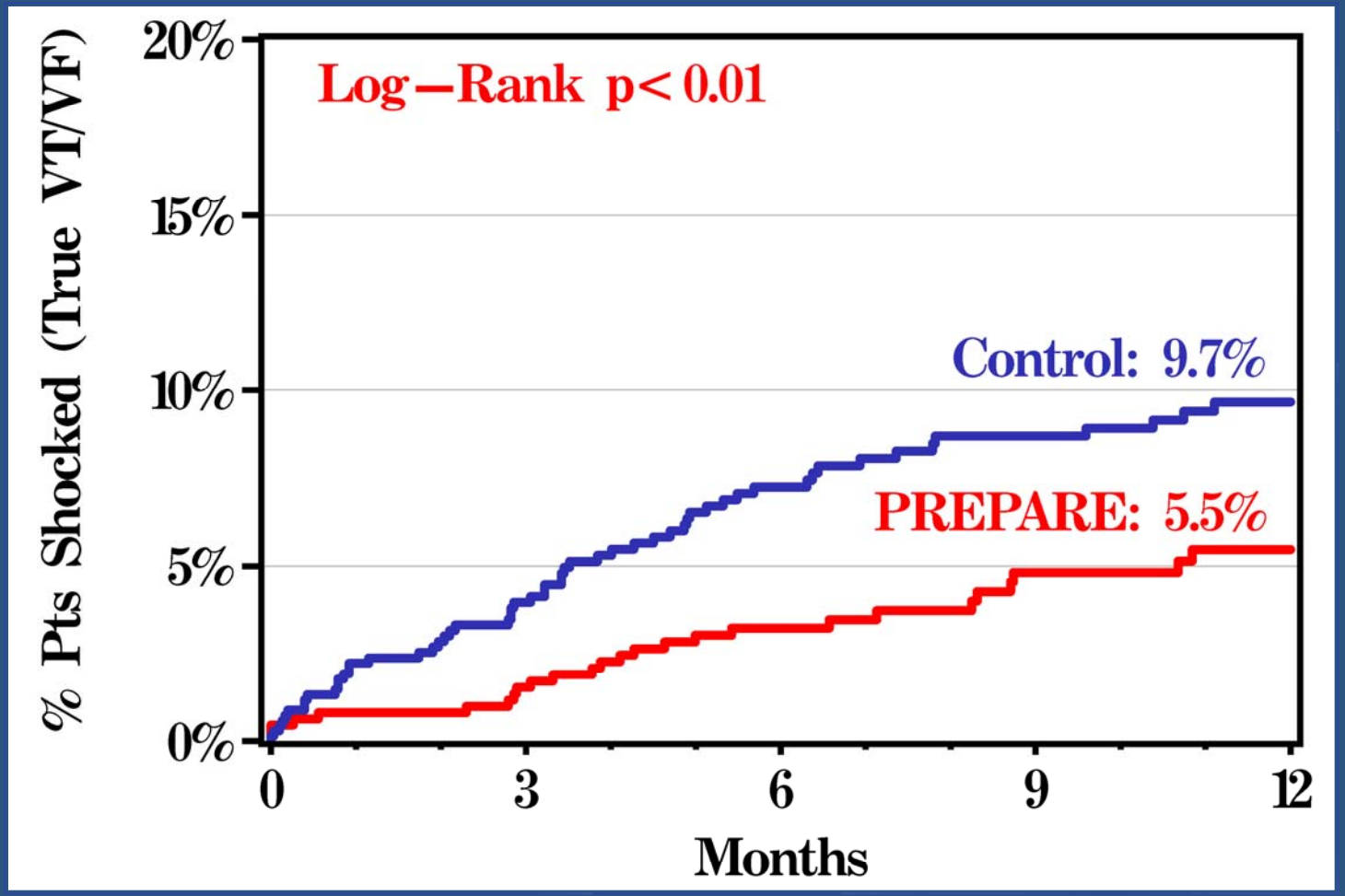


Morbidity Index incidence rate (events/pt-yr):
0.18 PREPARE vs. 0.69 Control

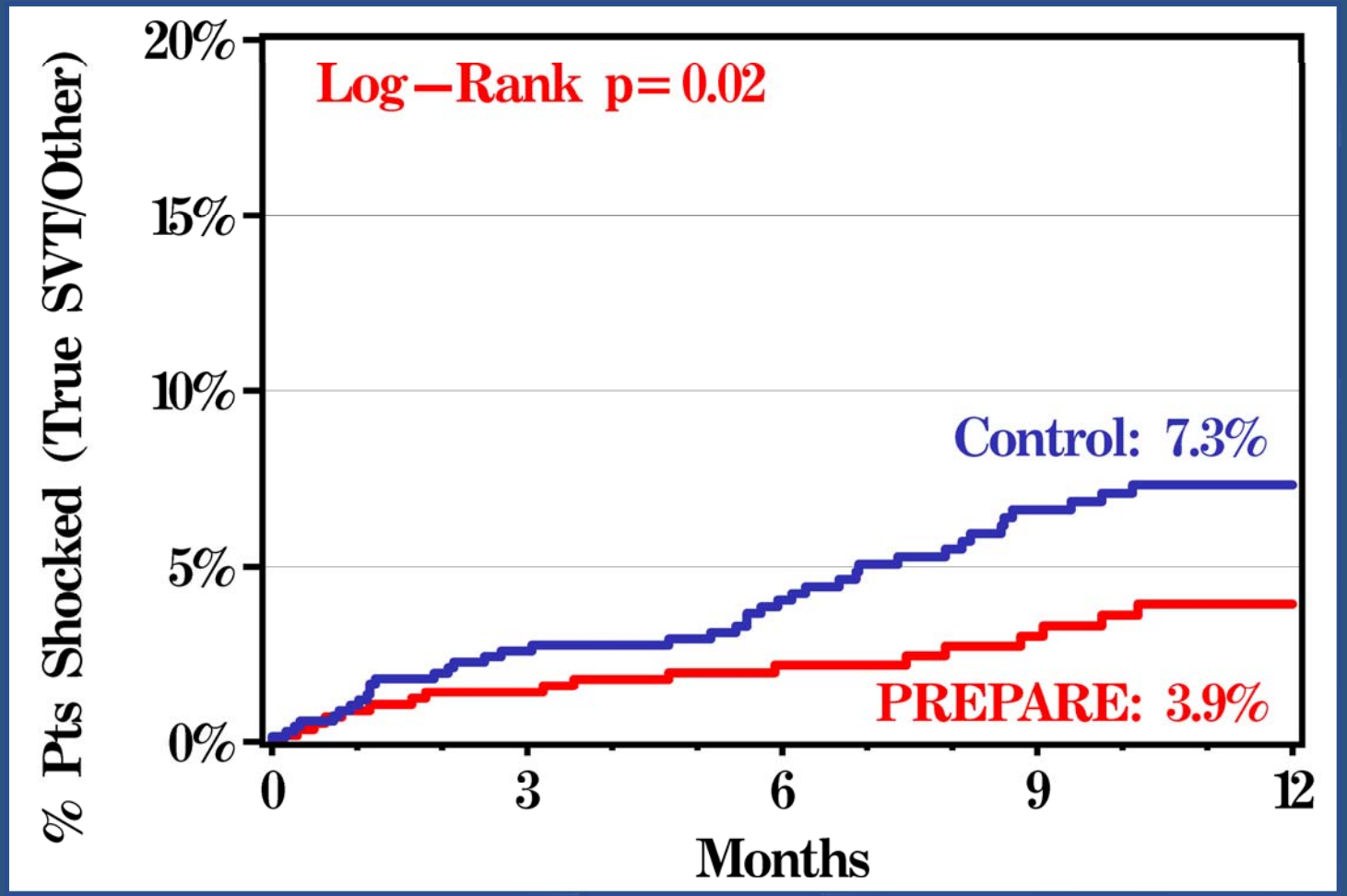
Time to First Shock: All-Cause



Time to First Shock – Appropriate



Time to First Shock – Inappropriate

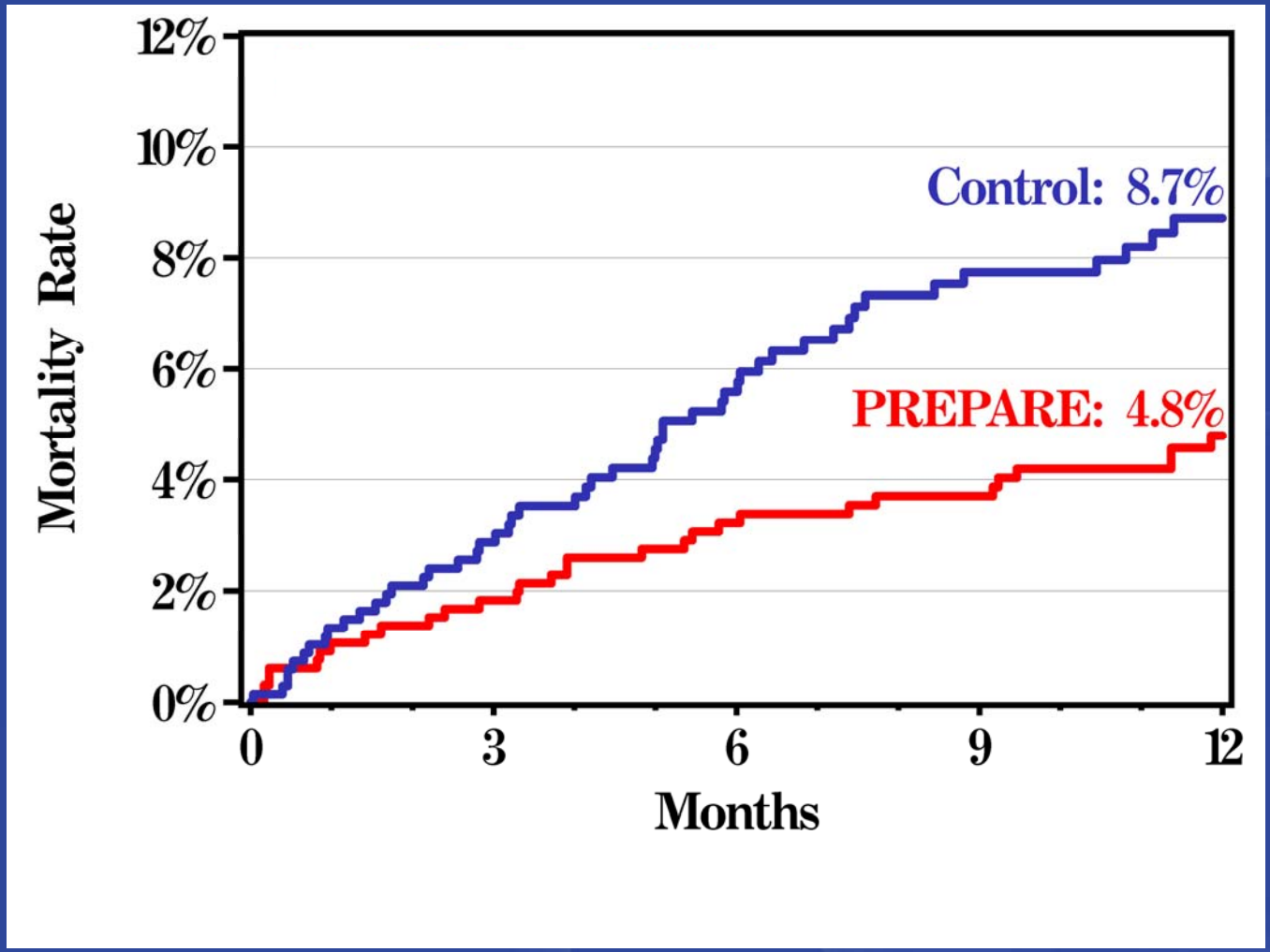


Syncope

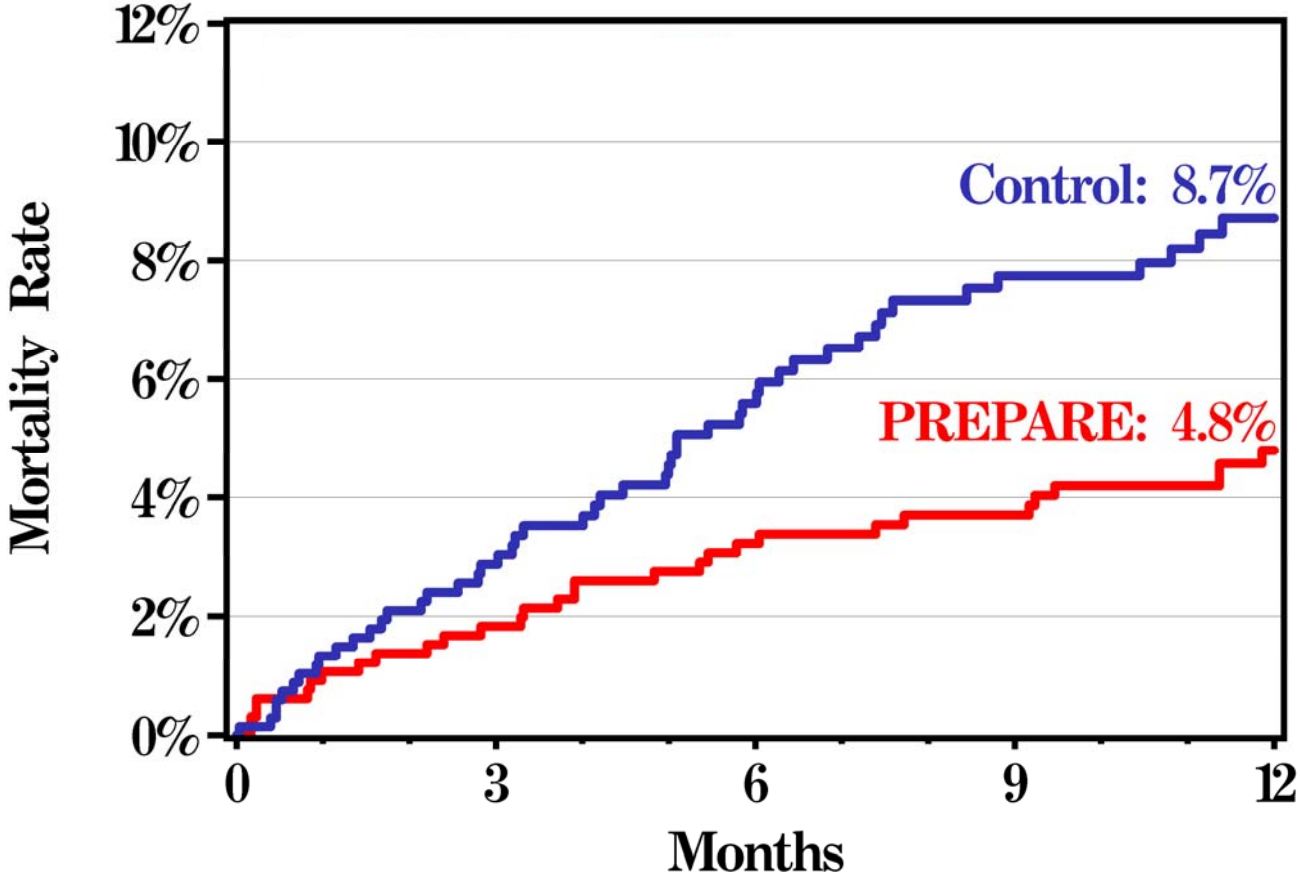
Adverse Event	Pts (%) Events (n=700)
Syncope and near-syncope	109 (17%) 241
Arrhythmia-related	19 (3%) 23
True syncope	23 (3.5%) 28
Arrhythmia-related	8 (1%) 9
Related to PREPARE programming	8 (1%) 8

- 8 events identified as possibly or probably related to PREPARE programming
  - None associated with injuries or death
  - 6 patients completed study
  - 2 patients withdrew for other reasons

Mortality


12%
10%
8%
6%
4%
2%
0%
Mortality Rate
Control: 8.7%
PREPARE: 4.8%
0
3
6
9
12
Months

Mortality



PREPARE	658	639 (2%)	613 (3%)	597 (4%)	369 (5%)
Control	689	605 (3%)	521 (6%)	445 (9%)	279 (9%)

Limitations

- Non-randomized trial
- Historical control cohort
- Differences in baseline characteristics between study group and control

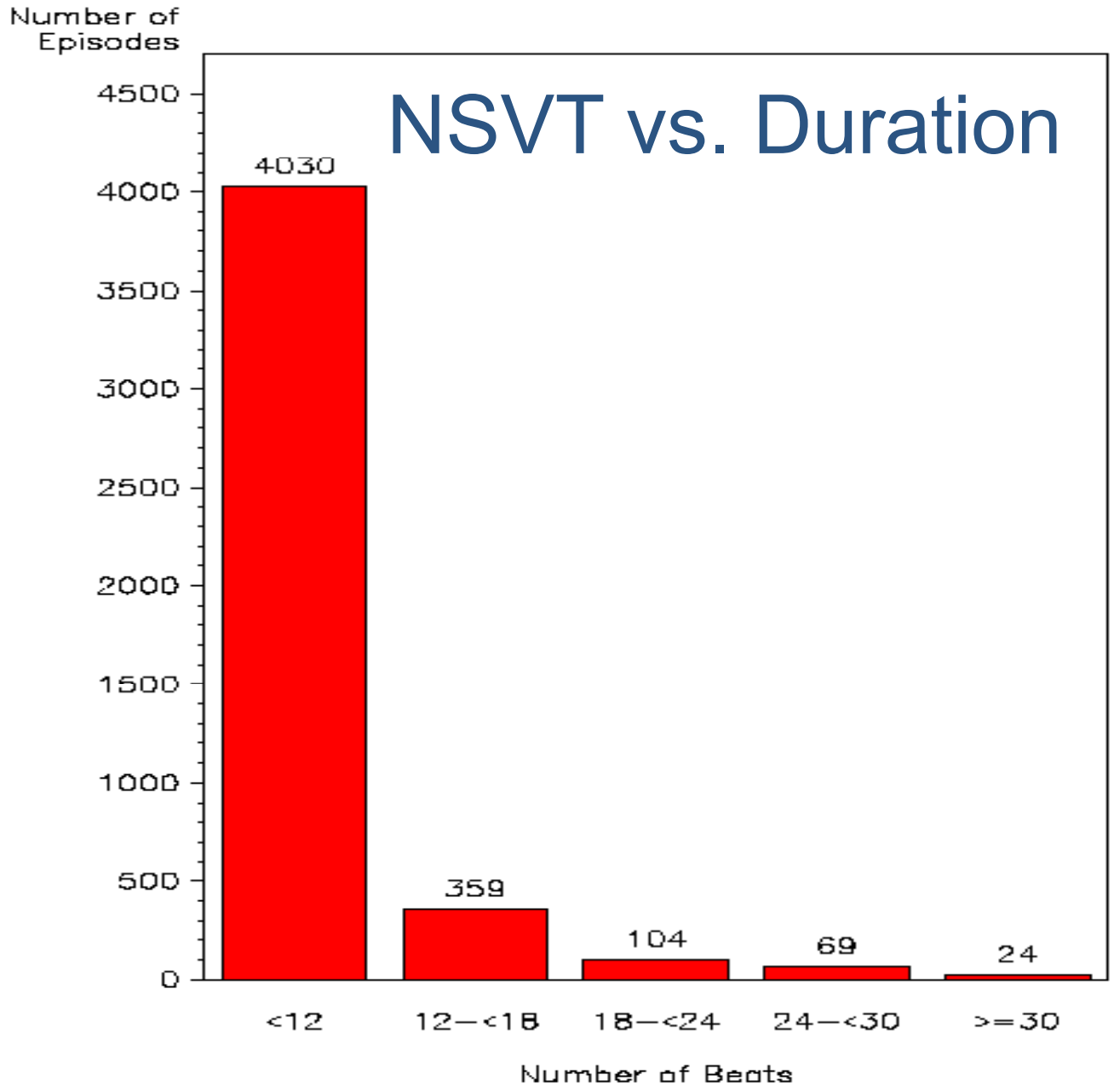
Conclusion

- Strategically chosen VT/VF detection and therapy options targeting primary prevention patients can safely reduce the morbidity related to ICD therapy
  - 74% reduction Morbidity index
  - 68% reduction Morbidity Tachycardia index

Implications

- Since the large majority of our ICD patients are primary prevention patients
- Most ICD patients receive too many shocks
- Strategic programming to treat:
  - Sustained and Fast tachycardias with ATP before shocks
  - Should safely reduce ICD morbidity

NSVT vs. Duration



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