Preliminary Results of the Post-Market Phase of the BeAT-HF Randomized Clinical Trial

March 21, 2023

CVRx
Outsmart the heart

Forward-looking statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements other than statements of historical facts are forward-looking statements, including statements regarding our future financial performance, our anticipated growth strategies, anticipated trends in our industry, our business prospects and our opportunities, including specifically those related to potential new indications, labelling or marketing opportunities, our continued review and analysis of trial data and future business and financial impacts. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "outlook," "guidance," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential" or "continue" or the negative of these terms or other similar expressions, although not all forward-looking statements contain these words.

The forward-looking statements in this press release are only predictions and are based largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition, and results of operations. These forward-looking statements speak only as of the date of this presentation and are subject to a number of known and unknown risks, uncertainties and assumptions, including, uncertainties related to obtaining regulatory approvals, further analysis and understanding of clinical trial data, physician and patient adoption, and other important factors that could cause actual results, performance or achievements to differ materially from those projected in the forward-looking statements that are found in "Part I, Item 1A. Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2022, as such factors may be updated from time to time in our other filings with the Securities and Exchange Commission. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

Baroreflex Activation Therapy (BAT) in Patients with Heart Failure and a Reduced Ejection Fraction (BeAT-HF) Trial: Long – Term Outcomes

BeAT-HF Executive Steering Committee:

Michael R. Zile

JoAnn Lindenfeld

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Study Sponsor: CVRx

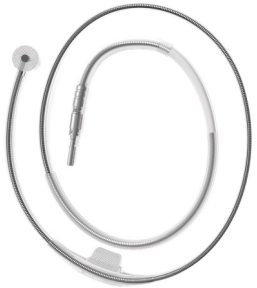
Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
Grant/Research Support	NHLBI, VA, DOD
Consulting Fees/Honoraria	Abbott, Boston Scientific, **CVRx**, Corvia, Edwards, EBR, Lilly, Medtronic, Merck, Novartis, Vectorious, V Wave
Major Stock Shareholder/Equity	None
Royalty Income	None
Ownership/Founder	None
Intellectual Property Rights	None
Other Financial Benefit	None

Faculty disclosure information can be found on the app

Baroreflex Activation Therapy (BAT) Device (Barostim)

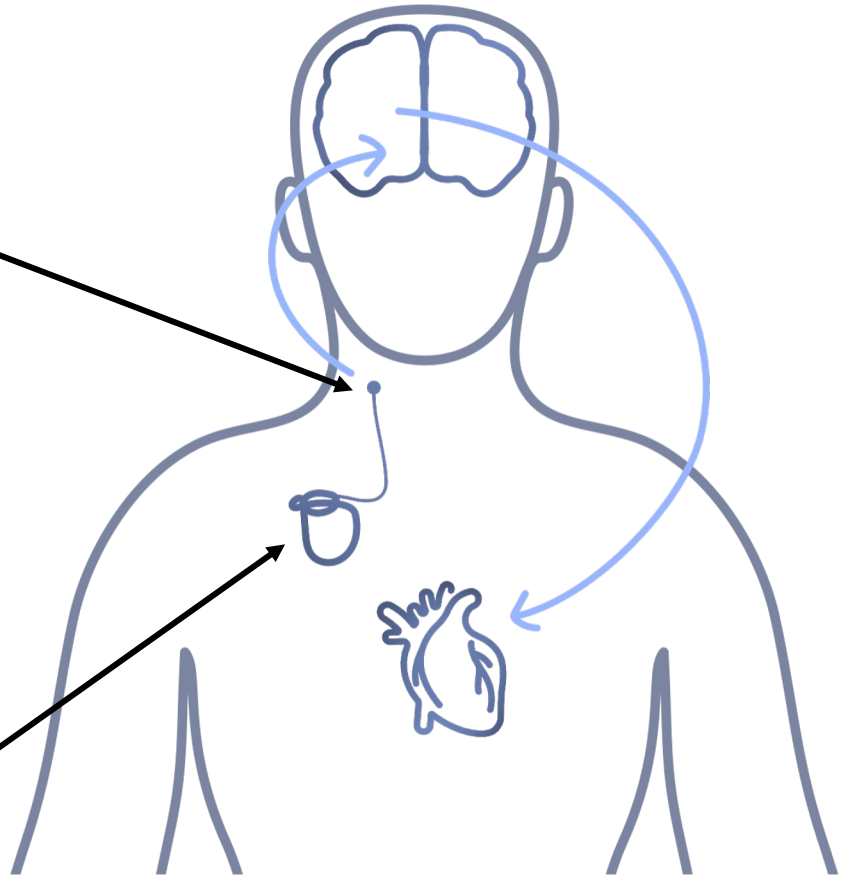


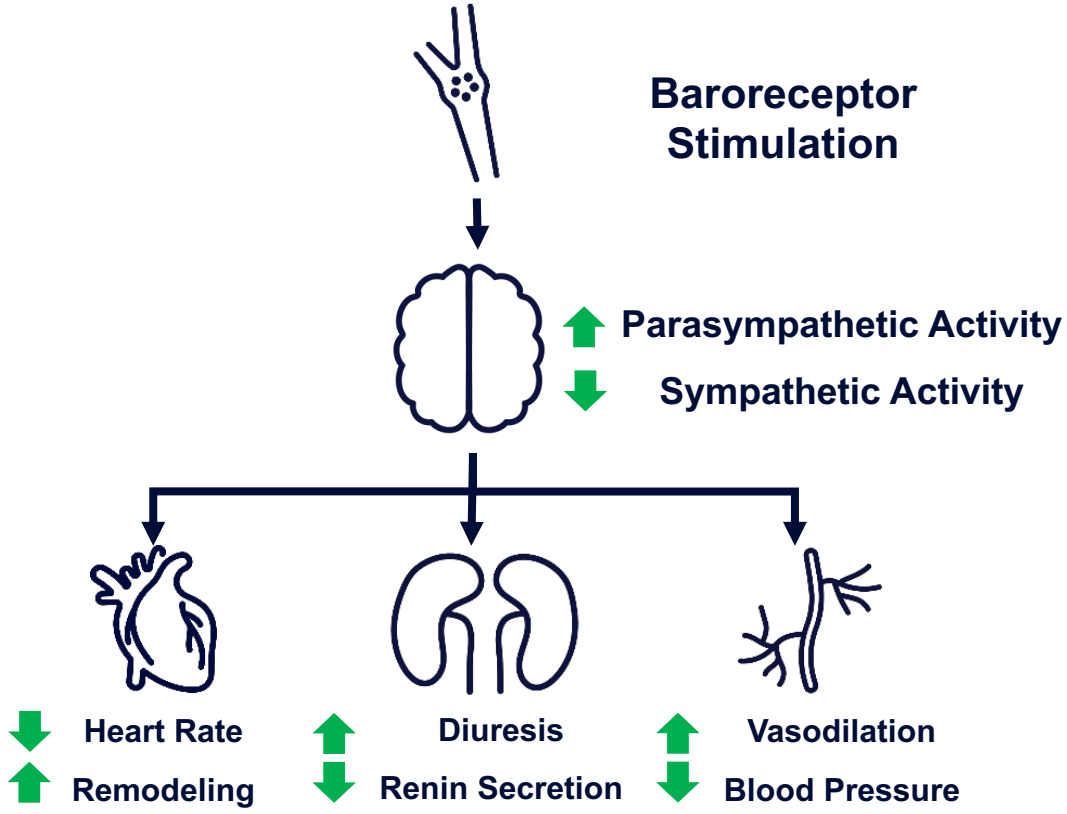
Carotid Sinus Lead

- Extravascular
- 2 mm electrode
- Unipolar design

IPG

- 5 year longevity
- Personalized therapy
- Average programming at 6 Mo:
  - 8.4 mA amplitude
  - 107 ms duration
  - 43 pps frequency





BeAT-HF Trial Design

Prospective, multicenter, randomized, 2-arm, parallel-group, open-label with blinded evaluation trial

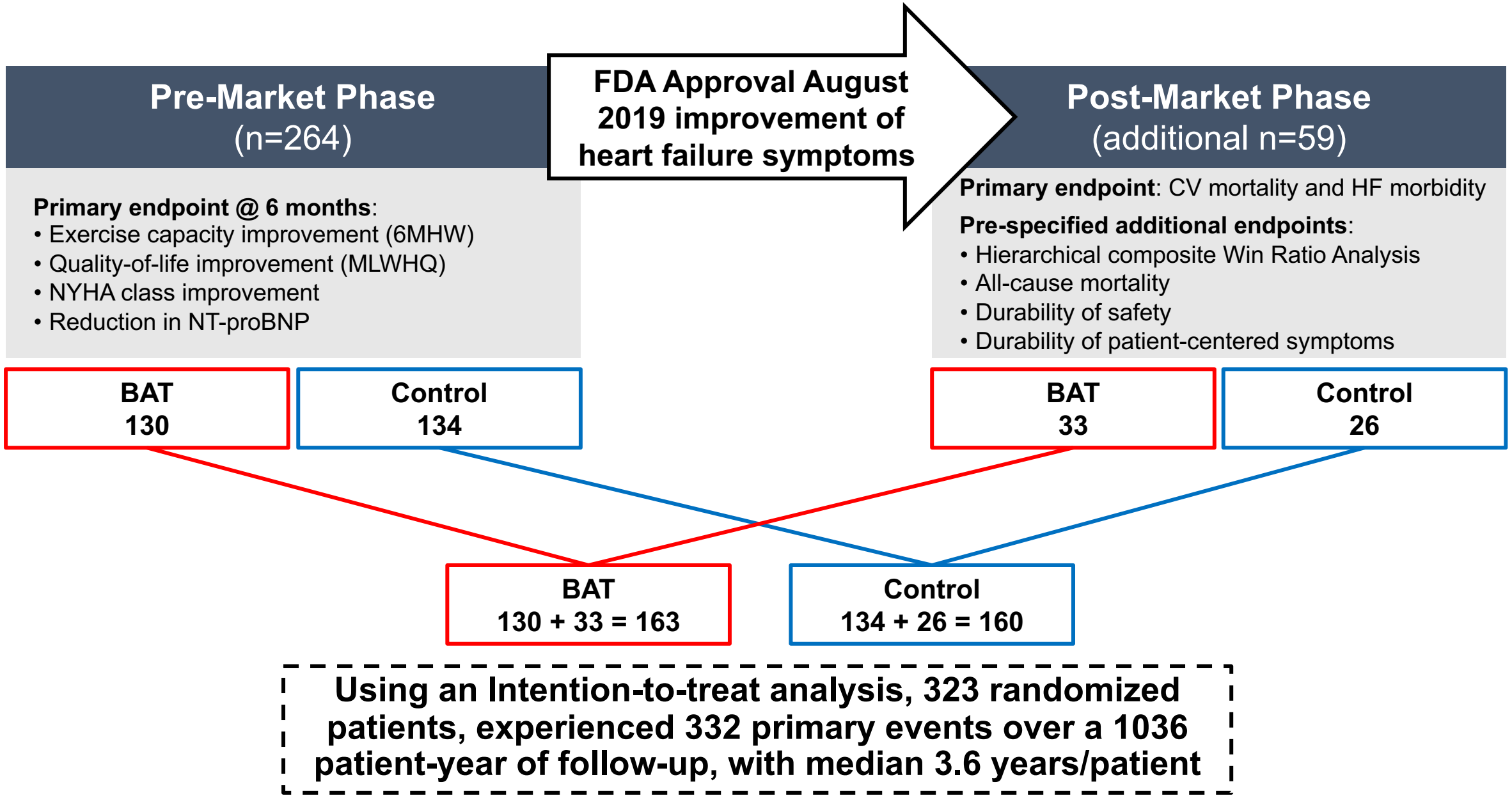
Groups: - BAT plus optimal medical management (**BAT group**)
- Optimal medical management alone (**Control group**)

Sites: 103 US centers and 5 United Kingdom centers

Eligibility criteria:
- NYHA Class III or Class II (with a recent history of Class III)
- Left ventricular EF ≤ 35%
- 6MHW 150 – 400 m
- HF Hospitalization or NT-proBNP > 400
- Stable optimal medical management ≥ 4 weeks
- No Class of Recommendation I indication for CRT
- NT-proBNP < 1600 pg/ml

Designated by FDA as Breakthrough Device in HFrEF

BeAT-HF Trial Design



BeAT-HF Baseline Characteristics

Baseline Characteristics	BAT (n=163)	Control (n=160)
Age at Screening (years)	63 ± 11	63 ± 10
Female	28 (17.2%)	35 (21.9%)
Race		
White	120 (73.6%)	116 (72.5%)
Black or African American	29 (17.8%)	24 (15.0%)
Asian	3 (1.8%)	2 (1.3%)
Other/Unknown	11 (6.7%)	18 (11.3%)
SBP (mmHg)	120 ± 16	121 ± 16
DBP (mmHg)	74 ± 10	73 ± 10
HR (bpm)	75 ± 10	75 ± 11
BMI (kg/m2)	31 ± 5	31 ± 5
eGFR	62.5 ± 16.3	61.1 ± 18.9
NYHA: Class III	155 (95.1%)	151 (94.4%)
LVEF (%)	27 ± 6	28 ± 6
6 Minute Walk (m)	314 ± 66	300 ± 71
QOL	53 ± 24	51 ± 24
NT-proBNP (pg/mL)	736 (474, 1057)	704 (442, 1044)
LBBB	4 (2.5%)	2 (1.3%)
At Least One HF Hospitalization	66 (40.5%)	79 (49.4%)
Number of HF Hospitalizations	0.6 ± 0.9	0.7 ± 0.8

No significant difference between BAT and Control

BeAT-HF Baseline Characteristics

Baseline Characteristics	BAT (n=163)	Control (n=160)
Coronary Heart Disease		
Coronary Artery Disease	104 (63.8%)	107 (66.9%)
Myocardial Infarction	89 (54.6%)	97 (60.6%)
CABG	35 (21.5%)	44 (27.5%)
PCI	72 (44.2%)	72 (45.0%)
Cardiac Arrhythmia		
Bradycardia	19 (11.7%)	18 (11.3%)
Tachycardia	54 (33.1%)	56 (35.0%)
Atrial Fibrillation	53 (32.5%)	66 (41.3%)
Stroke or TIA	29 (17.8%)	37 (23.1%)
Chronic Kidney Disease	45 (27.6%)	43 (26.9%)
Diabetes		
Type I	0 (0.0%)	2 (1.3%)
Type II	74 (45.4%)	80 (50.0%)

No significant difference between BAT and Control

BeAT-HF Baseline HF Treatment

Baseline Medications	BAT (n=163)	Control (n=160)
Number of Meds	4.0 ± 1.3	4.1 ± 1.5
ACE-I / ARB / ARNI	143 (88%)	129 (81%)
ARNI	57 (35%)	43 (27%)
Beta-Blocker	152 (93%)	147 (92%)
MRA	74 (45%)	64 (40%)
SGLT2i	1 (0.6%)	0 (0%)
Diuretic	138 (85%)	139 (87%)
Ivabradine	4 (2.5%)	9 (5.6%)
ICD	125 (77%)	127 (79%)
Pacemaker (non-ICD)	3 (1.8%)	2 (1.3%)
CRT	4 (2.5%)	5 (3.1%)
Other cardiac device (e.g., CardioMEMS)	8 (4.9%)	4 (2.5%)

No significant difference between BAT and Control

Study Endpoints

Primary Endpoint

Cardiovascular (CV) Mortality And Heart Failure (HF) Morbidity

- Assessed using a negative binomial model
- Includes recurrent HF morbidity events
- Pre-specified event–driven (n=320 events minimum)

CV Mortality:

- Cardiovascular deaths
- LVAD and heart transplants

HF Morbidity:

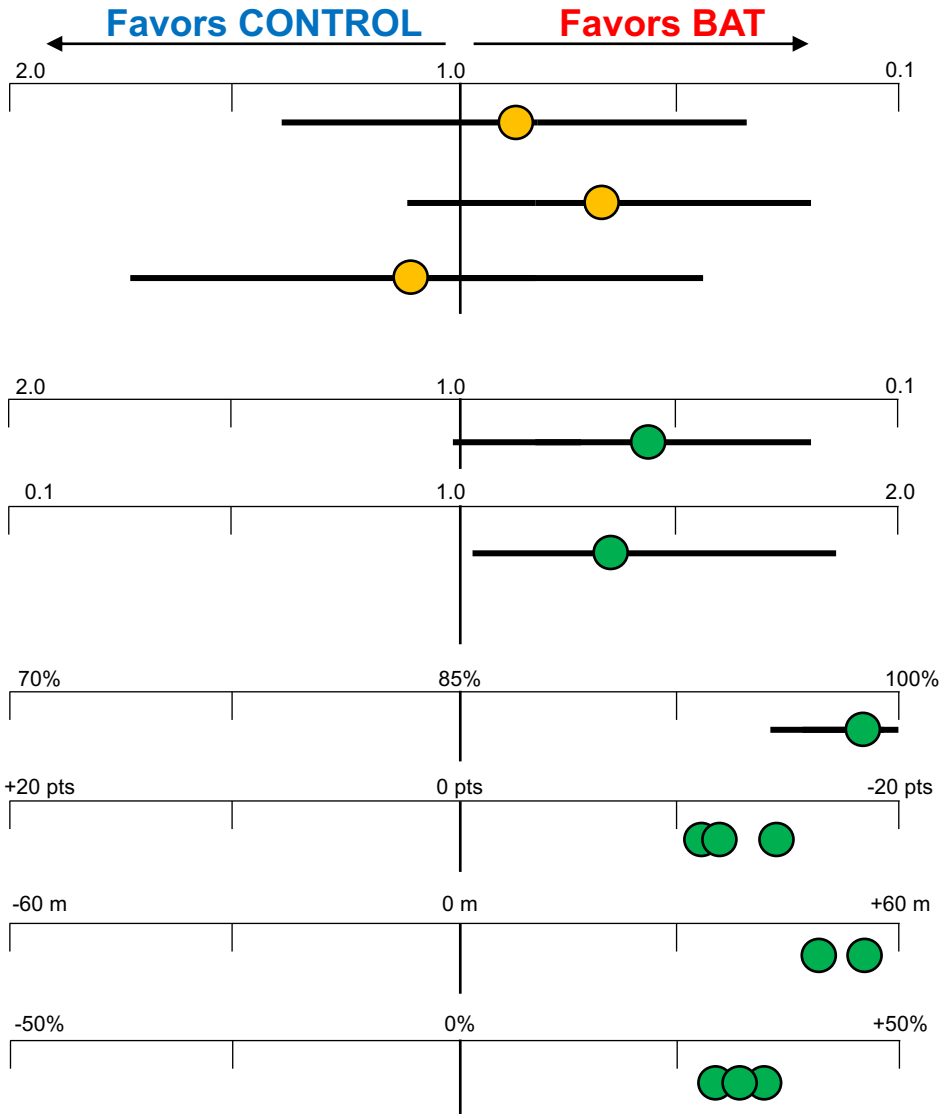
- Non-elective HF hospitalization
- HF emergency room visit

Pre-specified additional endpoints

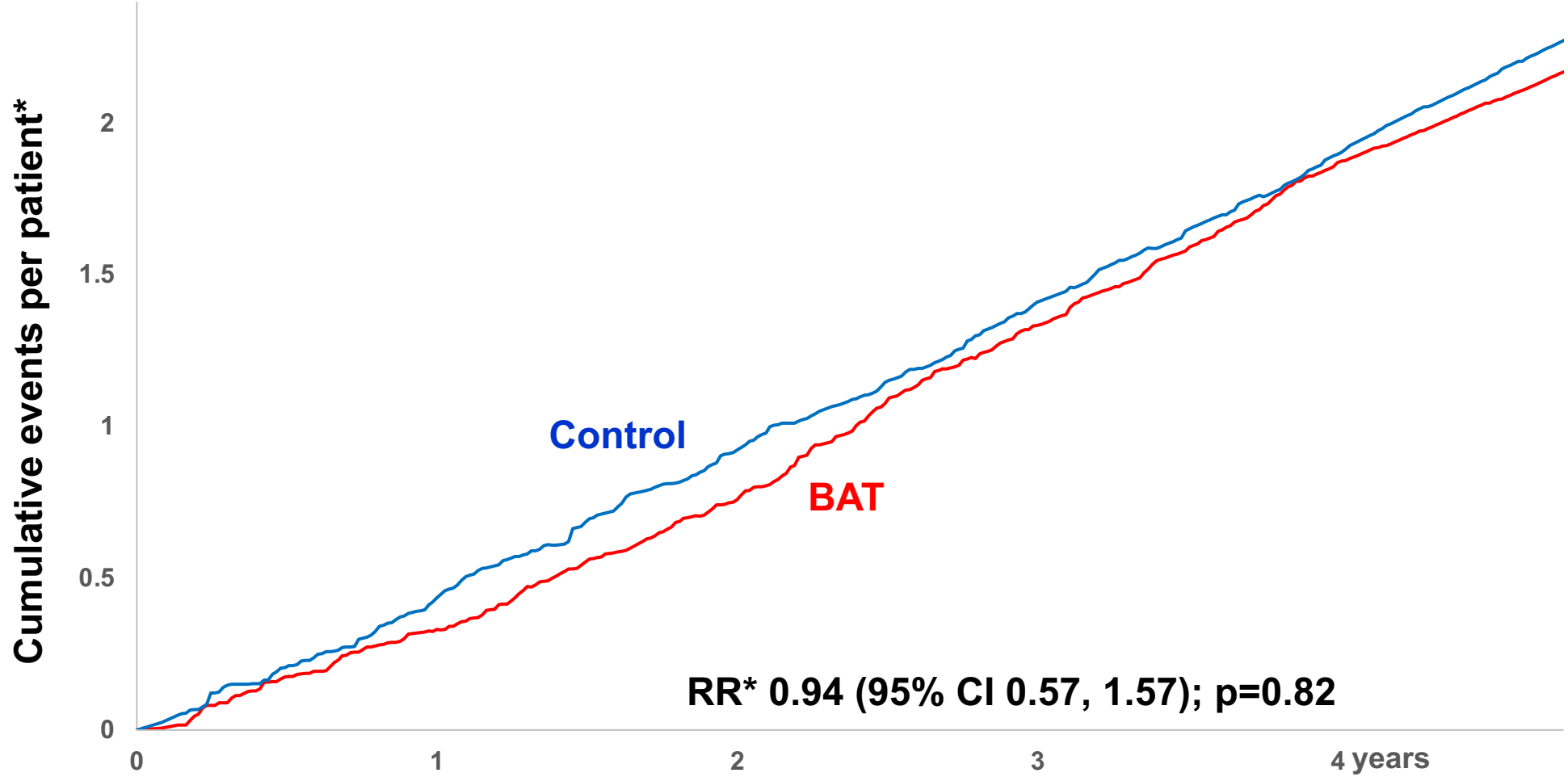
- Hierarchical composite analysis using Win Ratio
- All-cause mortality
- Durability of safety
- Durability of improved patient-centered symptom status
  - Quality of Life (MLWHFQ)
  - Exercise Capacity (6MHWD)
  - Functional Status (NYHA Class)

BeAT-HF Summary of Key Evidence

	Description	
Primary endpoint	**Composite CV Mortality and HF Morbidity**	Rate Ratio = 0.94
	CV Mortality (CV death, LVAD, heart transplant)	Hazard Ratio = 0.73
	HF Morbidity (Heart failure hospitalization, ER/ED visit)	Rate Ratio = 1.08
Additional Analyses	**All-cause Mortality** (death, LVAD, heart transplant)	Hazard Ratio = 0.66
	Hierarchical Win Ratio (CV mortality, HF morbidity, QOL)	Win Ratio = 1.26
Long-term Safety	**Related MANCE-free Rate*** *Major Adverse Neurologic and Cardiac Events	96.9%
Long-term Symptom Improvement	**Quality of Life – MLWHF** (6 / 12 / 24 Month)	-13 / -8 / -10
	Exercise Capacity – 6MHW (6 / 12 Month)	+55 / +44
	Functional Status – NYHA Class % Improved (6 / 12 / 24 Month)	30% / 32% / 27%



Primary Composite Endpoint: CV Mortality and HF Morbidity

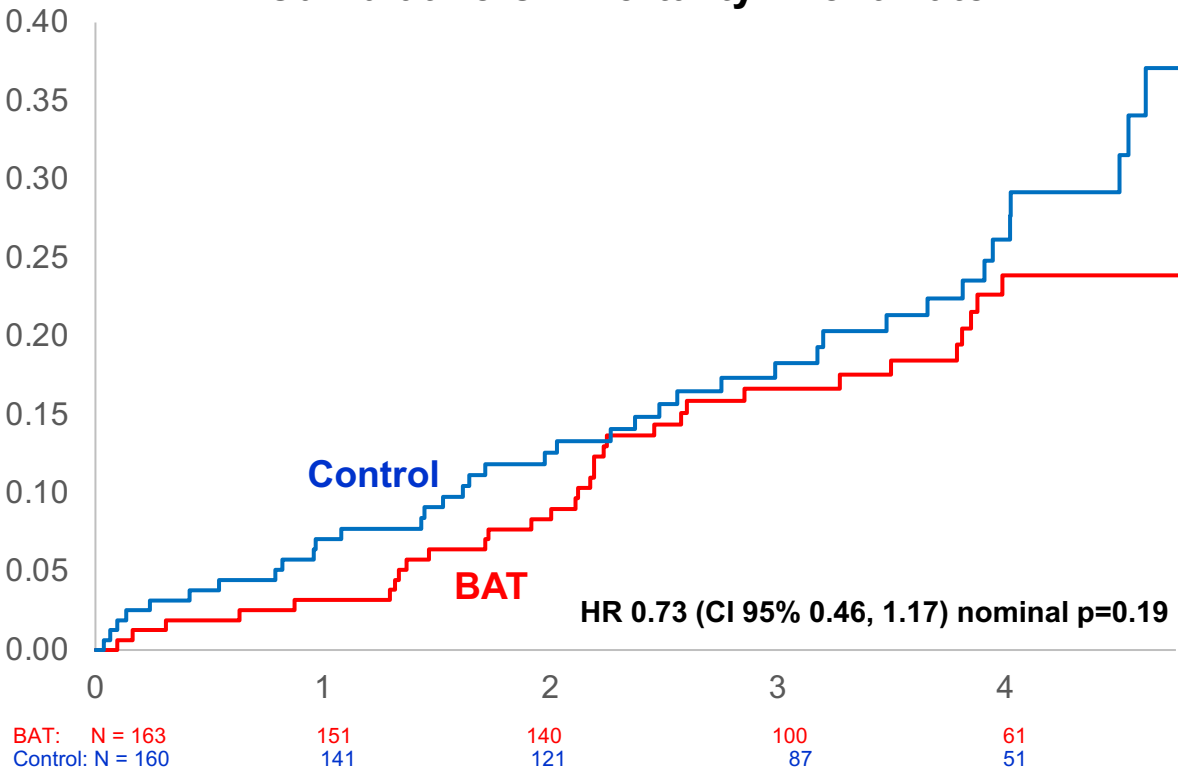


No statistically significant difference between BAT and Control

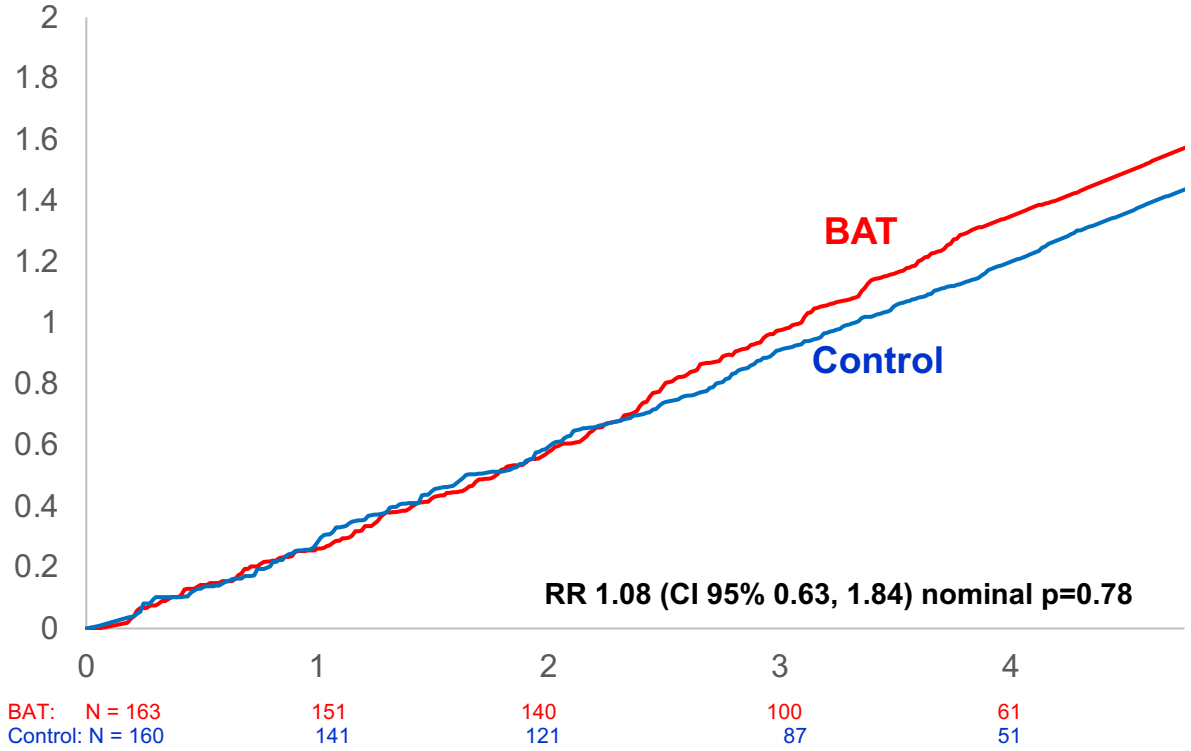
* Cumulative events per patient and rate ratio (RR) of treatment / control and 95% confidence interval estimated by negative binomial method

Components of Primary Endpoint

Cumulative CV Mortality Event Rate



Cumulative HF Morbidity Event Rate



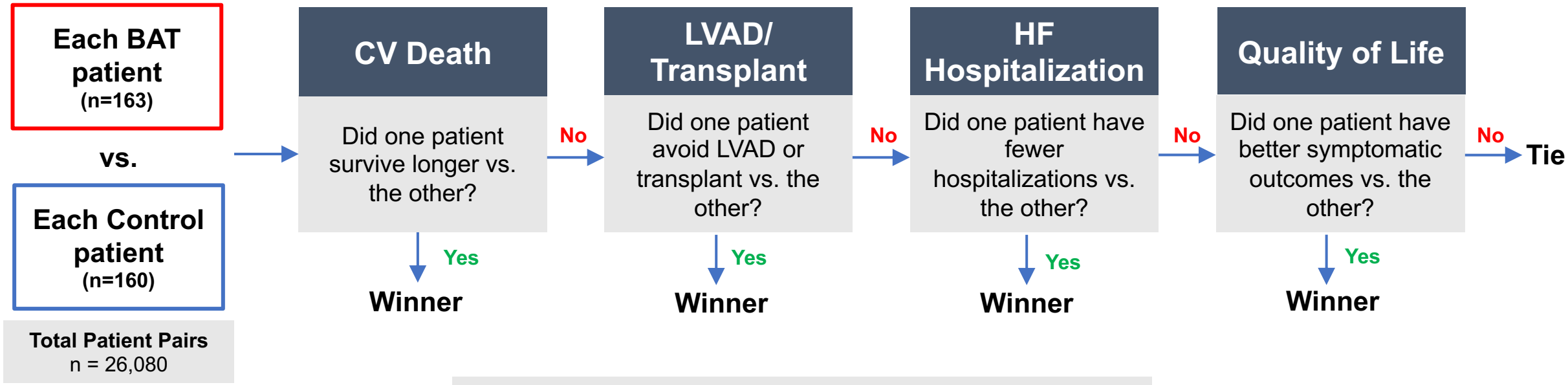
Event rate per 100 years (events / patient-years at risk)	BAT	Control
CV Mortality	5.8 (32 / 544)	7.9 (39 / 492)
HF Morbidity	26.6 (145 / 544)	23.6 (116 / 492)

No statistically significant difference between BAT and Control

Hierarchical Composite Using Win Ratio Analysis

Rationale:

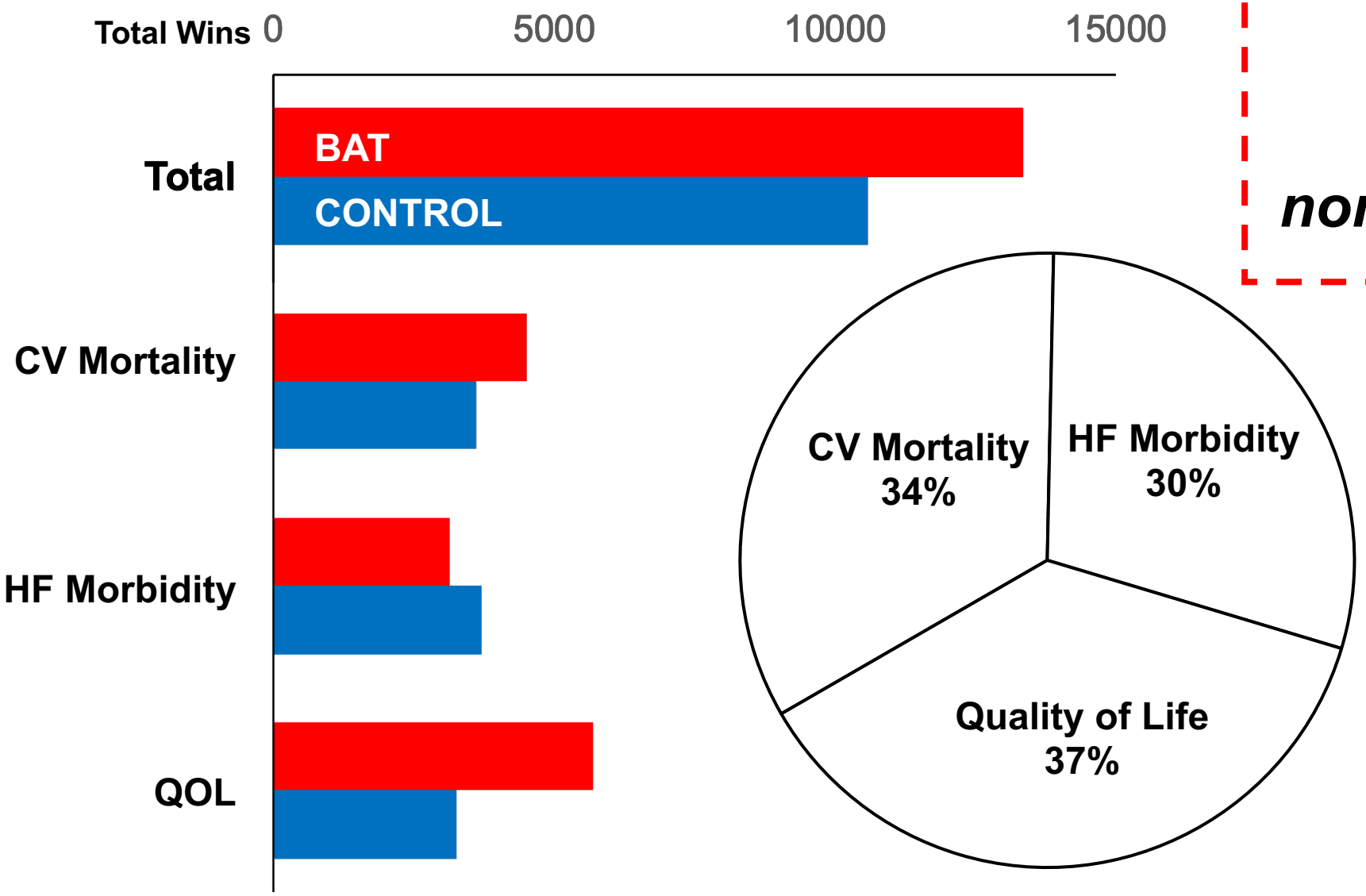
- CV Mortality + HF Morbidity: 40% of patients contributed to the end point
- Win ratio: 100% of patients contribute to the end point
- Used in many recent heart failure randomized controlled trial, drugs and devices



$$\text{Win Ratio} = \frac{\text{Total wins for BAT}}{\text{Total wins for Control}}$$

Stats: Finkelstein - Schoenfeld

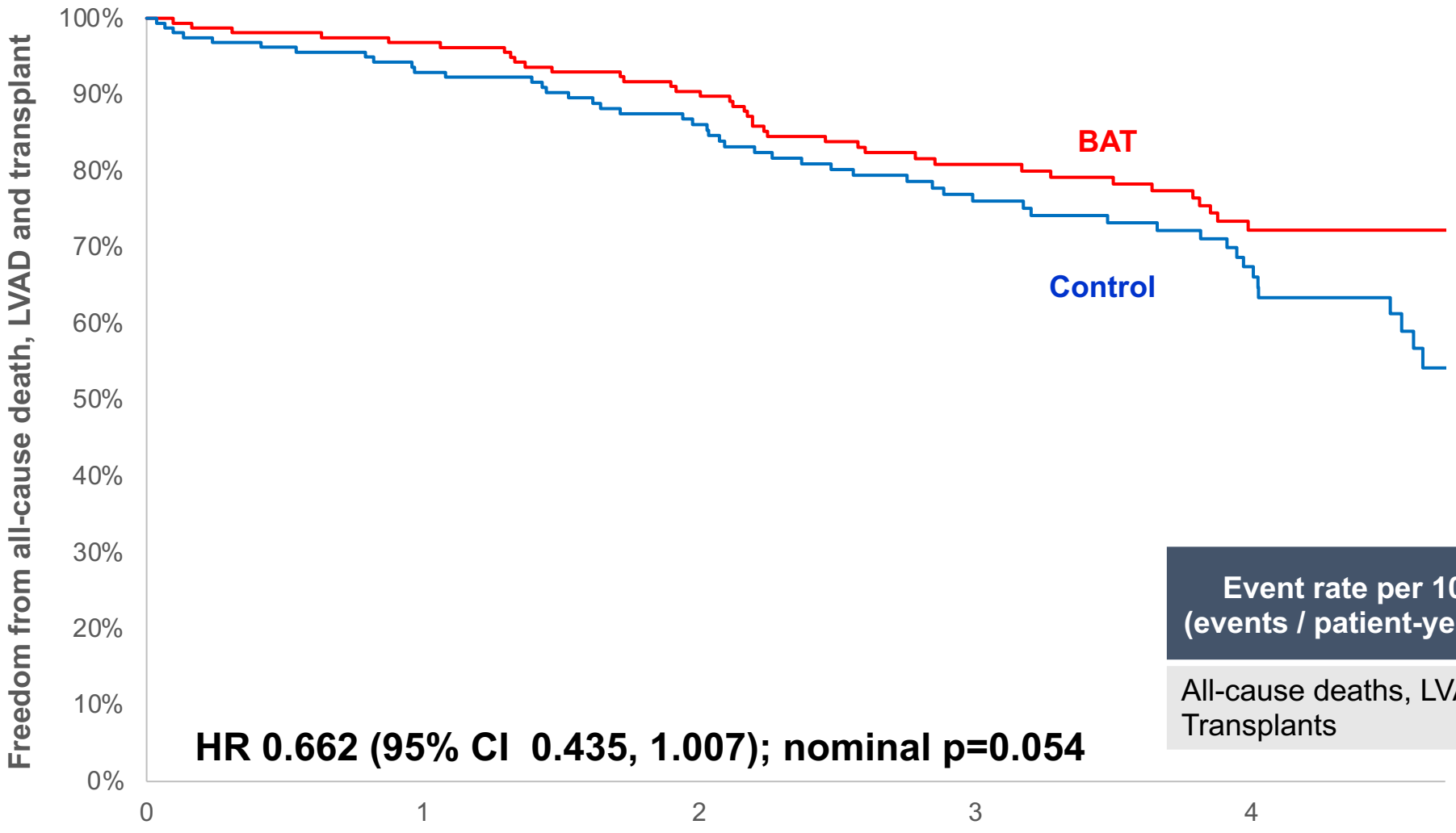
Hierarchical Composite Using Win Ratio Analysis



Win Ratio = 1.26
(1.02, 1.58)
nominal p-value = 0.04

* Sensitivity Test (All time M&M + 24 Month QOL) Win Ratio = 1.34 (95% CI 1.07, 1.68); nominal p=0.01

Freedom From All-cause Death, LVAD, and Transplant



BAT resulted in a 34% reduction in relative risk

Event rate per 100 years (events / patient-years at risk)	BAT	Control
All-cause deaths, LVAD, Heart Transplants	7.0 (38 / 544)	10.4 (51 / 492)

* Curves estimated using Kaplan-Meier method. Hazard ratio and p-value from Cox proportional hazards model.

Durable Safety Profile: MANCE*

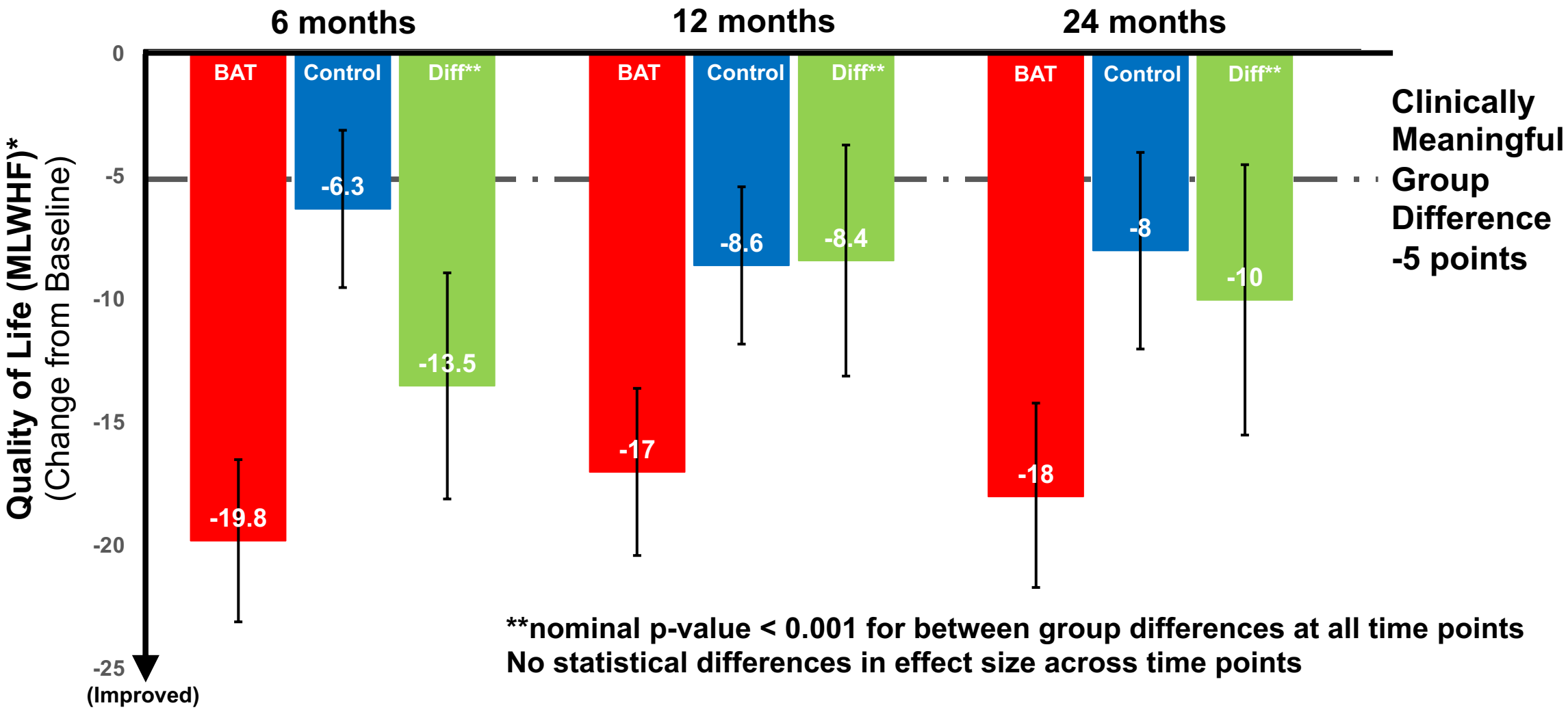
(Major Adverse Neurological or Cardiovascular system or procedure-related event rate)

Number of Subjects	Number of Subjects MANCE-Free	MANCE-Free Rate	One-Sided 95% Lower Bound	P-value**
159	154	96.9%	93.5%	<0.001

Device was surgically implanted in an outpatient procedure, totally extravascular

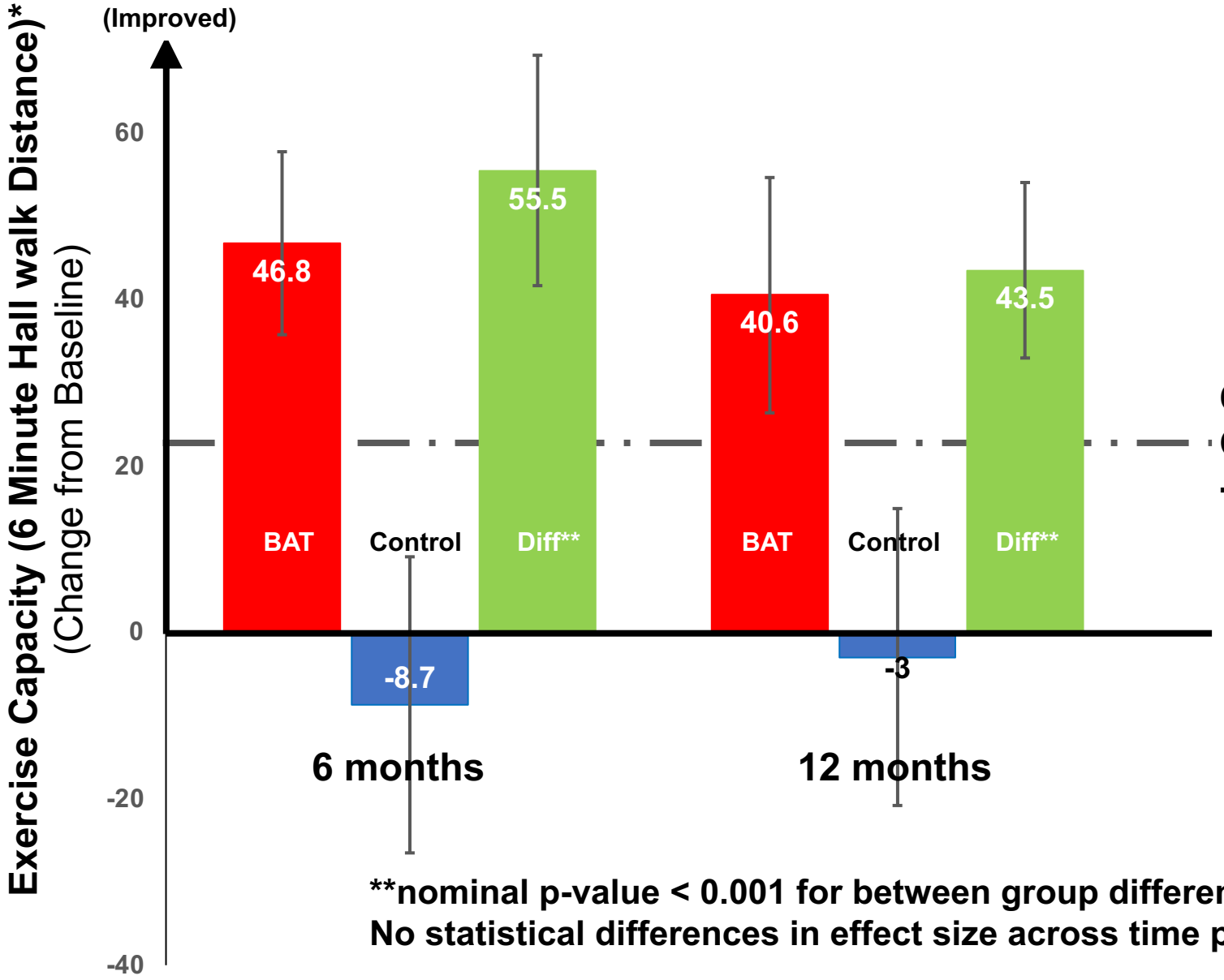
* Major Adverse Neurological or Cardiovascular system or procedure-related event rate
**Clopper-Pearson exact binomial method. One-sided hypothesis test p-value versus 85% performance goal.

Durable Improvement in Quality of Life (MLWHF)



*Statistics are estimated mean improvement and 95% confidence interval from repeated measures model
**From generalized estimating equation repeated measures model with covariate for baseline value

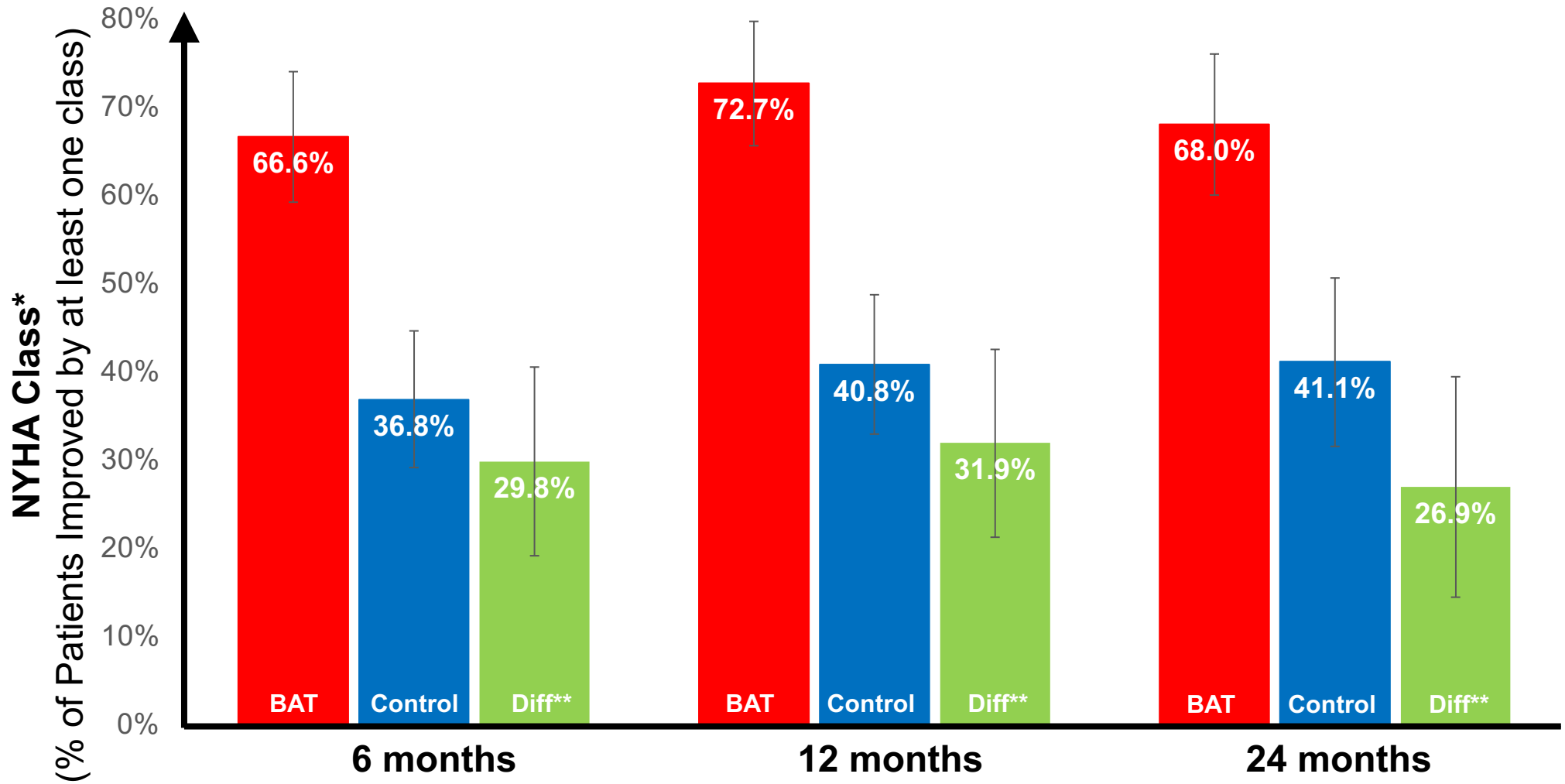
Durable Improvement in Exercise Capacity (6MHWD)



**nominal p-value < 0.001 for between group differences at all time points
No statistical differences in effect size across time points

*Statistics are estimated mean improvement and 95% confidence interval from repeated measures model
**From generalized estimating equation repeated measures model with covariate for baseline value

Durable Improvement in Functional Status (NYHA Class)



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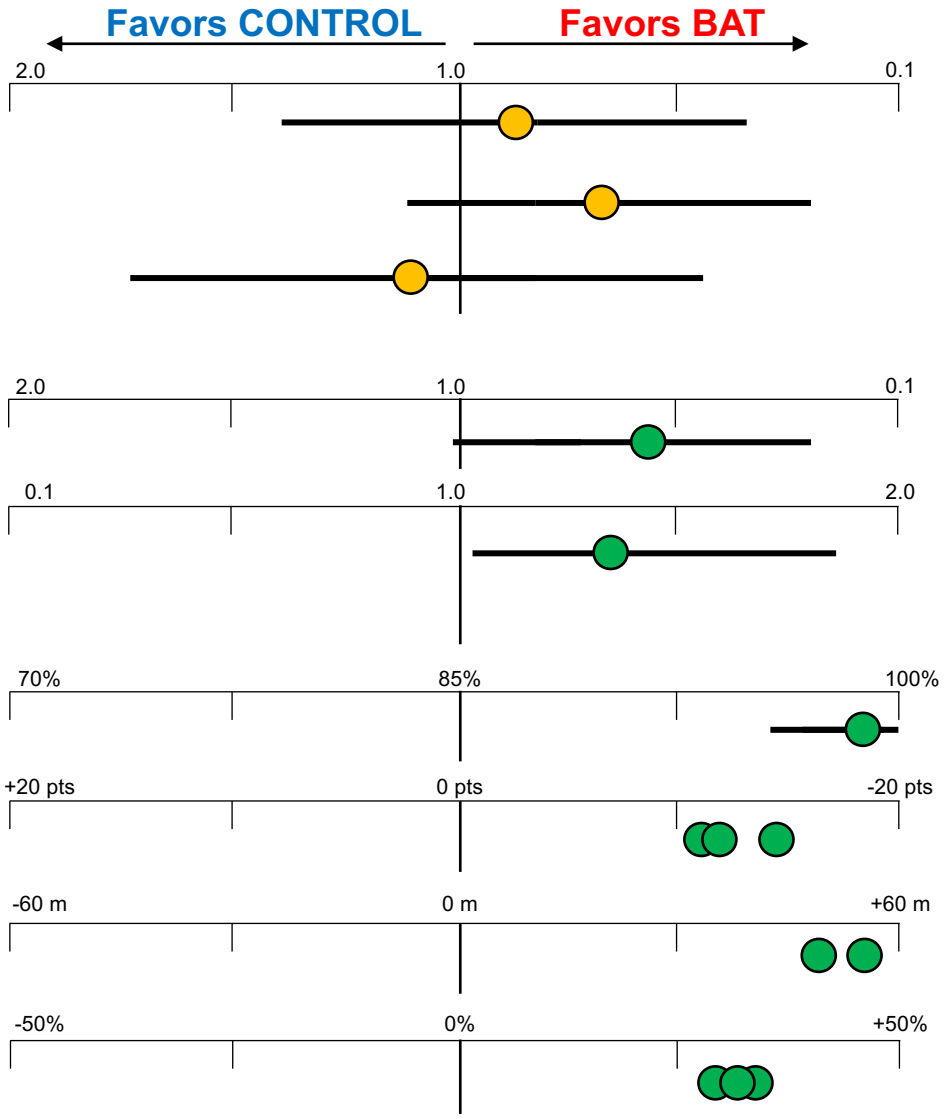
**From generalized estimating equation repeated measures model with covariate for baseline value

BeAT-HF Summary of Key Evidence

	Description	
Primary endpoint	**Composite CV Mortality and HF Morbidity**	Rate Ratio = 0.94
	CV Mortality (CV death, LVAD, heart transplant)	Hazard Ratio = 0.73
	HF Morbidity (Heart failure hospitalization, ER/ED visit)	Rate Ratio = 1.08
Additional Analyses	**All-cause Mortality** (death, LVAD, heart transplant)	Hazard Ratio = 0.66
	Hierarchical Win Ratio (CV mortality, HF morbidity, QOL)	Win Ratio = 1.26
Long-term Safety	**Related MANCE-free Rate*** *Major Adverse Neurologic and Cardiac Events	96.9%
Long-term Symptom Improvement	**Quality of Life – MLWHF** (6 / 12 / 24 Month)	-13 / -8 / -10
	Exercise Capacity – 6MHW (6 / 12 Month)	+55 / +44
	Functional Status – NYHA Class % Improved (6 / 12 / 24 Month)	30% / 32% / 27%



Totality of Data Favors BAT

Conclusion

Totality of evidence indicates that BAT is a safe, effective and durable treatment for patients with heart failure with reduced ejection fraction

Additional Excerpts from the Symposium

CVRx-Sponsored Lunch Symposium at 12:15 – 1:15 pm
Grand Ballroom A-B, Concourse Level

an in-depth discussion on the findings from BeAT-HF and potential confounders (COVID-19, Medications) and real-world experience using Barostim

Presented by:

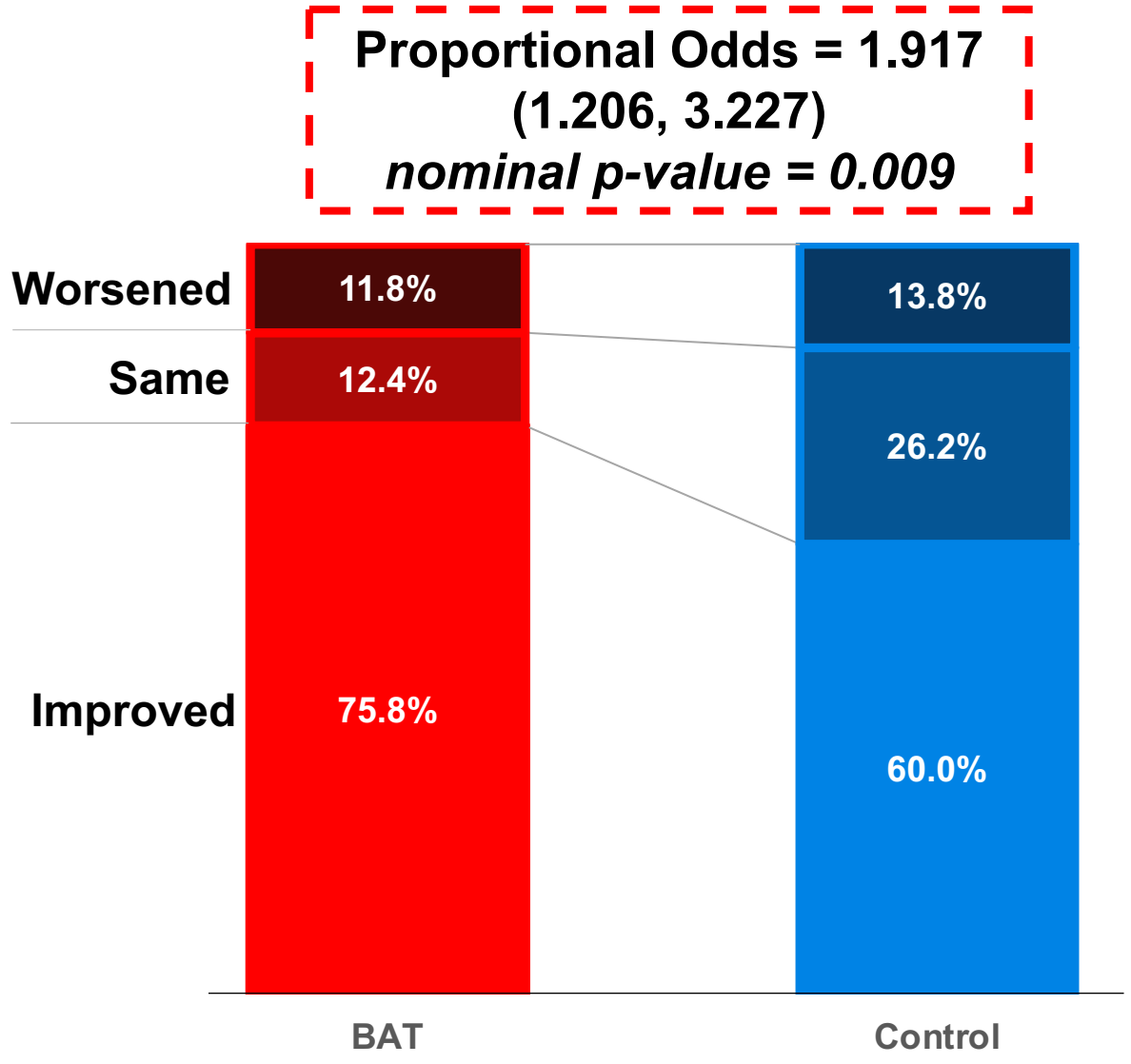
- **William T. Abraham**
- **JoAnn Lindenfeld**
- **Patrick J. McCann**
- **Michael R. Zile**

Clinical Stability Analysis *

Improved:
- Subject does not meet any worsening category AND
- Fewer HF hospitalizations in 12 months post-enrollment vs 12 months pre-enrollment,
- OR improved NYHA class at 12 months vs. baseline;

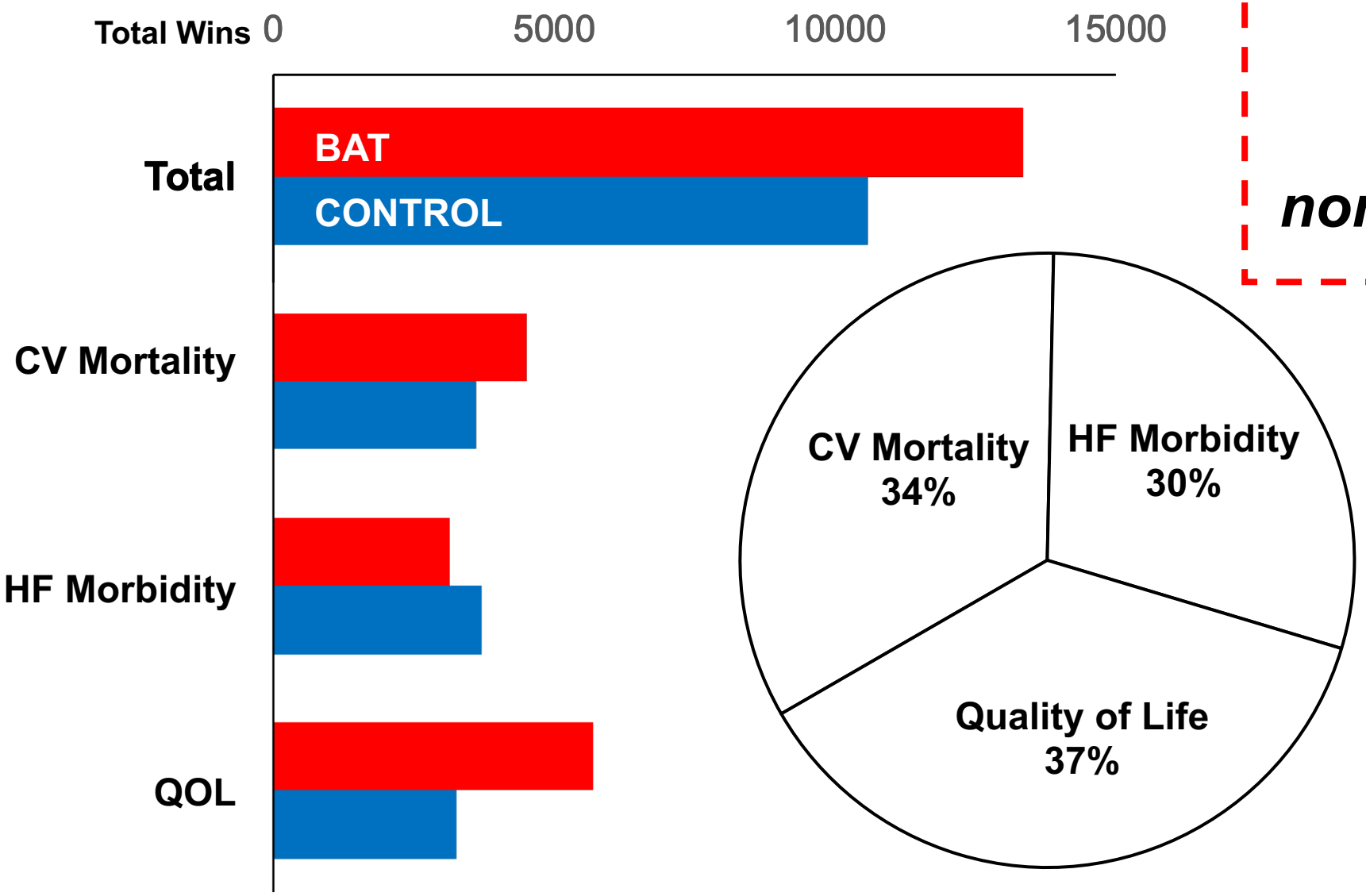
Same:
- Neither worsened nor improved
- AND evaluable for both HF hospitalizations and NYHA;

Worsened:
- Died prior to 12 months,
- OR more HF hospitalizations in 12 months post-enrollment as compared to 12 months pre-enrollment,
- OR higher NYHA class at 12 months vs. baseline



* Similar to that used in: Packer et al, Circulation. 2021;143:326–336, EMPEROR-Reduced Trial

Hierarchical Composite Using Win Ratio Analysis



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(1.02, 1.58)
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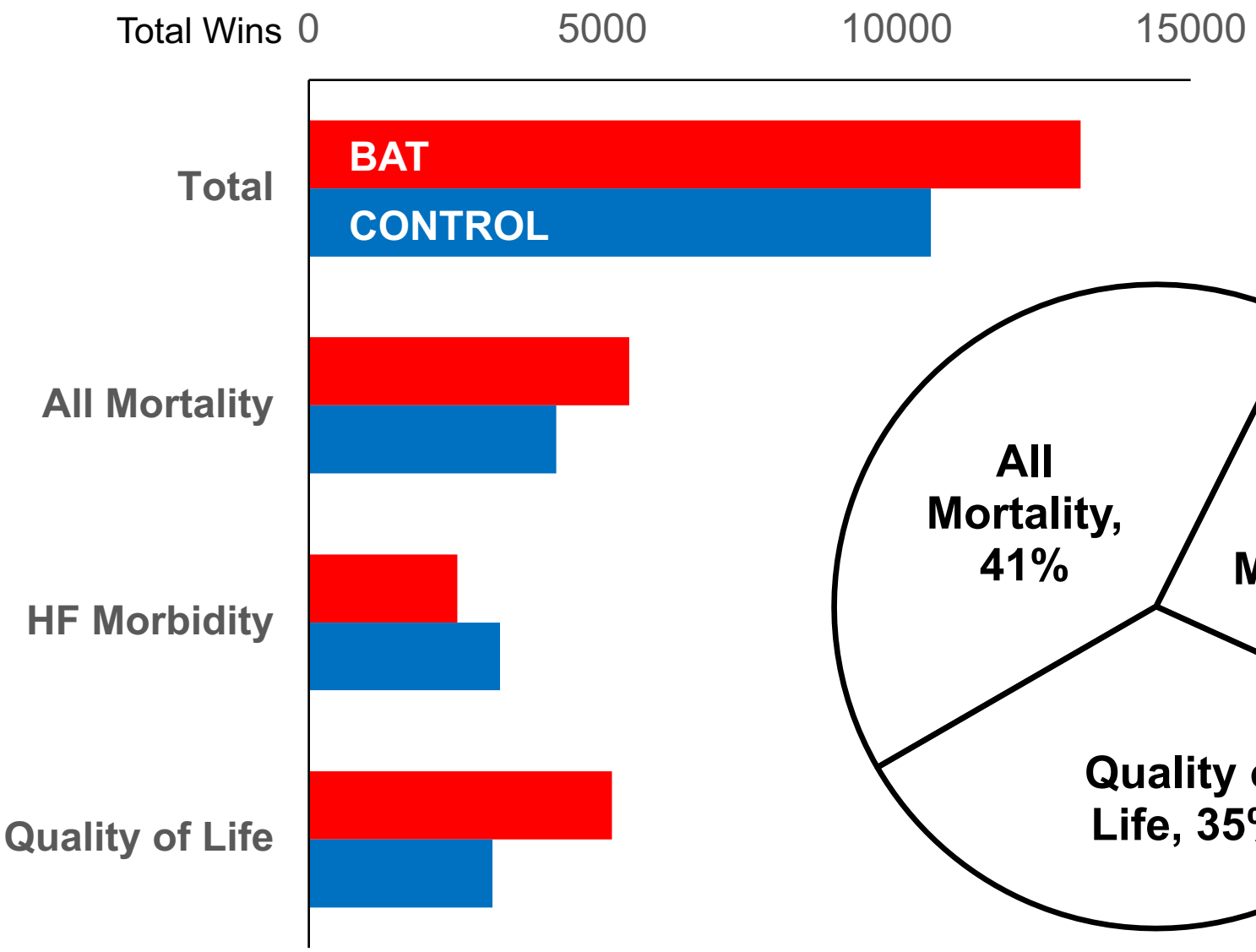
Sensitivity Analysis – All-Cause Mortality Win Ratio



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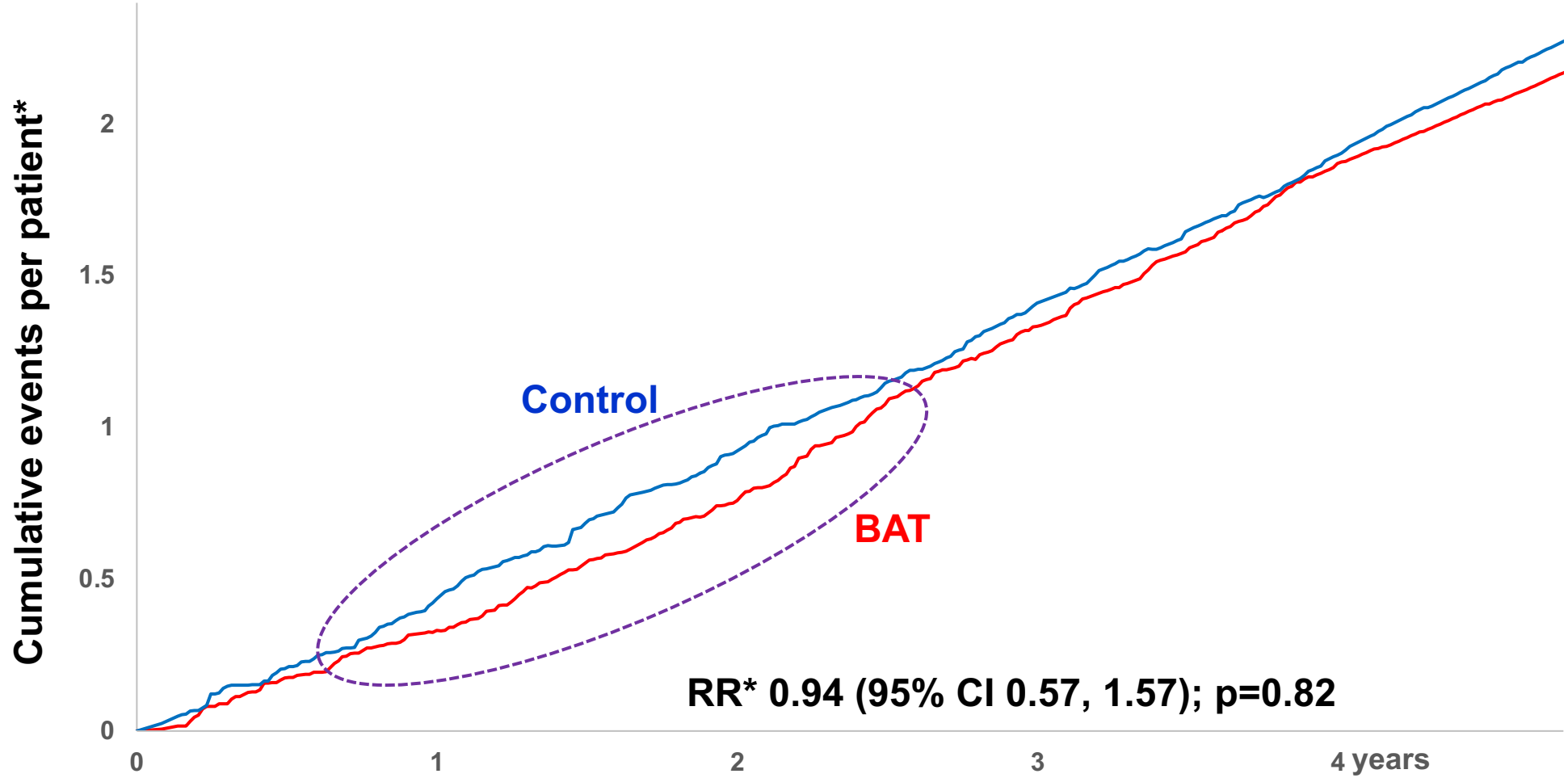
Primary Composite Endpoint: CV Mortality and HF Morbidity



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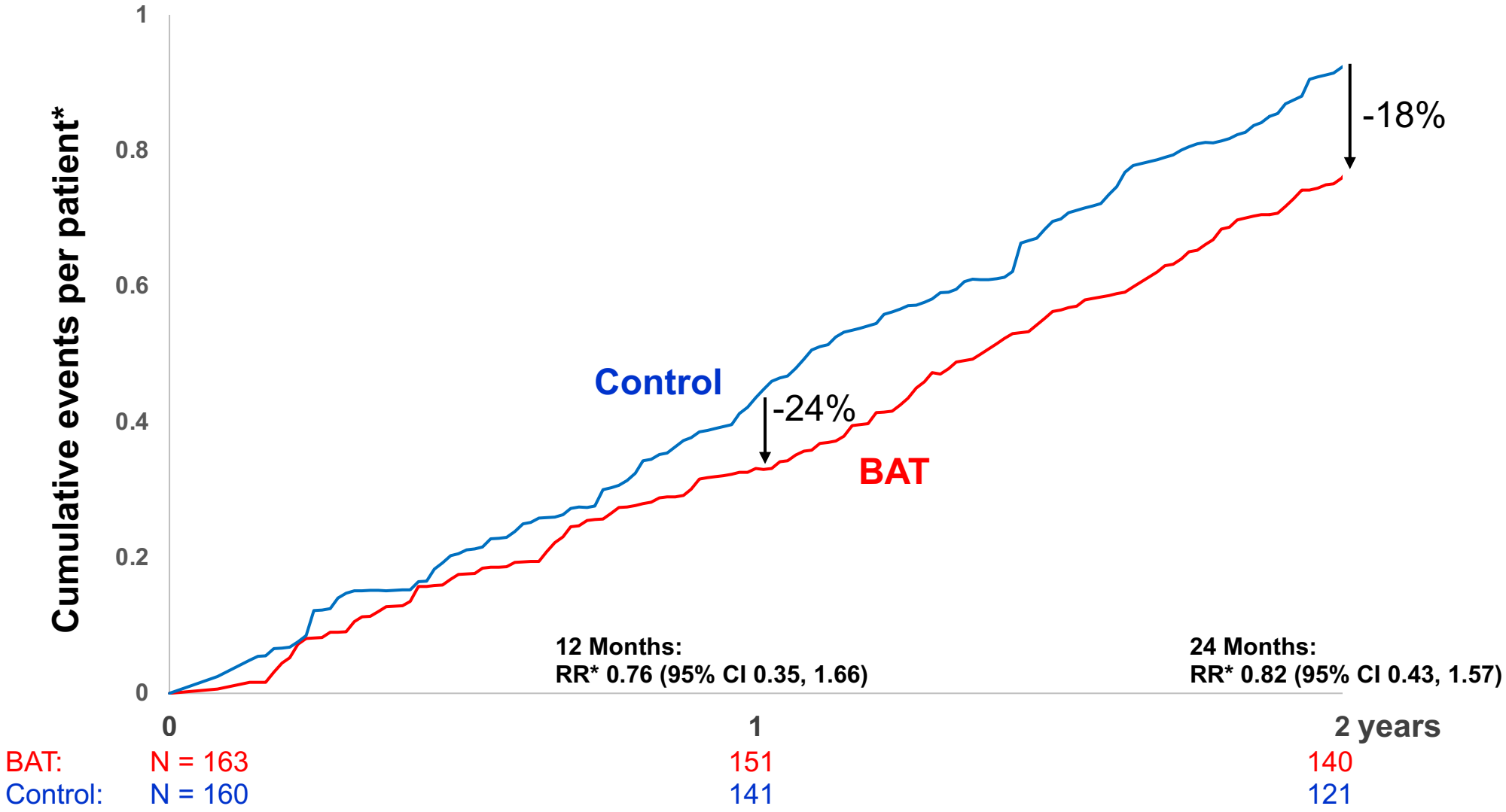
Primary Composite Endpoint at 12 and 24 Months



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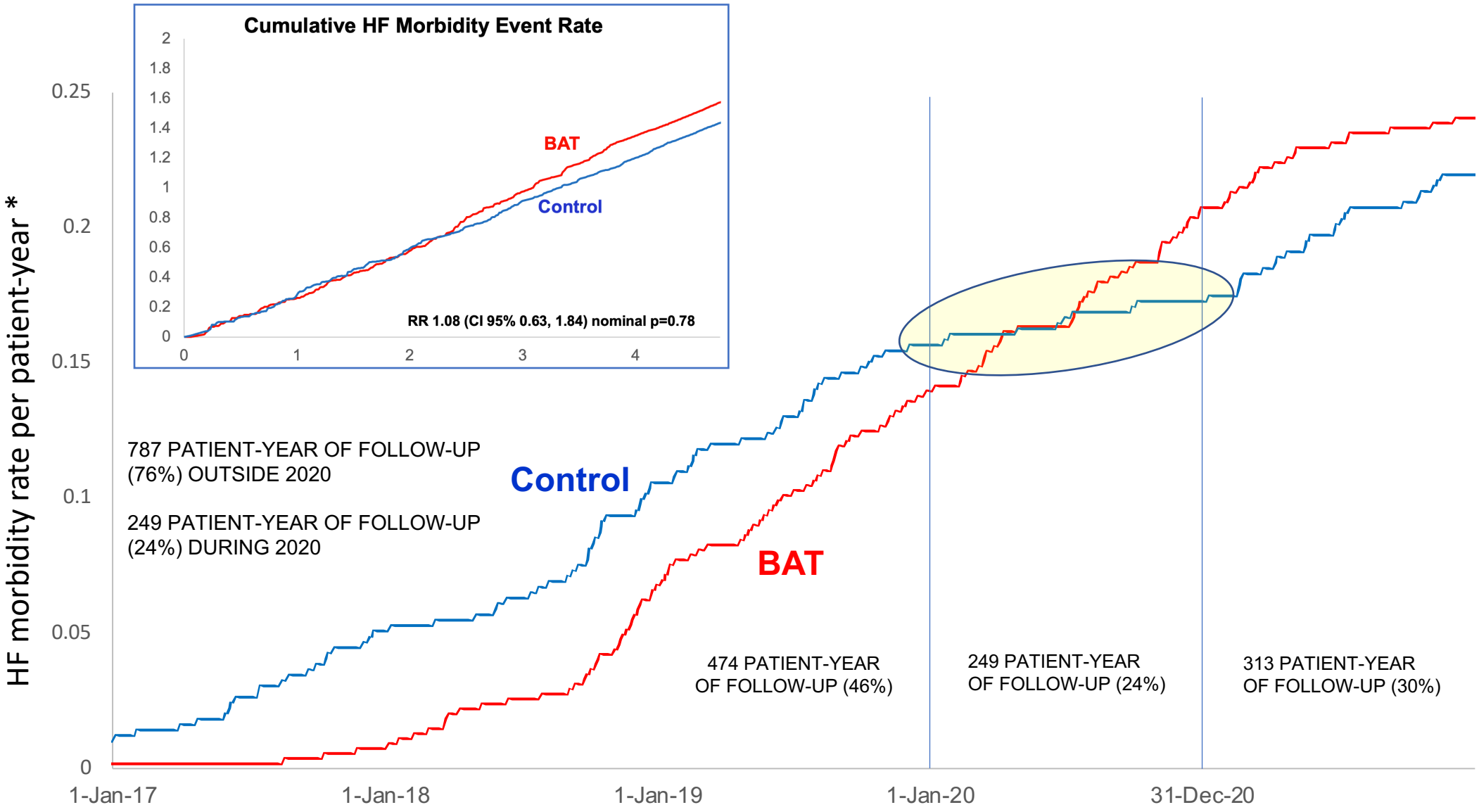
Impact of COVID-19 Pandemic on HF Morbidity



*Normalized by total patient-years of follow-up per arm (BAT: 544 patient-years, Control: 492 patient-years)

Potential Confounder: Impact of COVID Pandemic

Heart Failure Morbidity

Time Period	BAT †	Control†
2020	0.28	0.07
2016, 2017, 2018, 2019, 2021, 2022	0.26	0.29

† Number of hospitalizations or emergency department visits for heart failure per patient-year of follow-up

- **COVID definitely impacted the results of the study.**
- **The COVID impact was differentially expressed more in the control group than in the BAT group.**
- **Why COVID has these differential effects has not been thoroughly investigated yet.**
- **Whether and to what extent COVID acted to limit our ability to identify an effect of BAT on the HF Morbidity awaits further analysis.**

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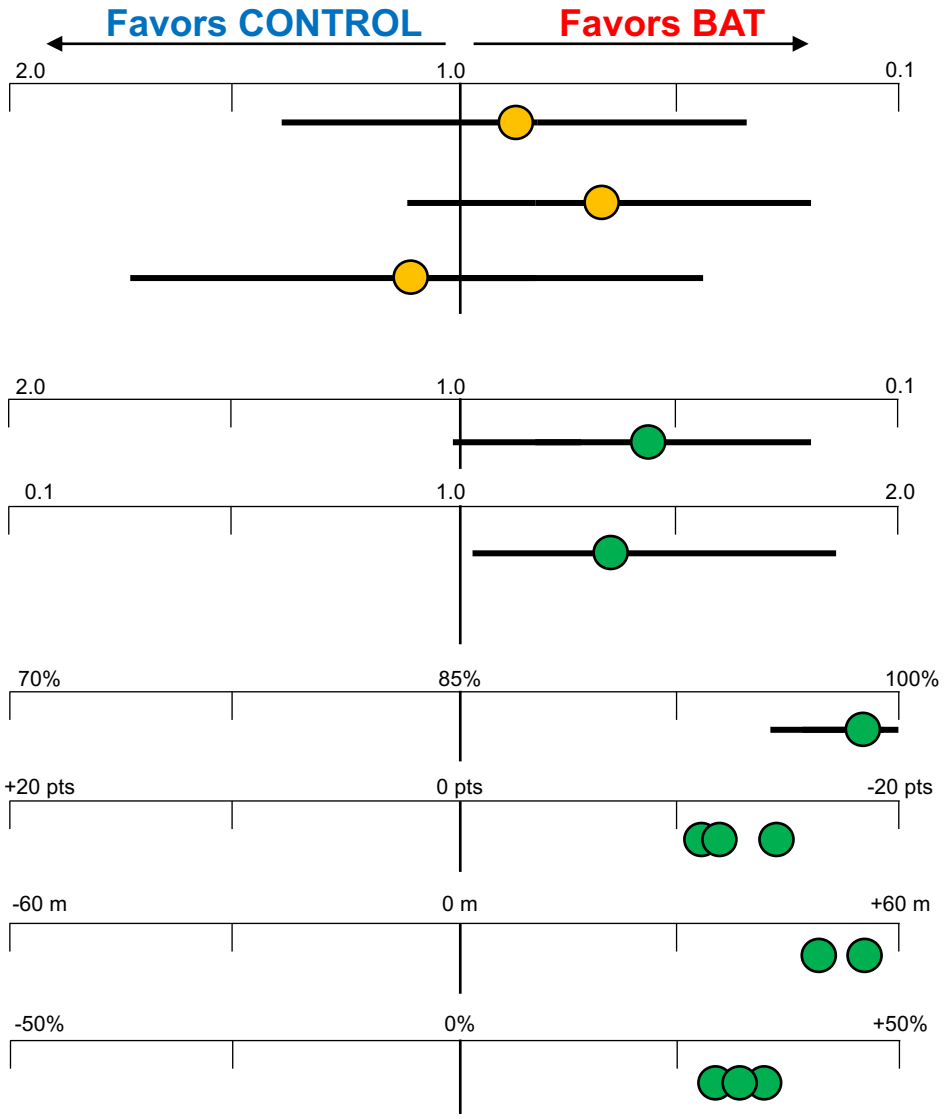

Totality of Data Favors BAT

Conclusion

Totality of evidence indicates that BAT is a safe, effective and durable treatment for patients with heart failure with reduced ejection fraction

Key takeaways

- Barostim is currently FDA-approved for the improvement of heart failure symptoms based on the pre-market phase of BeAT-HF at 6 months.
- The post-market phase of BeAT-HF confirmed the long-term durability of safety and symptomatic improvements, and the sustainability of the extent of the improvements.
- The reduction of all-cause death, LVAD and heart transplant is meaningful (34% reduction, nominal p-value 0.054).
- The pre-specified hierarchical composite endpoint was well balanced, and demonstrated meaningful benefit (Win ratio = 1.26, nominal p-value=0.04), stable over multiple sensitivity analyses

Next steps

- One or more manuscripts will be written by the executive steering committee for submission to peer-reviewed journals

- The PMA Clinical report is being prepared by CVRx to be submitted to FDA, to seek an expansion of the labeling, commensurate with the recommendation of the Executive Steering Committee of BeAT-HF. We agree with the committee that the totality of evidence supports the use of Barostim as a Treatment for heart failure

Questions?

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