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Late Breaking Clinical Trial Vignettes

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Blood-Pressure and Cholesterol Lowering in Persons without Cardiovascular Disease

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NEJM 2016; 374: 2021-2031

HOPE-3- Background

- Investigators evaluated the effects of **a MODERATE DOSE OF A POTENT STATIN VS PLACEBO**, and

- A **FIXED COMBINATION OF MODERATE DOSES OF AN ARB DIURETIC VS PLACEBO,** and **THE COMBINATION OF BOTH TREATMENTS VS DUAL PLACEBO** on the prevention of major cardiovascular events.

- Both systolic blood pressure and low density lipoprotein (LDL) cholesterol show graded associations with cardiovascular disease.

- This profile accounts for two thirds of the population-attributable risk of cardiovascular disease.

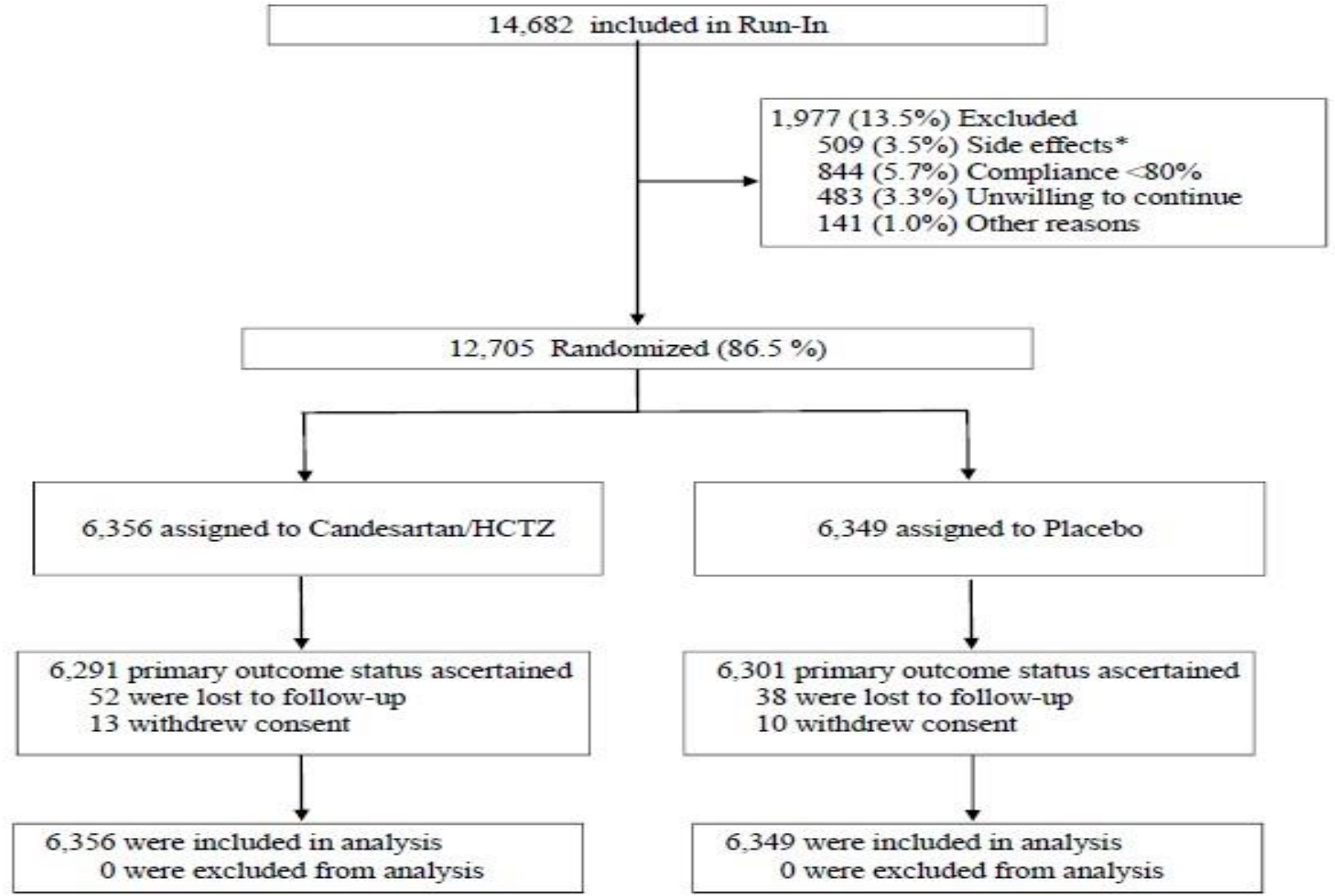
NEJM 2016; 374: 2021-2031

TRIAL DESIGN AND OVERSIGHT

- The **HEART OUTCOMES PREVENTION EVALUATION (HOPE)–3** trial is a multicenter, long-term, international,double-blind, randomized, placebo-controlled trial with a 2-by-2 factorial design among persons who did not have cardiovascular disease and who were at intermediate risk (defined as an annual risk of major cardiovascular events of approximately 1%).
- Conducted at 228 centers in 21 countries.

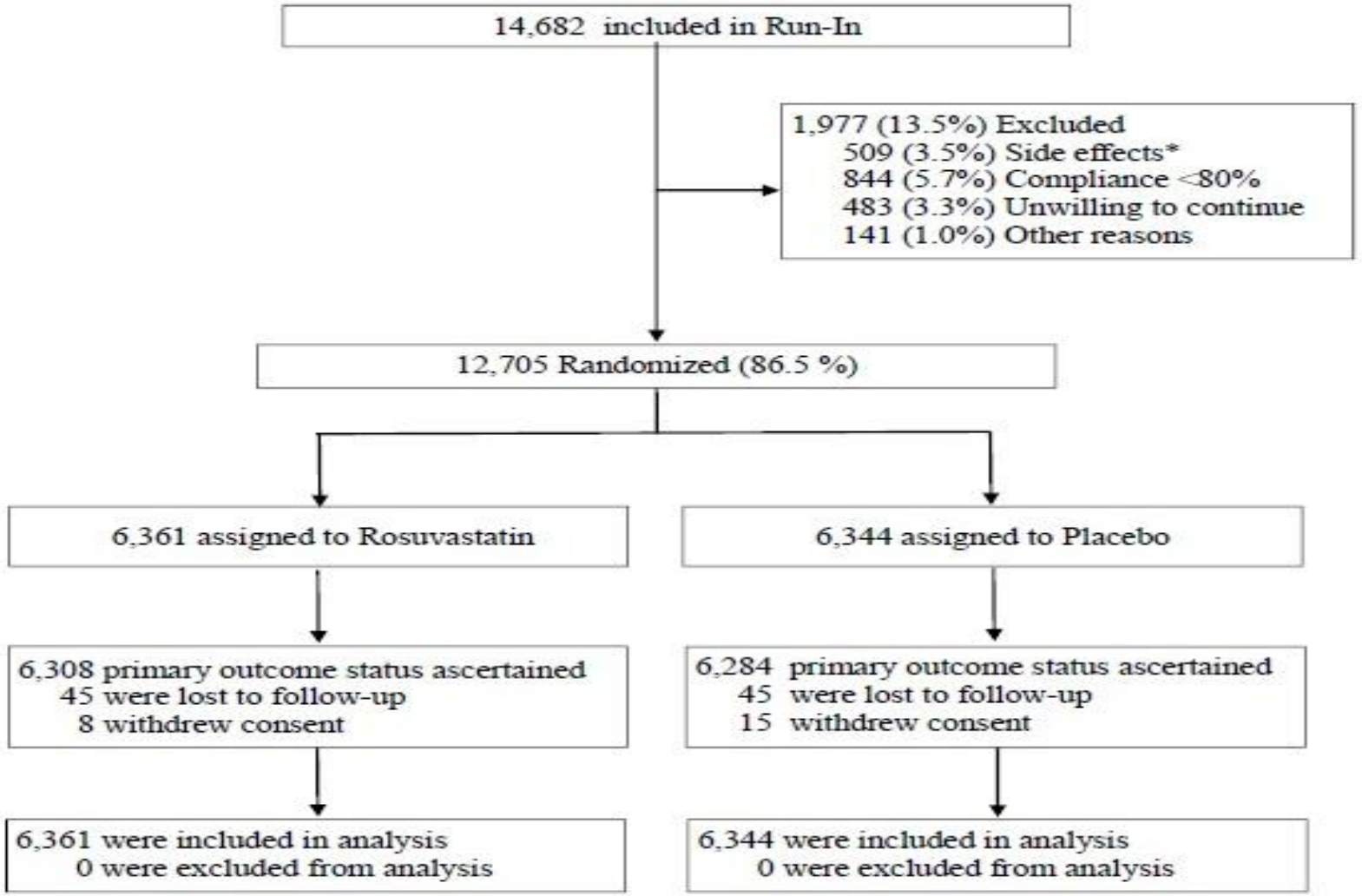
NEJM 2016; 374: 2021-2031

Figure S1: CONSORT Diagram for the Candesartan/HCTZ versus Placebo Comparison



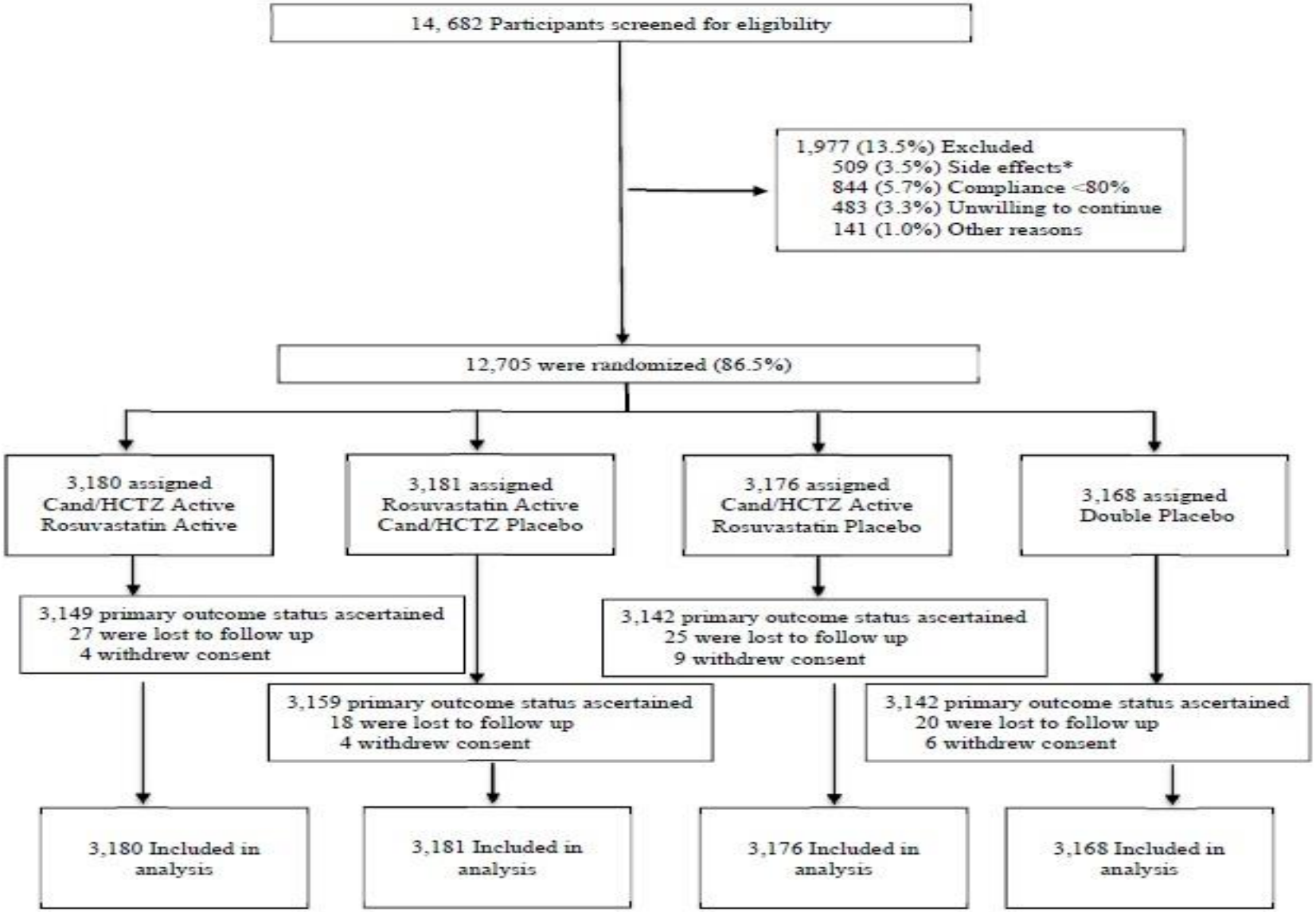
NEJM 2016; 374: 2021-2031

Figure S2: CONSORT Diagram for the Rosuvastatin versus Placebo Comparison



NEJM 2016; 374: 2021-2031

Figure S3: CONSORT Diagram for the Double Active versus Double Placebo Comparison



NEJM 2016; 374: 2021-2031

Table S1: The Heart Outcomes Prevention Evaluation (HOPE) - 3 Trial Design
(N=12,705)

Rosuvastatin	Candesartan/HCTZ		Rosuvastatin Margins
	Active	Placebo	
Active	Rosuvastatin Active/ Candesartan/HCTZ Active n=3,180	Rosuvastatin Active/ Candesartan/HCTZ Placebo n=3,181	**Rosuvastatin Active n=6,361**
Placebo	Rosuvastatin Placebo/ Candesartan/HCTZ Active n=3,176	Rosuvastatin Placebo/ Candesartan/HCTZ Placebo n=3,168	**Rosuvastatin Placebo n=6,344**
Candesartan/HCTZ Margins	**Candesartan/HCTZ Active n=6,356**	**Candesartan/HCTZ Placebo n=6,349**	

HCTZ=hydrochlorothiazide

NEJM 2016; 374: 2021-2031

TRIAL PROCEDURES

- Eligible persons entered a single-blind run-in phase, during which they received both active treatments for 4 weeks.
- Participants who adhered to the regimen and who did not have an unacceptable level of adverse events were randomly assigned to a **fixed combination of CANDESARTAN (16 mg per day) and HYDROCHLOROTHIAZIDE(12.5 mg per day) or placebo and to ROSUVASTATIN(10 mg per day) or placebo**.

NEJM 2016; 374: 2021-2031

Follow Up

- Follow-up visits occurred at 6 weeks and 6 months after randomization and every 6 months thereafter.
- Blood pressure was recorded at each visit in the first year and then annually.
- Lipid levels were measured at baseline in all participants and at 1 year, at 3 years, and at the end of the trial.

NEJM 2016; 374: 2021-2031

OUTCOMES

- There were **two co-primary outcomes**:

  1)the composite of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke.

  2)the composite of these events plus resuscitated cardiac arrest, heart failure, or revascularization.

- The **secondary outcome** was the composite of events comprising **the second co-primary outcome plus angina with evidence of ischemia**.

NEJM 2016; 374: 2021-2031

ADHERENCE TO TRIAL DRUGS

Table S3: Adherence to Study Drug and Open Label Use of ARBs, ACE-Is and Thiazides in the Candesartan/HCTZ and Placebo Groups

A. Candesartan

Visit	Candesartan/HCTZ					
	Eligible	On Study Drug	On Open Label			
		Cand/HCTZ N (%)	ARB N (%)	ACE-I N (%)	Thiazide N (%)	Other BP Lowering Drug(s)* N (%)
1 year	6314	5567(88.2)	14(0.2)	24(0.4)	1(0)	-
2 years	6267	5374(85.8)	28(0.4)	41(0.7)	10(0.2)	1011(16.5)
3 years	6205	5189(83.6)	45(0.7)	48(0.8)	15(0.2)	-
4 years	6101	4967(81.4)	52(0.9)	59(1.0)	30(0.5)	-
5 years	4854	3639(75.0)	60(1.2)	66(1.4)	30(0.6)	-
End	5990	4599(76.8)	93(1.6)	100 (1.7)	47(0.8)	1068(18.2)

B. Placebo

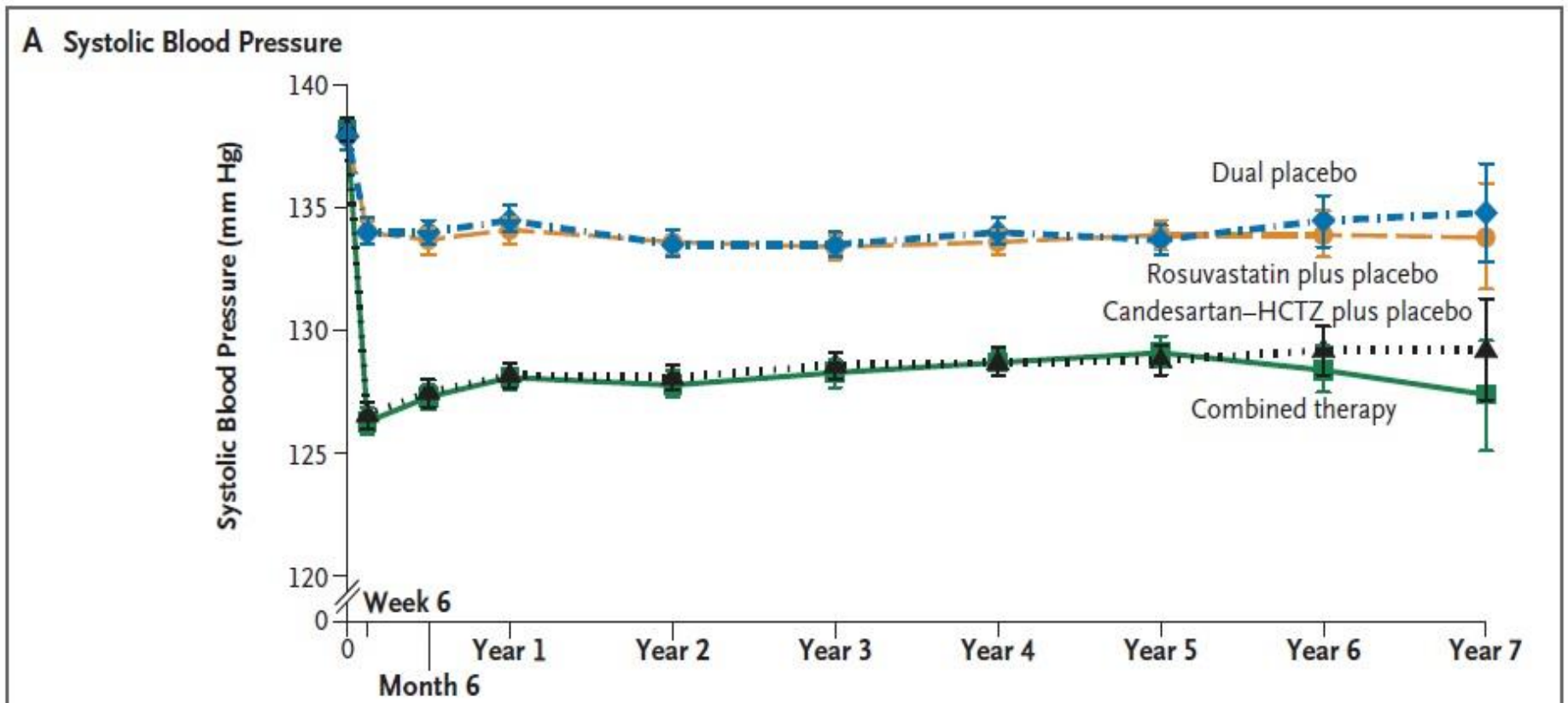
Visit	Placebo					
	Eligible	On Study Drug	On Open Label			
		Cand/HCTZ Placebo N (%)	ARB N (%)	ACE-I N (%)	Thiazide N (%)	Other BP Lowering Drug(s)* N (%)
	6306	5545(87.9)	30(0.5)	48(0.8)	9(0.1)	-
	6262	5359(85.6)	66(1.1)	67(1.1)	27(0.4)	1514(24.7)
	6188	5161(83.4)	76(1.2)	82(1.3)	45(0.7)	-
	6089	4953(81.3)	106(1.7)	102(1.7)	57(0.9)	-
	4818	3588 (74.5)	104(2.2)	110(2.3)	57(1.2)	-
	5985	4530(75.7)	146(2.4)	137(2.3)	79 (1.3)	1688(28.8)

NEJM 2016; 374: 2021-2031

BLOOD PRESSURE AND LIPID LEVELS

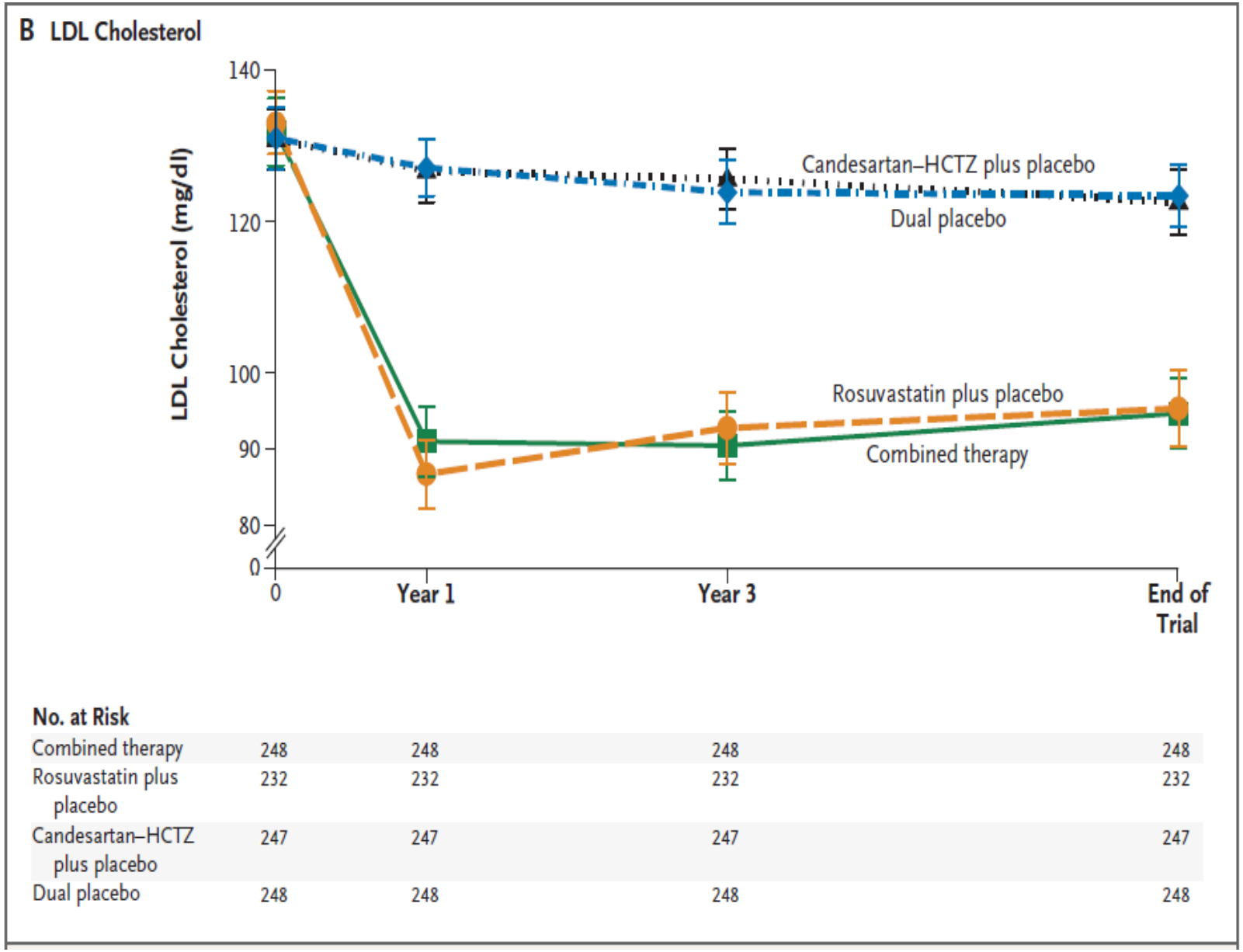
- On average , the **mean SBP was lower by 6.2 mm Hg** in the combined-therapy group than in the dual placebo group, the **mean DBP was lower by 3.2 mm Hg**, and the **mean LDL cholesterol level was lower by 33.7 mg per deciliter .**
- The difference in blood pressure was similar for participants assigned to candesartan– hydrochlorothiazide alone versus placebo.
- The difference in LDL cholesterol level was similar for participants assigned to rouvastatin alone versus placebo.

NEJM 2016; 374: 2021-2031



No. at Risk										
Combined therapy	3180	3091	3009	2953	2836	2718	2594	1921	731	178
Rosuvastatin plus placebo	3181	3105	3033	2957	2832	2741	2615	1929	728	167
Candesartan–HCTZ plus placebo	3176	3109	3022	2954	2831	2728	2619	1941	706	172
Dual placebo	3166	3093	3000	2922	2791	2701	2571	1893	696	167

NEJM 2016; 374: 2021-2031



No. at Risk

Combined therapy	248	248	248	248
Rosuvastatin plus placebo	232	232	232	232
Candesartan–HCTZ plus placebo	247	247	247	247
Dual placebo	248	248	248	248

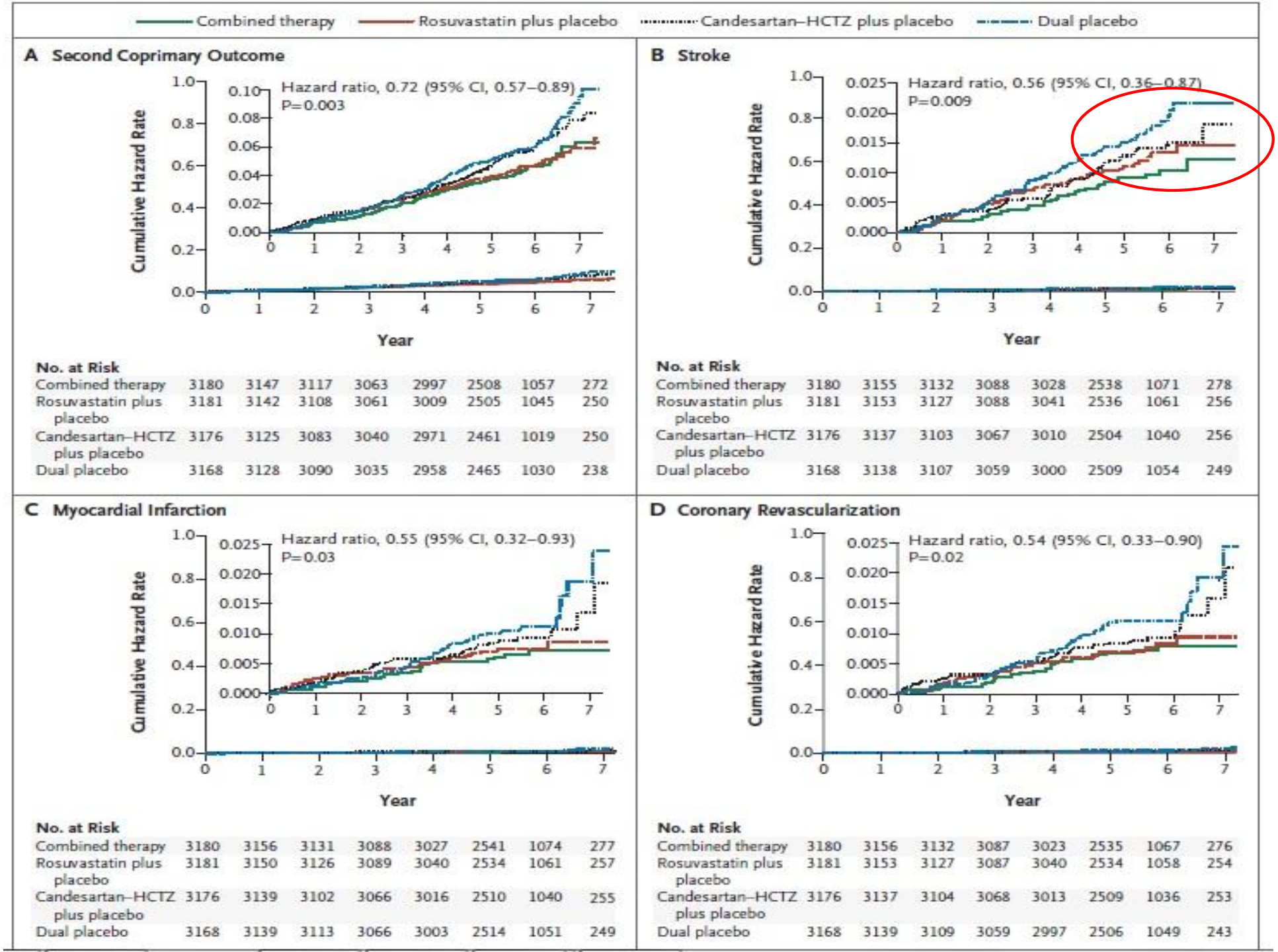
NEJM 2016; 374: 2021-2031

Table 2. Primary, Secondary, and Other Outcomes.*

Outcome	Candesartan–Hydrochlorothiazide plus Rosuvastatin (N=3180)	Rosuvastatin plus Placebo (N=3181)	Candesartan–Hydrochlorothiazide plus Placebo (N=3176)	Placebo plus Placebo (N=3168)	Candesartan–Hydrochlorothiazide plus Rosuvastatin vs. Placebo plus Placebo	
					Hazard Ratio (95% CI)	P Value
Coprimary outcomes — no. (%)						
First coprimary outcome	113 (3.6)	122 (3.8)†	147 (4.6)‡	157 (5.0)	0.71 (0.56–0.90)	0.005
Second coprimary outcome	136 (4.3)	141 (4.4)§	176 (5.5)¶	187 (5.9)	0.72 (0.57–0.89)	0.003
Secondary outcome — no. (%)‖	147 (4.6)	159 (5.0)	188 (5.9)	205 (6.5)	0.71 (0.57–0.87)	0.001
Components of the coprimary and secondary outcomes — no. (%)						
Death from cardiovascular causes	75 (2.4)	79 (2.5)	80 (2.5)	91 (2.9)	0.82 (0.60–1.11)	
Fatal or nonfatal myocardial infarction	21 (0.7)	24 (0.8)	31 (1.0)	38 (1.2)	0.55 (0.32–0.93)	
Fatal or nonfatal stroke	31 (1.0)	39 (1.2)	44 (1.4)	55 (1.7)	0.56 (0.36–0.87)	
Resuscitated cardiac arrest	1 (<0.1)	3 (0.1)	1 (<0.1)	3 (0.1)	0.33 (0.03–3.18)	
Revascularization	27 (0.8)	29 (0.9)	37 (1.2)	45 (1.4)	0.59 (0.37–0.95)	
Heart failure	10 (0.3)	11 (0.3)	11 (0.3)	18 (0.6)	0.55 (0.25–1.19)	
Angina with objective evidence of ischemia‖	25 (0.8)	31 (1.0)	26 (0.8)	38 (1.2)	0.65 (0.39–1.08)	
Other outcomes						
Death from any cause — no. (%)	163 (5.1)	171 (5.4)	179 (5.6)	178 (5.6)	0.91 (0.73–1.12)	
New-onset diabetes — no./total no. (%)	123/2982 (4.1)	109/3001 (3.6)	113/2984 (3.8)	113/2999 (3.8)	1.09 (0.85–1.41)	
Hospitalization — no. (%)**						
For cardiovascular causes	141 (4.4)	140 (4.4)	178 (5.6)	191 (6.0)	0.73 (0.59–0.91)	0.005
For noncardiovascular causes	463 (14.6)	418 (13.1)	436 (13.7)	443 (14.0)	1.04 (0.92–1.19)	0.52
First and recurrent events of the second coprimary outcome††						
No. of participants with ≥1 event	136	141	176	187		
No. of participants with ≥2 events	29	39	30	59		
No. of participants with ≥3 events	2	4	3	13		
Total no. of events	169	184	211	262	0.66 (0.52–0.84)	0.001

* The first coprimary outcome was the composite of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke; the second coprimary outcome was the composite of cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, resuscitated cardiac arrest, heart failure, or revascularization; and the secondary outcome was the composite of cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, resuscitated cardiac arrest, heart failure, revascularization, or angina with objective evidence of ischemia. CI denotes confidence interval.

NEJM 2016; 374: 2021-2031



NEJM 2016;
374: 2021-2031

Complications

- **No significant differences** between the combined-therapy group and the dual placebo group were seen **in the rate of new-onset diabetes, renal dysfunction, syncope, liver-function abnormalities, eye problems, or cancers**.
- The **rates of muscle weakness or pain and of dizziness were higher in the combined-therapy group** than in the dual-placebo group.
- These effects were reversible by temporary is continuation of the trial drug.

NEJM 2016; 374: 2021-2031

True Prevention

- Investigators approach of selecting persons on the basis of age and easily measured risk factors meant that neither complex screening nor blood tests are required to initiate treatment with low doses of combination therapy.

- Trial included persons of diverse racial and ethnic groups from 21 countries with broadly consistent benefits and safety.

NEJM 2016; 374: 2021-2031

CONCLUSION

- Treatment with fixed doses of rouvastatin and two antihypertensive agents was associated with a significantly lower risk of cardiovascular events than the risk with placebo among intermediate-risk persons without previous cardiovascular disease.

NEJM 2016; 374: 2021-2031

The Third DANish Study of Optimal Acute Treatment of Patients with ST-segment Elevation Myocardial Infarction: DEFERred stent implantation in connection with primary PCI: DANAMI 3-DEFER

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Lancet 2016; 387(10034): 2199-2206

Deferred versus conventional stent implantation in patients with ST-segment elevation myocardial infarction (DANAMI 3-DEFER): an open-label, randomised controlled trial

Henning Kelbæk, Dan Eik Høfsten, Lars Køber, Steffen Helqvist, Lene Kløvgaard, Lene Holmvang, Erik Jørgensen, Frants Pedersen, Kari Saunamäki, Ole De Backer, Lia E Bang, Klaus F Kofoed, Jacob Lønborg, Kiril Ahtarovski, Niels Vejlstrup, Hans E Bøtker, Christian J Terkelsen, Evald H Christiansen, Jan Ravkilde, Hans-Henrik Tilsted, Anton B Villadsen, Jens Aarøe, Svend E Jensen, Bent Raungaard, Lisette O Jensen, Peter Clemmensen, Peer Grande, Jan K Madsen, Christian Torp-Pedersen, Thomas Engstrøm

Summary

Background Despite successful treatment of the culprit artery lesion by primary percutaneous coronary intervention (PCI) with stent implantation, thrombotic embolisation occurs in some cases, which impairs the prognosis of patients with ST-segment elevation myocardial infarction (STEMI). We aimed to assess the clinical outcomes of deferred stent implantation versus standard PCI in patients with STEMI.

Methods We did this open-label, randomised controlled trial at four primary PCI centres in Denmark. Eligible patients (aged >18 years) had acute onset symptoms lasting 12 h or less, and ST-segment elevation of 0·1 mV or more in at least two or more contiguous electrocardiographic leads or newly developed left bundle branch block. Patients were

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See Online/XXX
http://dx.doi.org/10.1016/PII

Department of Cardiology, Roskilde Hospital, Roskilde, Denmark (H Kelbæk MD);

Lancet 2016; 387(10034): 2199-2206

Aim of DANAMI-3-DEFER study

To evaluate whether the prognosis of STEMI patients treated with pPCI can be improved by deferred stent implantation

Lancet 2016; 387(10034): 2199-2206

Participants

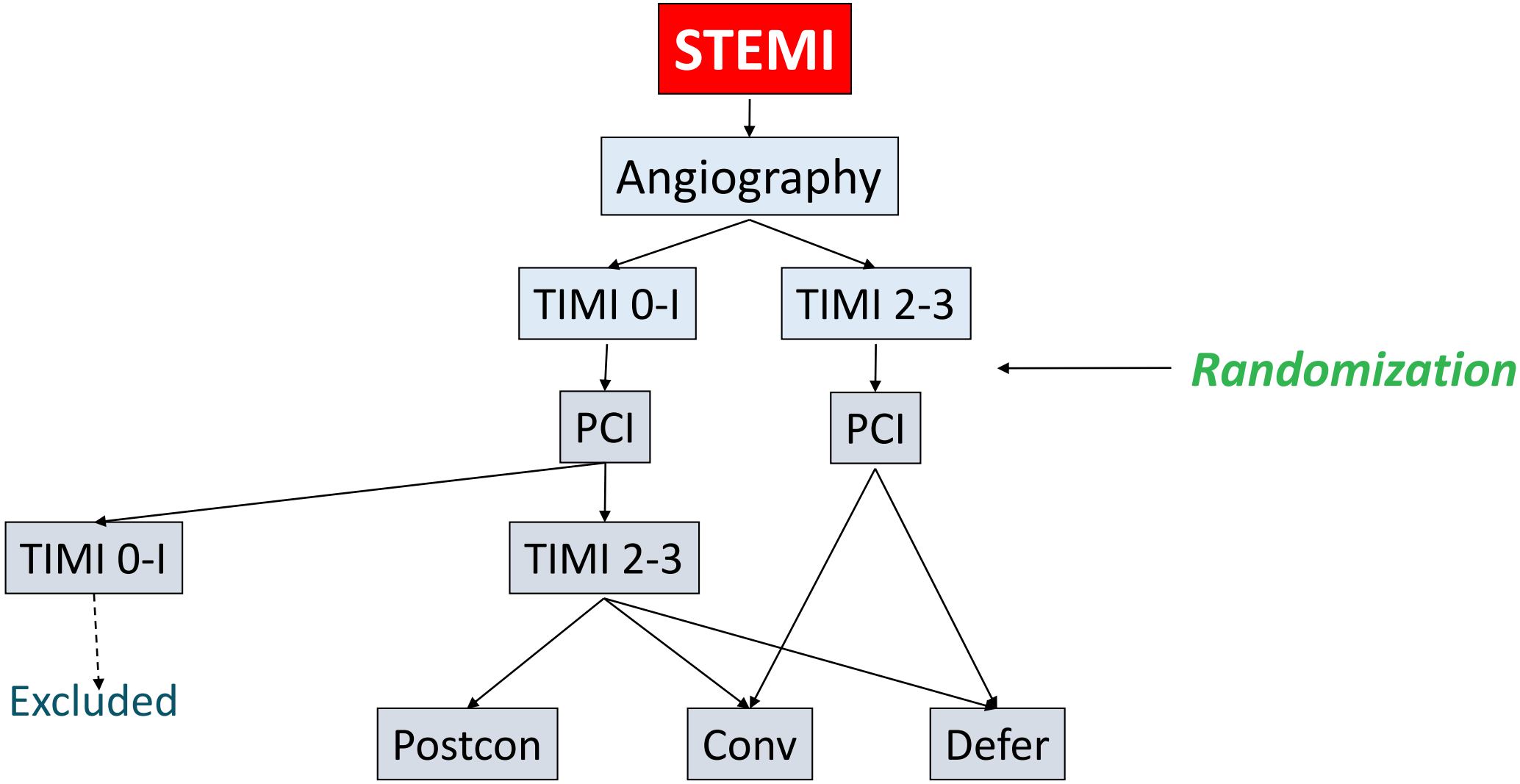
Inclusion criteria:

- chest pain of <12 hours' duration
- ST-segment elevation > 0·1 mV in at least 2 contiguous leads

Exclusion criteria Lancet 2016; 387(10034): 2199-2206

- Known intolerance of contrast media, anticoagulant or DAPT
- unconsciousness or cardiogenic shock
- stent thrombosis
- indication for acute CABG
- increased bleeding risk

Flow Chart DANAMI-3



Lancet 2016; 387(10034): 2199-2206

Primary Endpoints

A composite of:

- All cause mortality
- Hospitalization for heart failure
- Re-infarction
- Target vessel revascularization

Lancet 2016; 387(10034): 2199-2206

Methods

DEFER:

- **Minimal acute manipulation to restore stable flow in IRA**
- **Stent implantation 48 hours later**

Conventional PCI:

- **Immediate stent implantation**

Lancet 2016; 387(10034): 2199-2206

Procedural Data

	Conventional (n = 612)	DEFER (n = 603)
Median stent diameter (mm)	3·5	3·5
Median stent length (mm)	22	18 *
No stenting	3%	15%*
Use of GP-inhibitor or Bivalirudin	92%	93%
Thrombus aspiration	58%	63%
TIMI flow before PCI**		
0 - 1	38%	38%
2 - 3	62%	62%
TIMI flow after PCI**		
0 - 1	1·0%	1.0%
2 - 3	99%	99%

* P < 0.001 ** self-reported

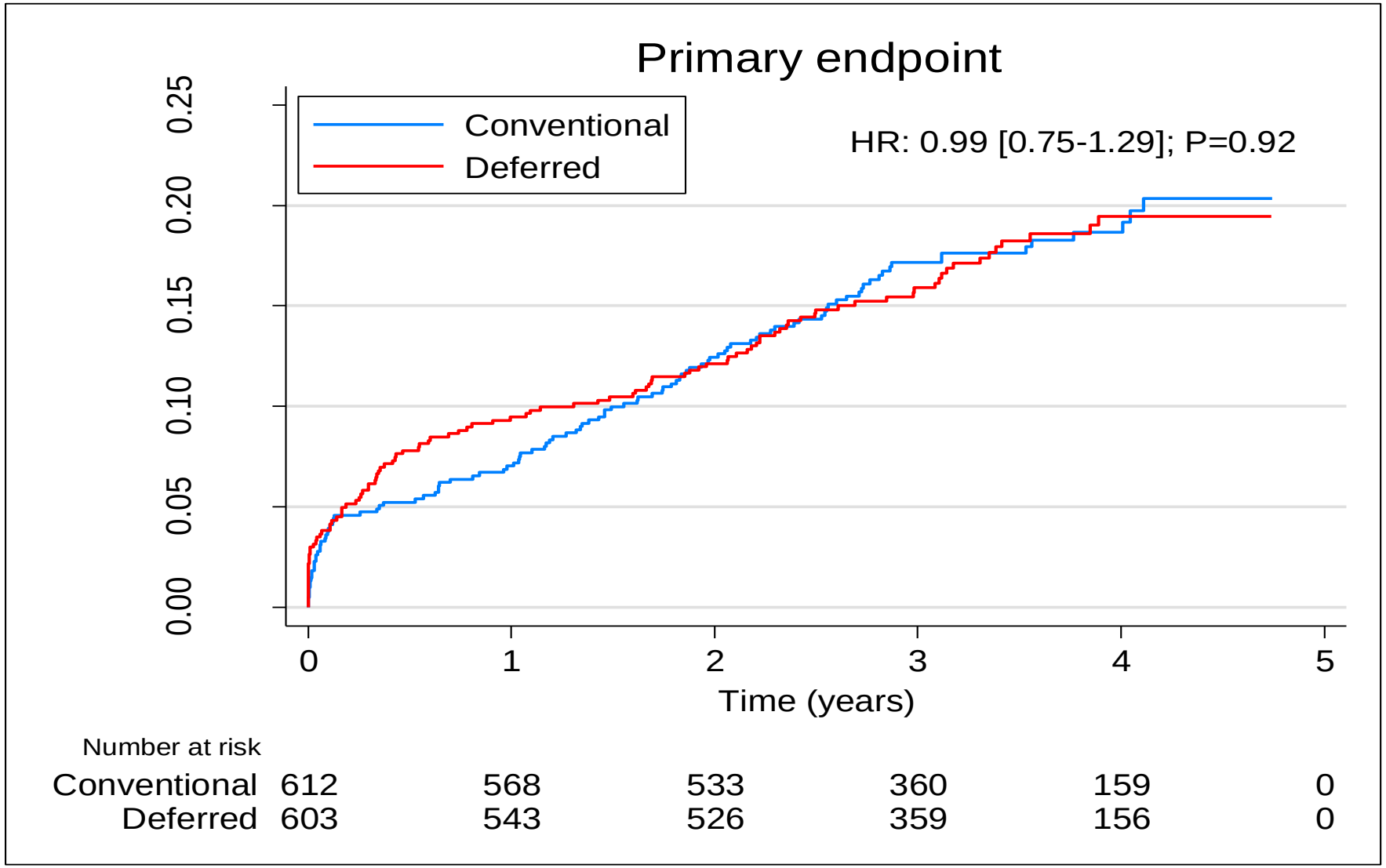
Lancet 2016; 387(10034): 2199-2206

Clinical Status at Discharge

	Conventional (n = 612)	DEFER (n = 603)
Killip Class II - IV at any time	7%	7%
Median LVEF	50%	50%
Medical treatment at discharge		
Antiplatelet drug		
Aspirin	98%	98%
Clopidogrel /Prasugrel/Ticagrelor	99%	99%
Statin	98%	98%
Betablocker	90%	92%
ACE inhibitor or ARB	44%	41%

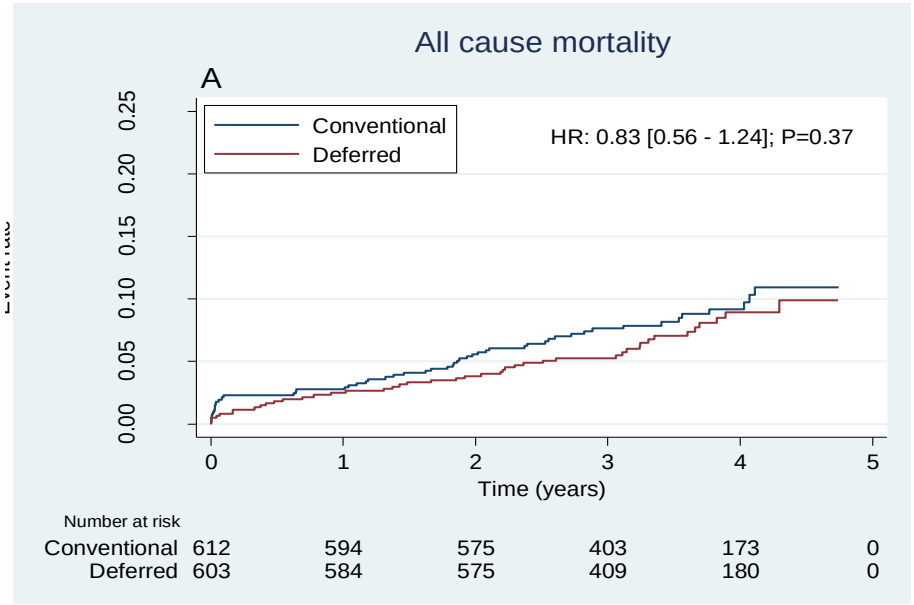
Lancet 2016; 387(10034): 2199-2206

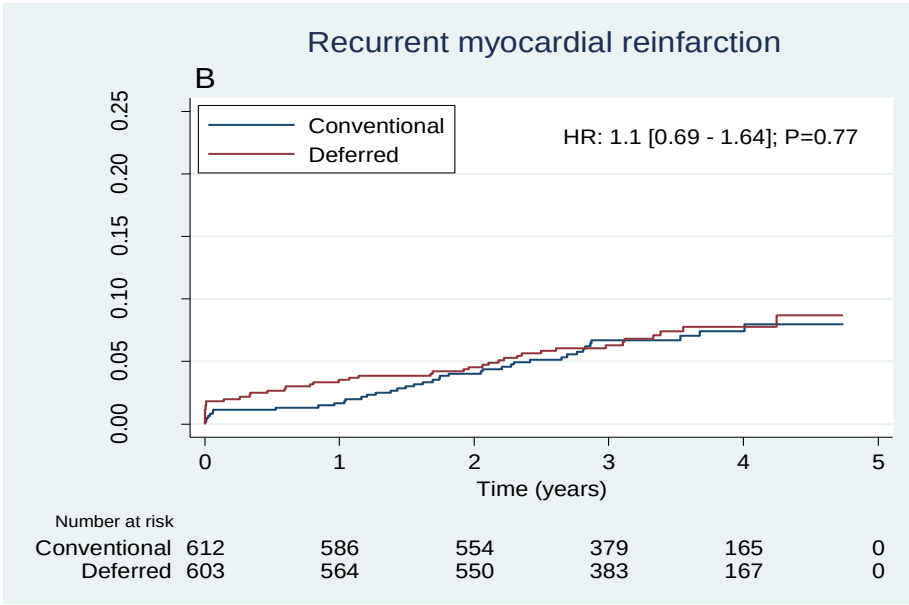
Primary Endpoint

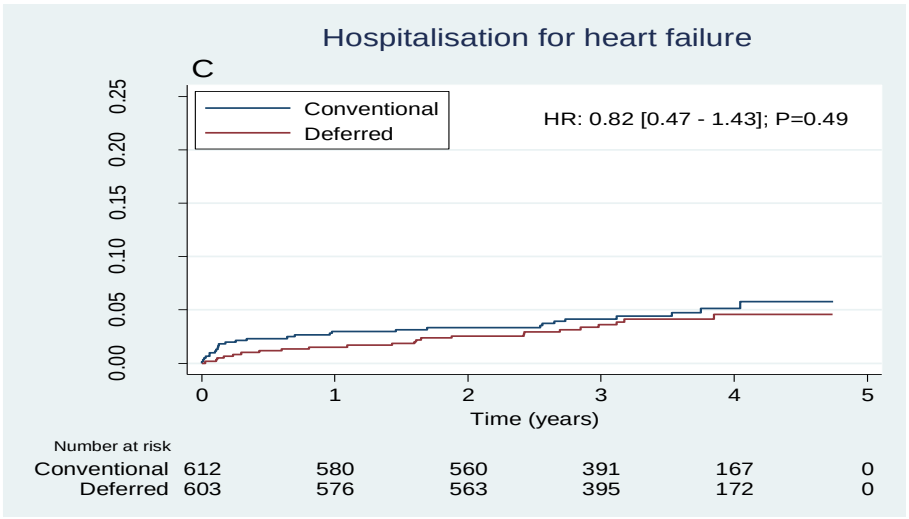


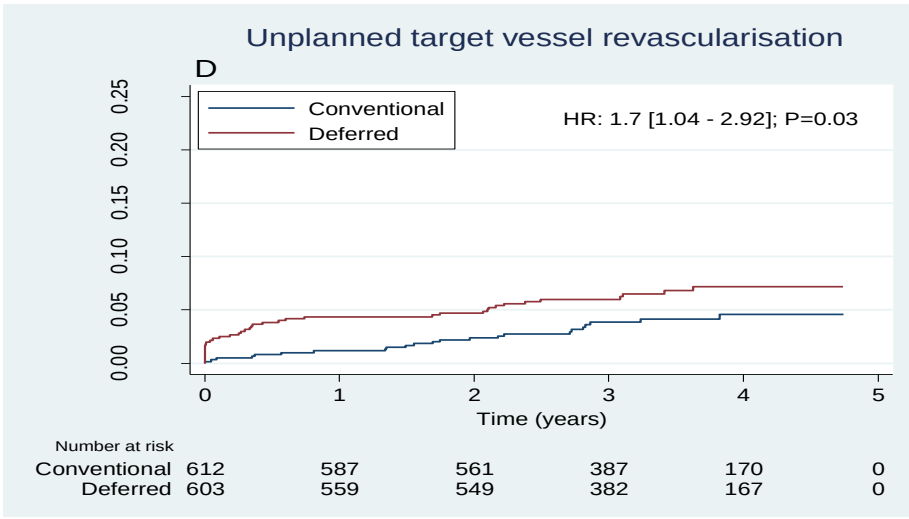
Lancet 2016; 387(10034): 2199-2206

Components of the primary endpoint



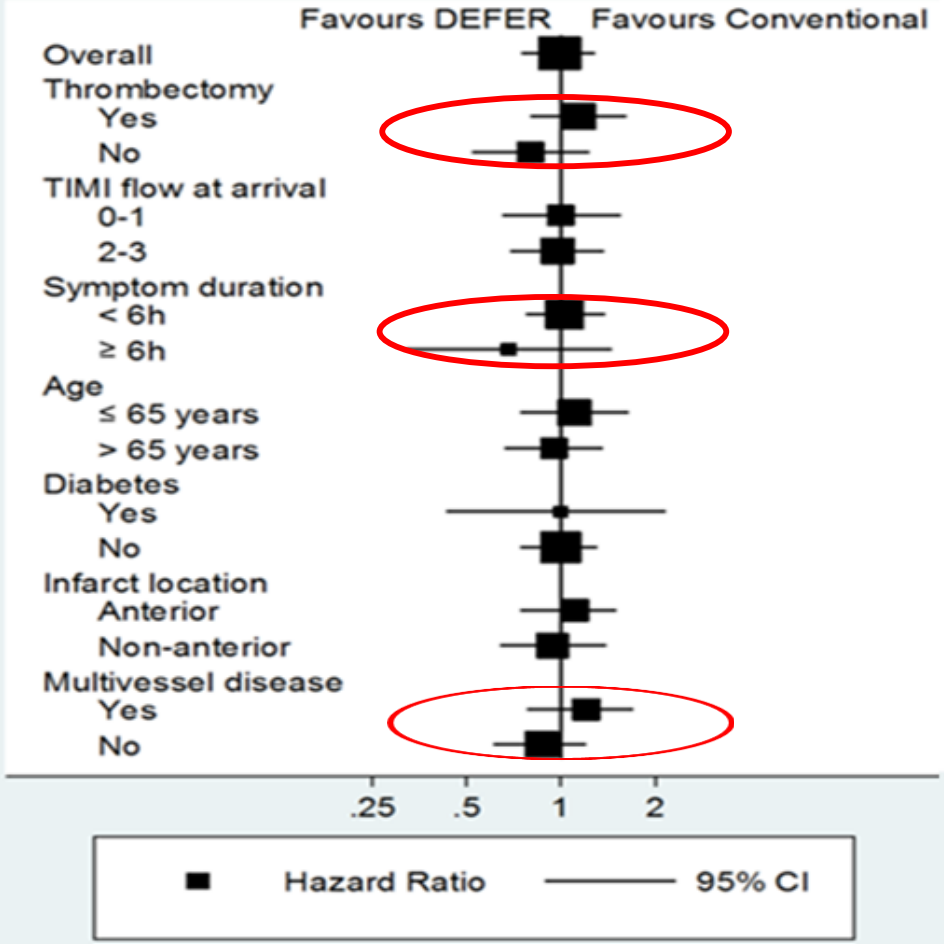






Lancet 2016; 387(10034): 2199-2206

Subgroup analysis



	Hazard ratio (95% CI)	$P_{interaction}$
Overall	0·99 (0·75 – 1·29)	
Thrombectomy		
Yes	1·14 (0·80 – 1·62)	0·20
No	0·80 (0·52 – 1·23)	
TIMI flow at arrival		
0-1	1.00 (0·65 - 1·55)	0.90
2-3	0·98 (0·69 – 1·37)	
Symptom duration		
< 6h	1·03 (0·77 - 1·39)	0.30
≥ 6h	0·68 (0·32 - 1·46)	
Age		
≤ 65 years	1·10 (0·74 - 1·64)	0·60
> 65 years	0·95 (0·66 - 1·36)	
Diabetes		
Yes	0·97 (0·43 - 2·15)	0·96
No	0·99 (0·74 - 1·31)	
Infarct location		
Anterior	1·07 (0·74 - 1·55)	0·64
Non-anterior	0·94 (0·64 - 1·38)	
Multivessel disease		
Yes	1·16 (0·78 - 1·74)	0·30
No	0·87 (0·61 - 1·25)	

Lancet 2016; 387(10034): 2199-2206

Secondary Endpoint

Left ventricular ejection fraction (LVEF) at 18 months			
	Conventional	DEFER	P
Median LVEF	57%	60%	0·04
No of patients with LVEF ≤45%	18%	13%	0·05

Lancet 2016; 387(10034): 2199-2206

Complications

Procedure-related MI, bleeding *, contrast-induced nephropathy or stroke occurred in

28 (5%) patients in the conventional group and

27 (4%) in the DEFER group

* Requiring blood transfusion or surgical intervention

Lancet 2016; 387(10034): 2199-2206

Conclusions

Deferred stent implantation in patients with STEMI did not reduce the risk of death, heart failure, or reinfarction compared with standard immediate stent implantation.

Left ventricular function and target vessel revascularization is slightly better after deferred stent implantation.

Lancet 2016; 387(10034): 2199-2206

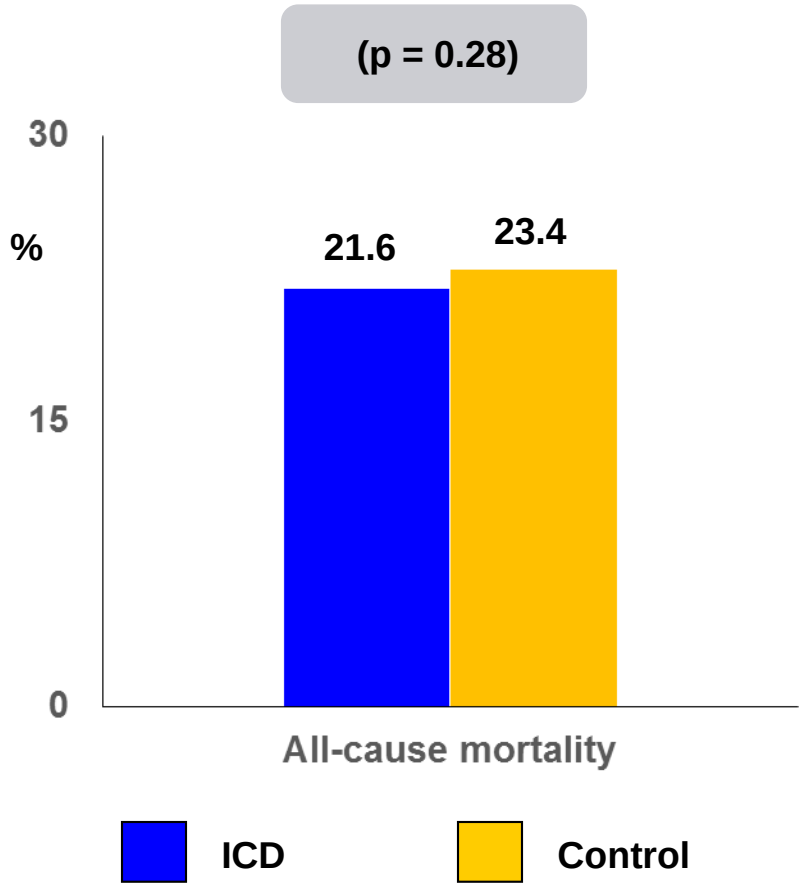
Defibrillator Implantation in Patients with Non-ischemic Systolic Heart Failure

Keber et al.

NEJM 2016

DANISH

Trial design: Patients with nonischemic cardiomyopathy were randomized to ICD implantation (n = 556) versus usual care (n = 560).



Results

- All-cause mortality: 21.6% of the ICD group versus 23.4% of the control group (p = 0.28)
- Younger patients (<59 years) appeared to derive greater benefit from ICD implantation versus older patients (p for interaction = 0.009)
- Sudden cardiac death: 4.3% versus 8.2%; respectively, for ICD versus control (p = 0.005)

Conclusions

- Among patients with a nonischemic cardiomyopathy, ICD implantation did not reduce long-term mortality compared with usual care; however, there was suggestion of benefit among younger patients

Køber L, et al. N Engl J Med 2016;375:1221-30

Non-invasive Lung IMPEDANCE-Guided Preemptive Treatment in Chronic Heart Failure Patients: a Randomized Controlled Trial (IMPEDANCE-HF trial)

Michael Kleiner Shochat, MD, BSc, PhD[a], Avraham Shotan, MD[a], David S Blondheim, MD[a], Mark Kazatsker, MD[a], Iris Dahan, MSIT[a], Aya Asif, MD[a], Yoseph Rozenman, MD[b], Ilia Kleiner, MD[c], Jean Marc Weinstein, MBBS, FRCP[c], Aaron Frimerman, MD[a], Lubov Vasilenko, MD[a], Simcha R Meisel, MD, MSc[a]

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American College of Cardiology. Chicago.
Late Braking Clinical Trial Session. Apr.04. 2016

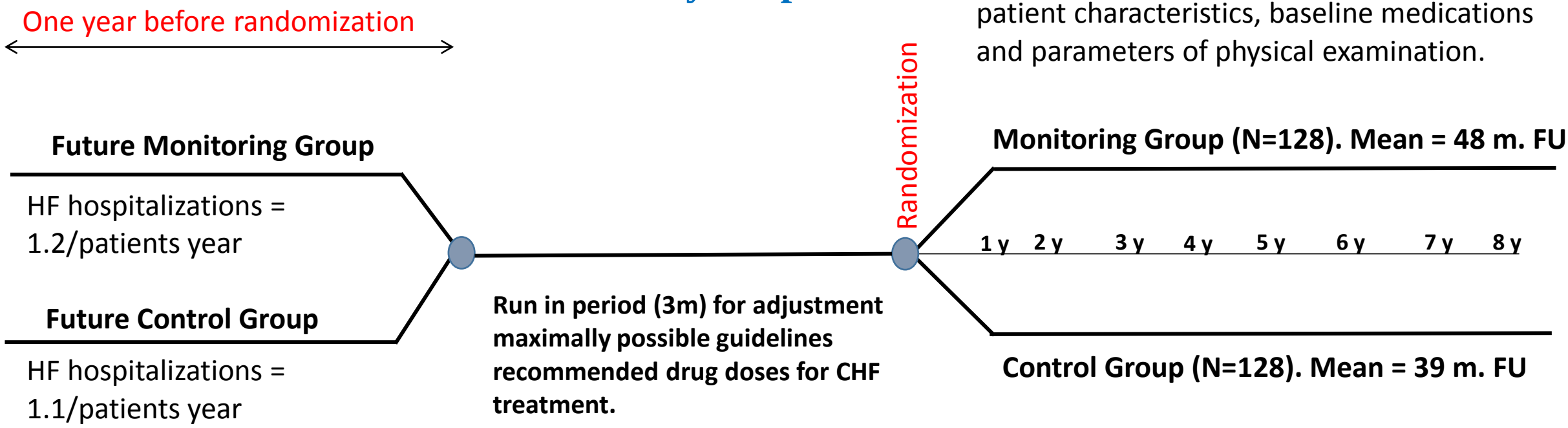
Presenter - Michael Kleiner Shochat

Now Published in the Journal of Cardiac Failure 2016 On Line

Conflict of interest: Michael Kleiner Shochat is a co-founder and member of the board of directors of the RSMM Company that manufactured and supplied the devices for the study.

Study design: Randomized, single blinded, two centers.
Study population.
Efficacy endpoints.

Mean age in both groups 67 y. Men – 80%. Both groups were well adjusted by baseline patient characteristics, baseline medications and parameters of physical examination.



Primary efficacy endpoints:

1. Acute heart failure hospitalizations up to 12 months.

2. Acute heart failure hospitalizations during entire follow up

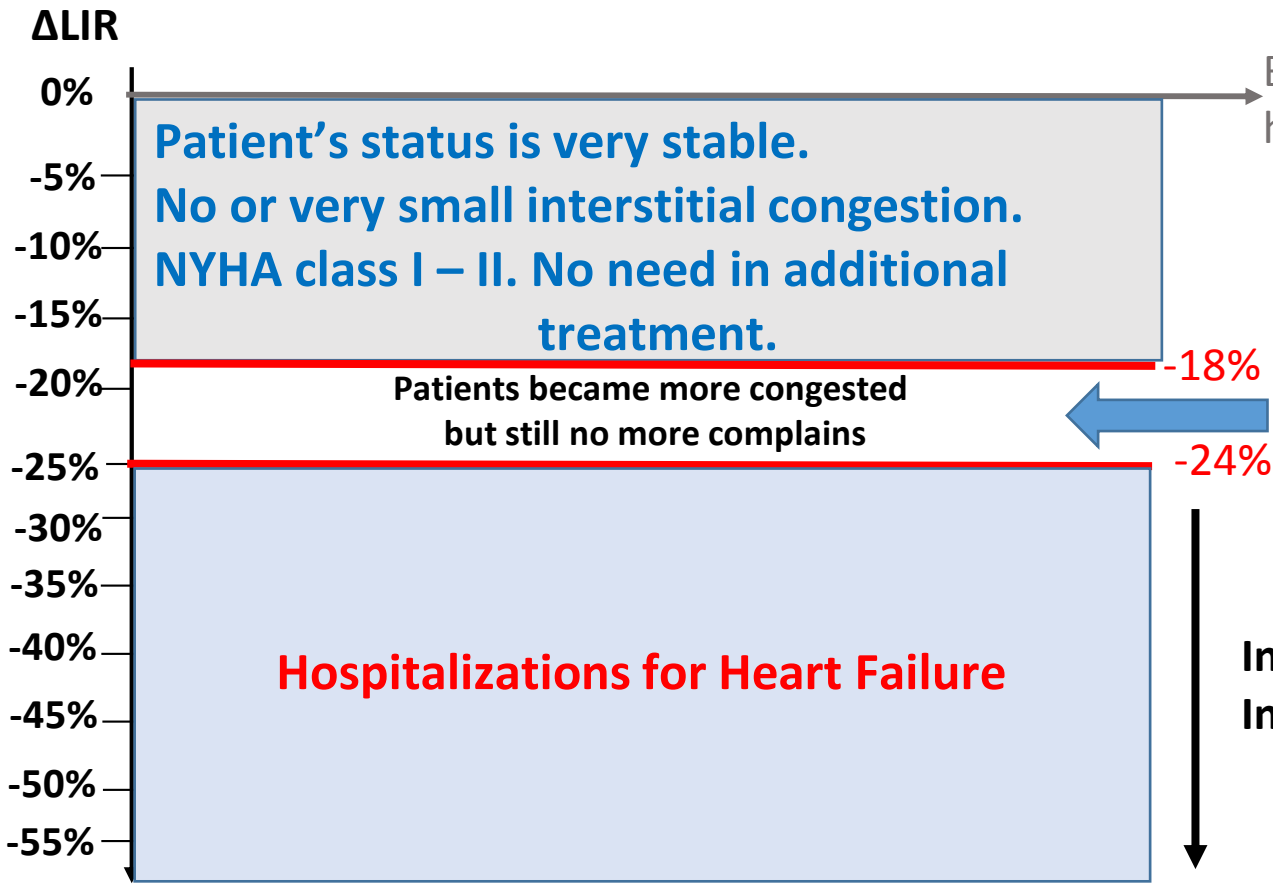
Secondary efficacy endpoints:

1. All –cause, Cardiac hospitalizations during entire follow up .

2. All-cause, Cardiac and Heart Failure mortality during entire follow up.

J. Card Failure 2016; http://dx.doi.org/10.1016/jcardfail.2016.03.015.

Strategy of drug adjustment



Baseline (dry) lung impedance (BLI). As if patient is healthy.

-18%

Target zone for adjustment treatment

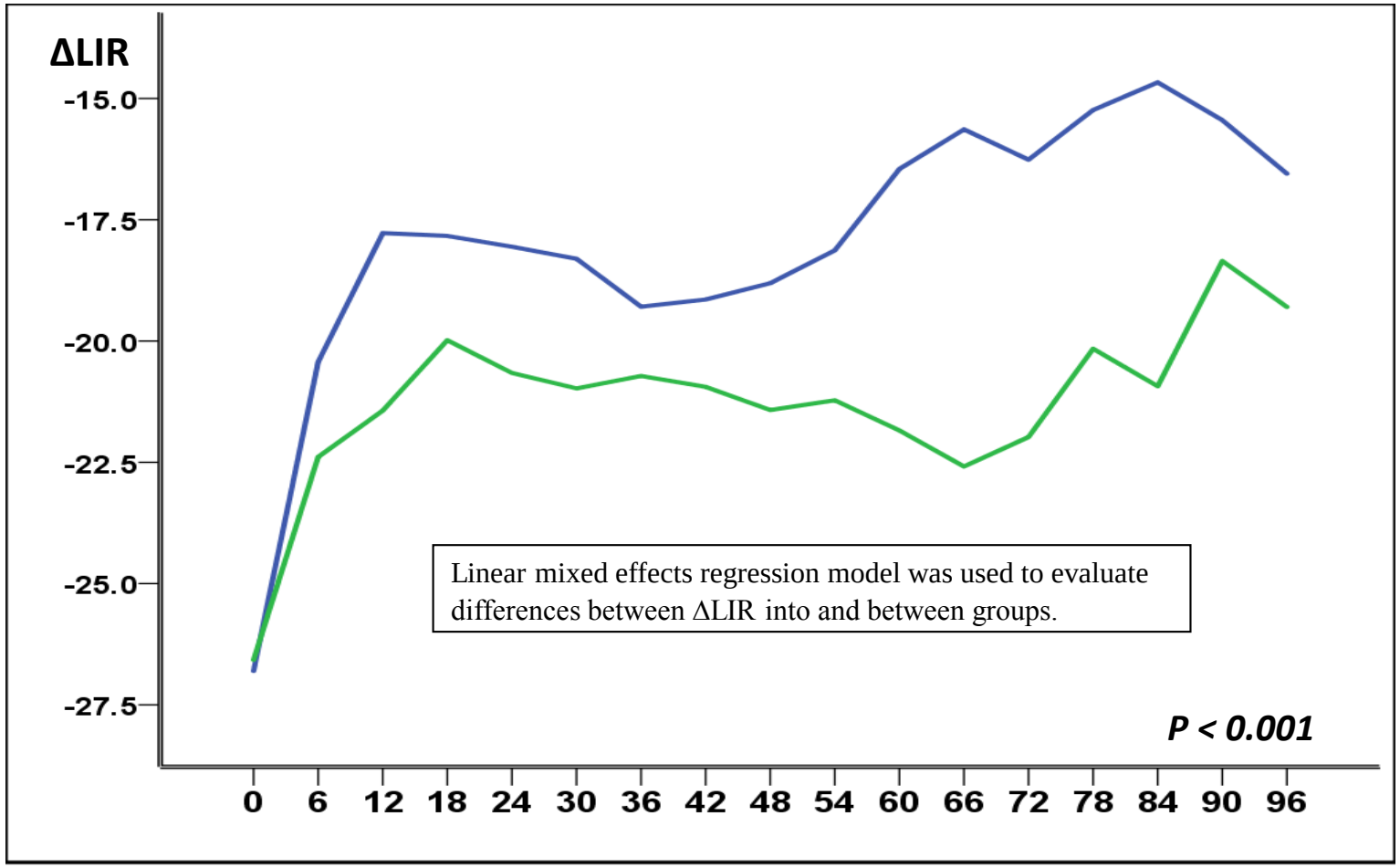
-24% Beginning Heart Failure hospitalizations

Increasing in congestions
Increased risk of Heart Failure hospitalizations

(ΔLIR) = [current LI/BLI)-1]

J. Card Failure 2016; http://dx.doi.org/10.1016/jcardfail.2016.03.015.

Results

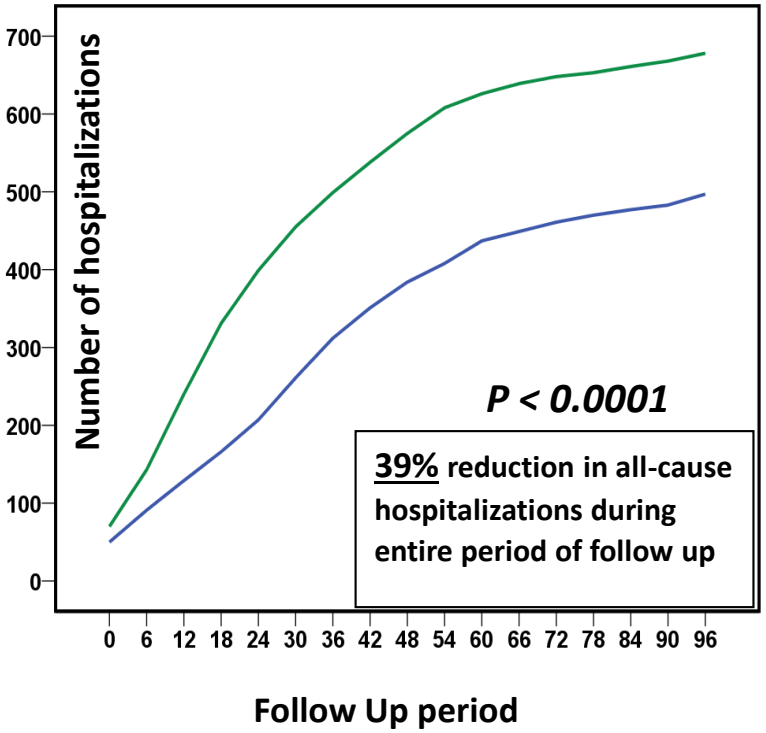


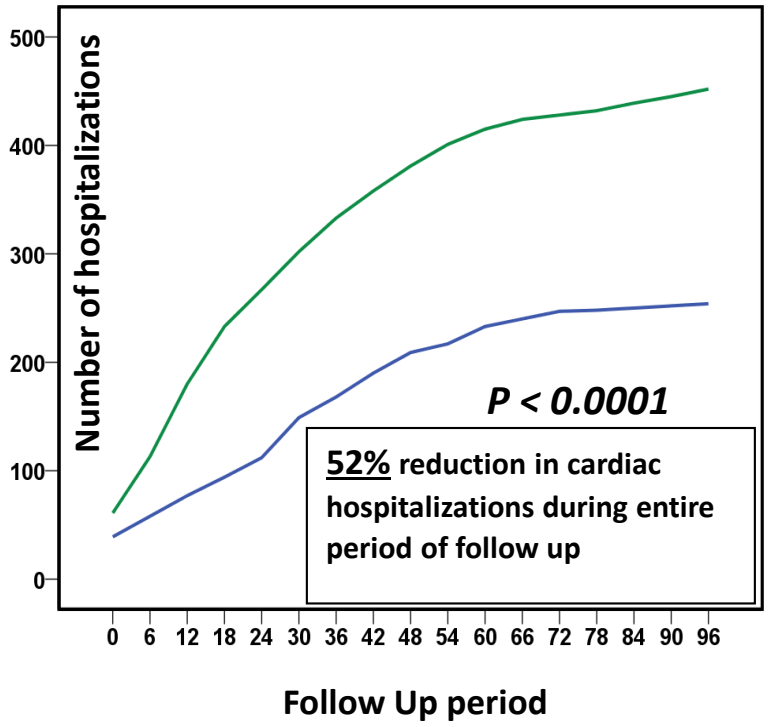
Difference in pulmonary congestion between groups during follow up period

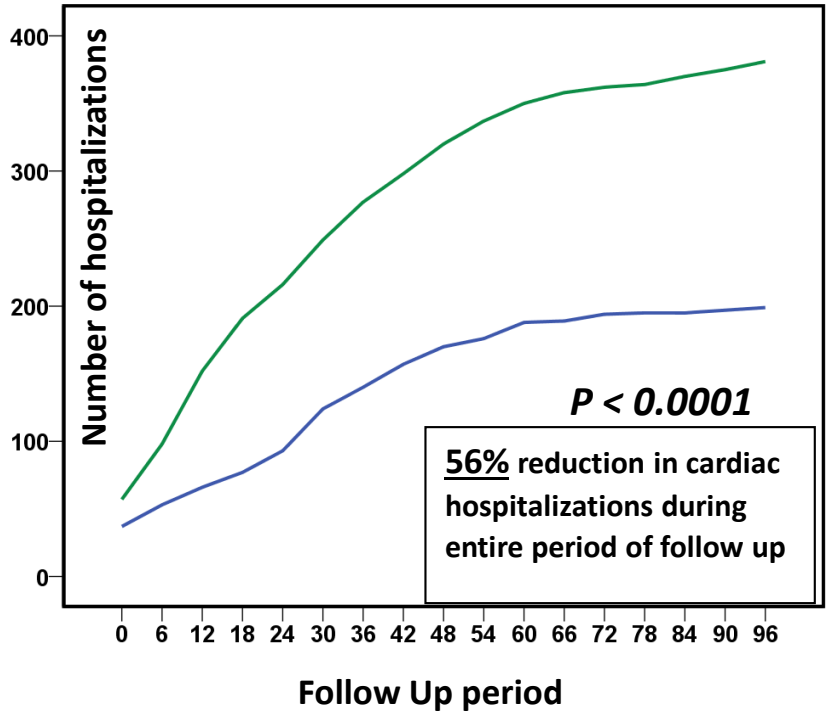
J. Card Failure 2016; http://dx.doi.org/10.1016/jcardfail.2016.03.015.

Results

Hospitalizations







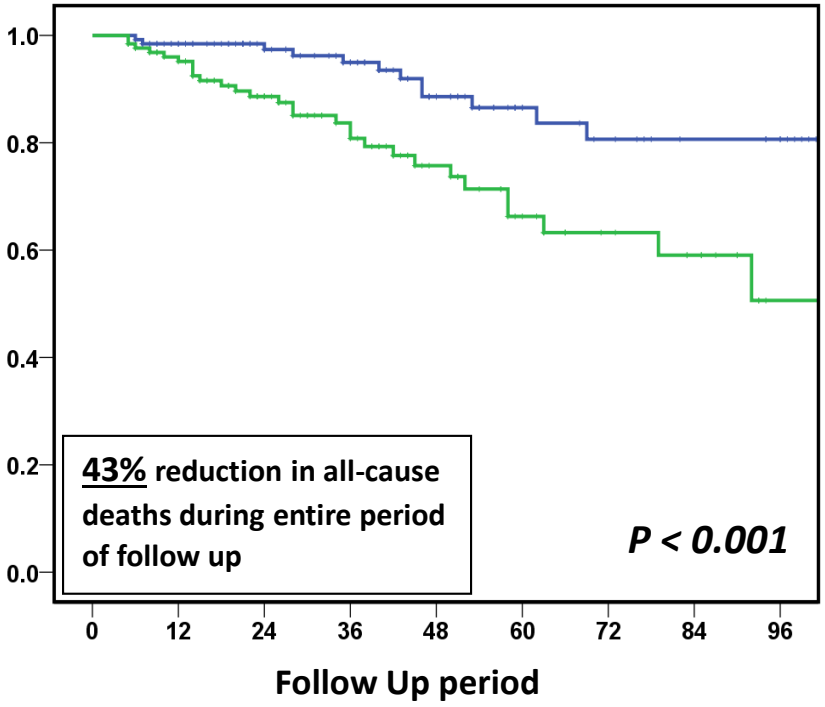
All-cause Hospitalizations ***Cardiac Hospitalizations*** ***Heart Failure Hospitalizations***

Method of statistics: Cox regression analyses

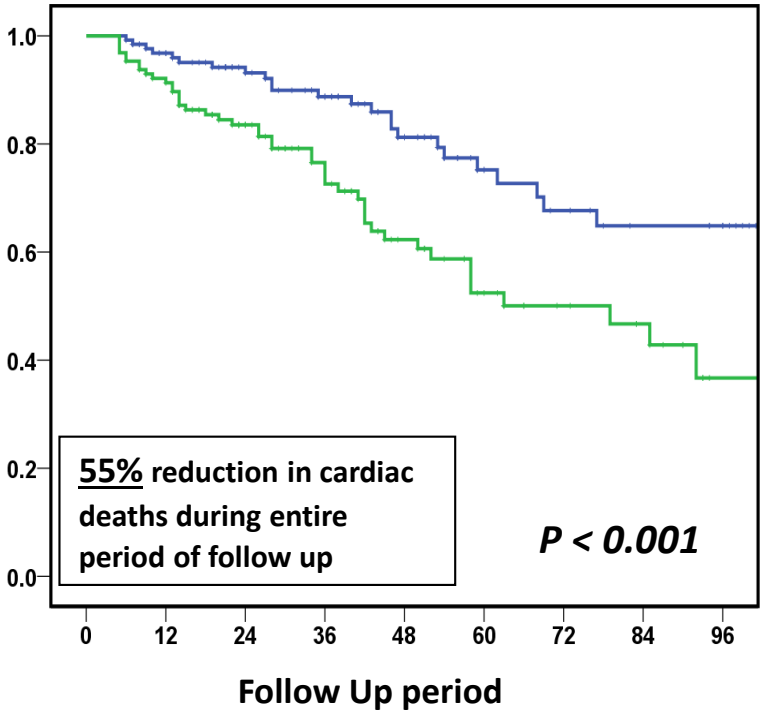
J. Card Failure 2016; http://dx.doi.org/10.1016/jcardfail.2016.03.015.

Results

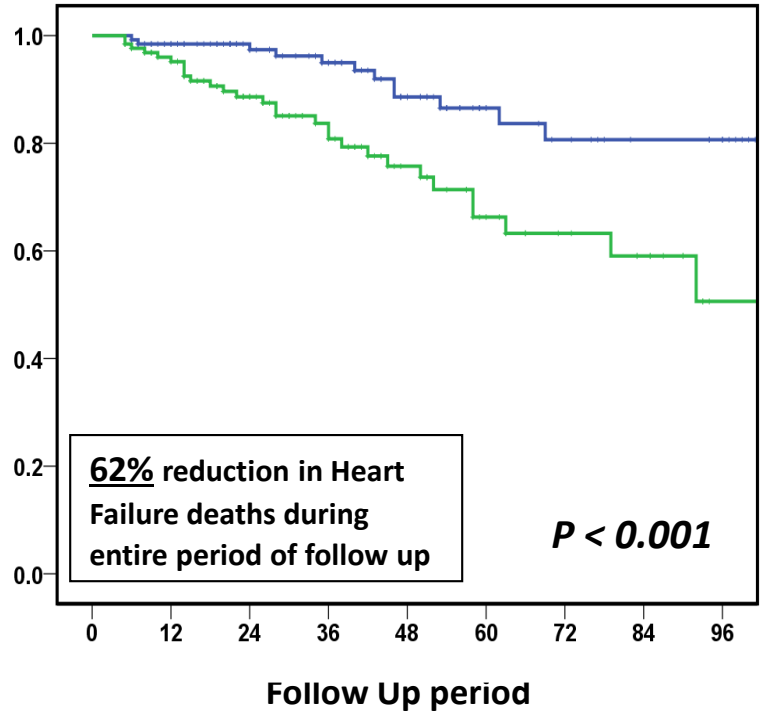
Mortality



All-cause Death



Cardiac Death



Heart Failure death

Method of statistics: Kaplan Meyer analyses

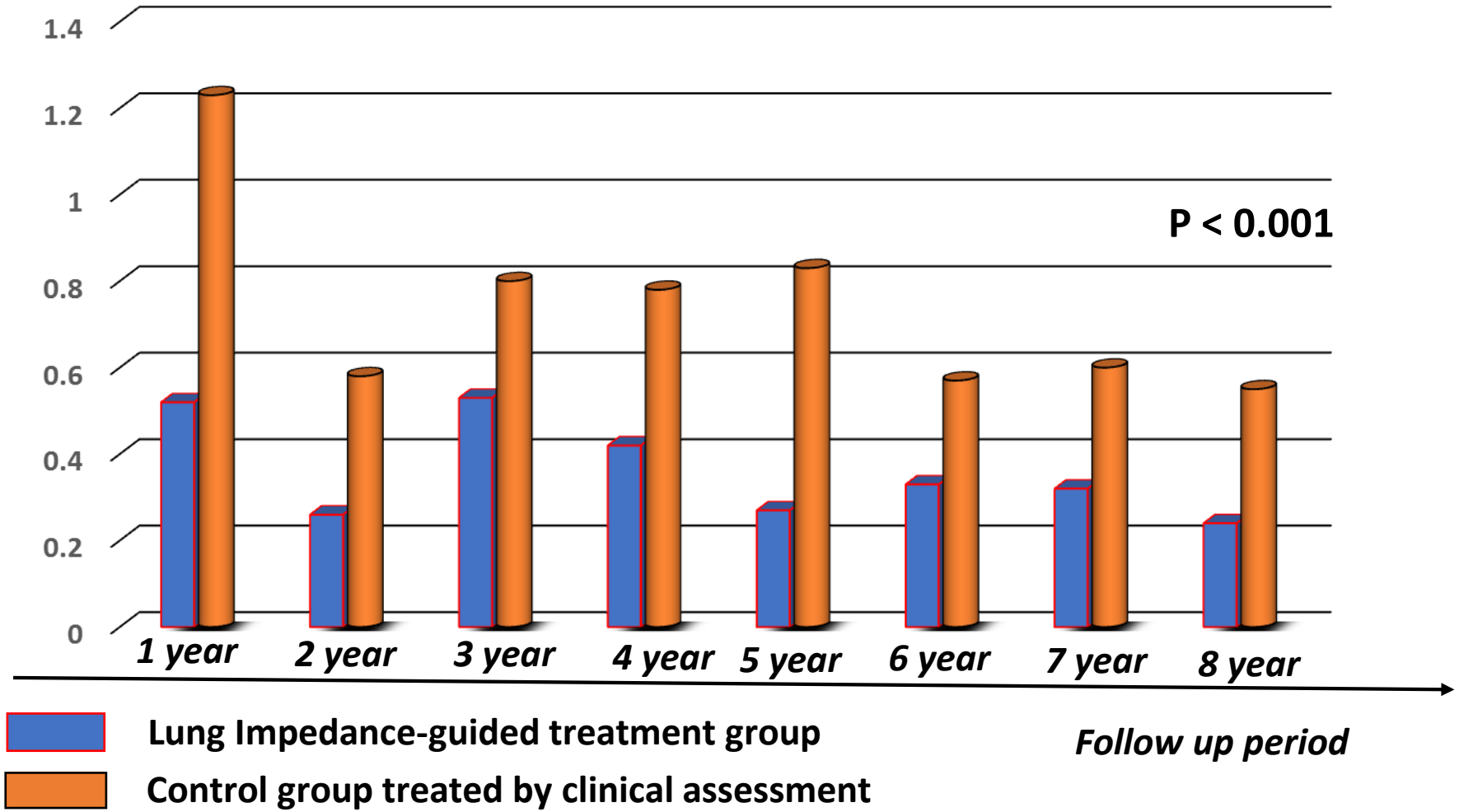
J. Card Failure 2016; http://dx.doi.org/10.1016/jcardfail.2016.03.015.

TABLE Drug modifications during entire follow up				
Medications	**Monitored Group**	**Control Group**	**p**	**Monitoring /Control group. Ratio of drug adjustment**
Rate of changes in medical therapy				
Total	**3166 (6.2)†**	**1244 (3.0)†**	**<0.05**	**2.1 times**
Diuretics	**1530 (48%)‡**	**515 (42%)‡**	**<0.05**	
Diuretics	**1530 (3.0)†**	**515 (1.3)†**	**<0.05**	**2.3 times**
Beta Blockers	**792 (25%)‡**	**303 (24%)‡**	**<0.05**	
Beta Blockers	**792 (1.6)†**	**303 (0.7)†**	**<0.05**	**2.3 times**
ACE inh /ARB	**410 (13%)‡**	**142 (11%)‡**	**<0.05**	
ACE inh /ARB	**410 (0.8)†**	**142 (0.3)†**	**<0.05**	**2.7 times**
Nitrates	**166 (5%)‡**	**78 (6%)‡**	**<0.05**	
Nitrates	**166 (0.3)†**	**78 (0.2)†**	**<0.05**	**1.5 times**
MRA	**154 (5%)‡**	**144 (12%)‡**	**NS**	
MRA	**154 (0.3)†**	**144 (0.4)†**	**NS**	**0.9 times**
Digoxin	**114 (4%)‡**	**62 (5%)‡**	**<0.05**	
Digoxin	**114 (0.2)†**	**62 (0.15)†**	**<0.05**	**1.5 times**

J. Card Failure 2016; http://dx.doi.org/10.1016/jcardfail.2016.03.015.

Results

Rate of Heart Failure hospitalizations (per patient*year)



J. Card Failure 2016; http://dx.doi.org/10.1016/jcardfail.2016.03.015.

Conclusions

Data of "IMPEDANCE-HF" trial shows that Lung Impedance guided treatment in compare with treatment based on clinical assessment of HFrEF patients:

Hospitalizations (Primary endpoint)

1. ***Reduces rate of HF hospitalizations during first year by 58%.***
2. ***Reduces rate of HF hospitalizations during 4 years by 56%.***

Hospitalizations (Secondary endpoint)

3. ***Reduces rate of all-cause hospitalizations during 4 years by 39%.***
4. ***Reduces rate of cardiac hospitalization during 4 years by 52%.***
5. ***Reduces rate of Non-cardiac hospitalization during 4 years by 9%, (p=0.6).***

Deaths (Secondary endpoint)

7. ***Reduces rate of All-cause mortality during 4 years by 43%.***
8. ***Reduces rate of Cardiac mortality during 4 years by 55%.***
9. ***Reduces rate of Heart Failure mortality during 4 years by 62%.***
10. ***No changes in Non-cardiac mortality during 4 years.***

J. Card Failure 2016; http://dx.doi.org/10.1016/jcardfail.2016.03.015.

These results support

Non-invasive Lung Impedance technology is enough sensitive to detect a very early stage of evolving pulmonary congestion and Lung Impedance-guided treatment is reliable for improving hospitalization and survival of Heart Failure patients.

Thank you very much for attention!

J. Card Failure 2016; http://dx.doi.org/10.1016/jcardfail.2016.03.015.