Heart Failure Facts

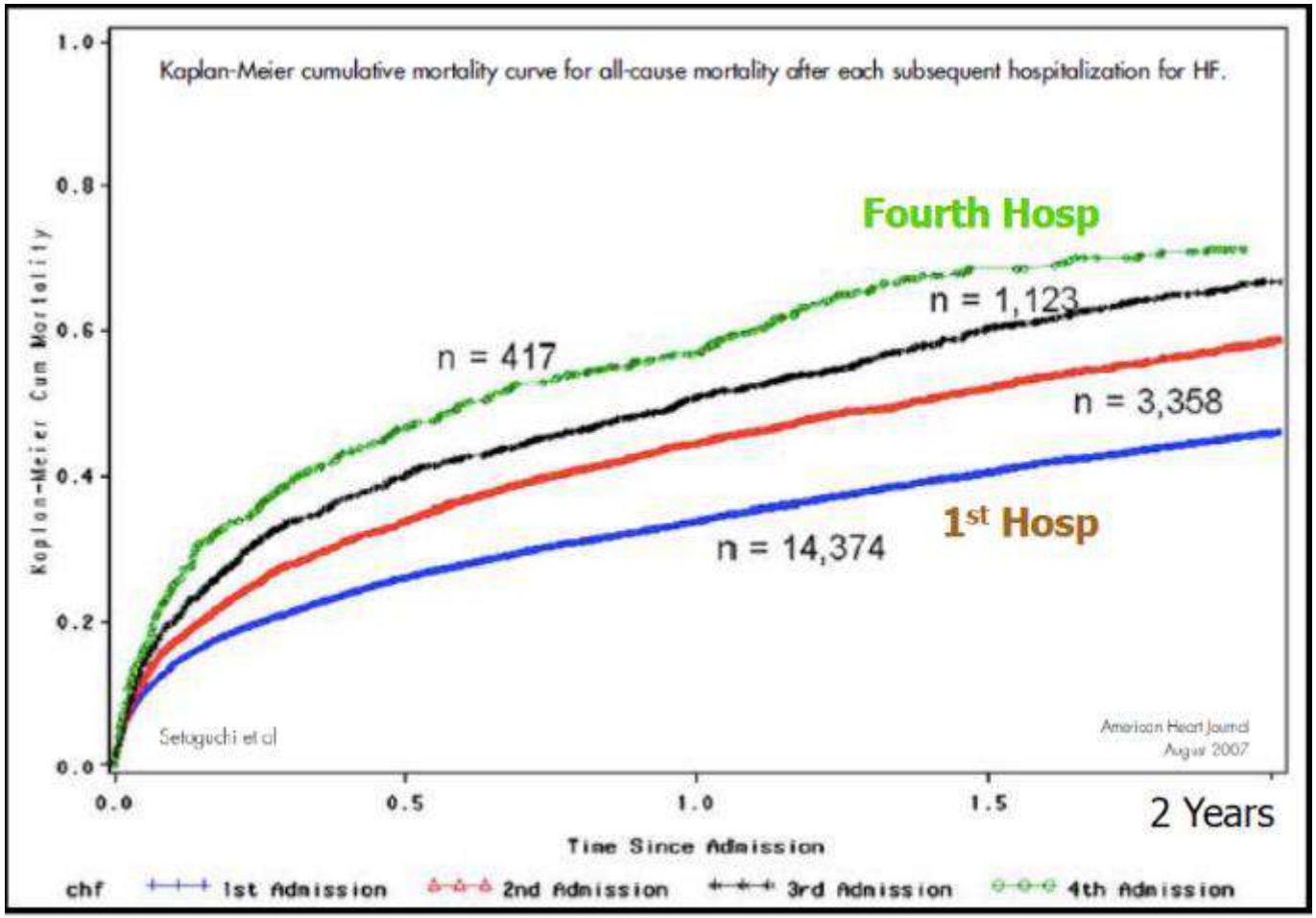
- The primary economical and social burden of HF syndrome is hospitalization rate whose **costs represent the highest ones ($40B per year in USA) within the entire health care management** [1].

- Approximately **80% of HF hospital admissions are driven by pulmonary congestion symptoms** [2].

1. 2014 American Heart Association Heart and Stroke Statistics.

2. O'Connor CM J Cardiac Fail 2005; 11: 200-205

Worsening Outlook After Each HF Admission



Il perché di una Società Scientifica dedicata ai temi dello Scompenso CV

Gianfranco Gensini

ELSEVIER

The European Journal of Heart Failure 7 (2005) 343–349

The European Journal of Heart Failure

www.elsevier.com/locate/heafai

Review

Health care professionals in a heart failure team

Tiny Jaarsma

Department of Cardiology, University Medical Centre Groningen, Groningen, The Netherlands

Received 18 May 2004; received in revised form 21 October 2004; accepted 11 January 2005

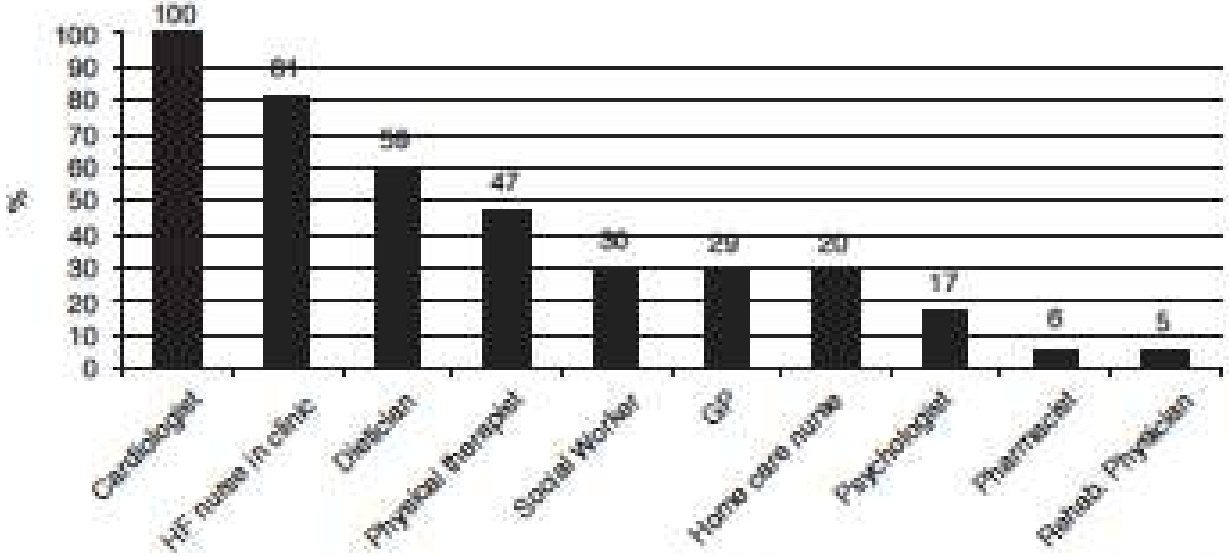


Fig. 1. Health care professionals involved in heart failure clinics in the Netherlands in 2003 (n=83*); *(85 hospitals had a HF clinic but 2 hospitals did not complete these data).

INTER-PROFESSIONAL TEAM APPROACH TO PATIENTS WITH HEART FAILURE

Tiny Jaarsma

Heart 2005; **91**:832–838. doi: 10.1136/hrt.2003.025296

Take the online multiple choice questions associated with this article (see page 846)

In most developed countries worldwide, the number of patients with chronic heart failure is growing, with 1–3% of the adult population suffering from this syndrome, rising to about 10% in the very elderly. Because the incidence of heart failure increases with age, its prevalence will

Need for inter-professional team approach

- Health care providers
  - complexity of diagnosis of heart failure
  - complexity of heart failure treatment
  - co-morbidities
- Patients
  - elderly
  - coping with complex lifestyle changes
  - possible impaired cognitive function and/or depression

Tiny Jaarsma

Heart 2005; **91**:832–838. doi: 10.1136/hrt.2003.025296

Table 3 Components of multidisciplinary care

- Appropriate diagnosis
  - assess severity of symptoms
  - determine aetiology
- Optimal medical management
- Intense education and counselling
- Discharge planning
- Vigilant follow up
- Attention to behavioural strategies
- Address barriers to compliance
- Early attention to signs and symptoms (for example, daily weighing, telemonitoring)
- Flexible diuretic regimen
- Increased access to health care providers
- Exercise programme

Tiny Jaarsma

Heart 2005; **91**:832–838. doi: 10.1136/hrt.2003.025296

15 **Rich MW, Beckham V, Wittenberg C, et al. A multidisciplinary intervention to prevent readmission of elderly patients with congestive heart failure.**
N Engl J Med 1995;333:1190–5.
First properly powered randomised study of a multidisciplinary intervention in heart failure.
16 **McDonald K, Ledwidge M, Cahill J, et al. Elimination of early rehospitalization**
in a randomized, controlled trial of multidisciplinary care in a high-risk, elderly heart failure population: the potential contributions of specialist care,
clinical stability and optimal ACE-inhibitor dose at discharge. Eur J Heart Fail
2001;3:209–15.
Irish study reporting a very high success of a multidisciplinary intervention.

Tiny Jaarsma

Heart 2005;**91**:832–838. doi: 10.1136/hrt.2003.025296

Il perché di una Società Scientifica dedicata ai temi dello Scompenso CV

Gianfranco Gensini

ITAlian Heart Failure Association

-
- **1)** …E' costituita…una associazione denominata: **ITAHFA – the Italian Heart Failure Association**, con sede in Firenze, viale Matteotti n. 60.
- 2) **Gli scopi perseguiti dall'associazione sono: promuovere una politica pubblica atta a:**
- **migliorare le cure dei cittadini affetti da scompenso cardiaco o a rischio di averlo,**
- **ridurne l'incidenza e la prevalenza nella popolazione e il numero delle morti,**
- **consentirne quanto più possibile una gestione extraospedaliera del paziente, in sicurezza e grazie a moderne tecnologie,**
- **migliorare la qualità di vita dei pazienti.**

- **armonizzazione sul territorio nazionale della gestione del paziente con scompenso cardiaco, attraverso la realizzazione di linee guida, protocolli e programmi inerenti la specifica patologia,**

ITAHFA
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- Massimo Fini — **Geriatria** IRCCS
- Gino Gerosa — **Cardiochirurgia** Universitaria
- Gian Franco Gensini — **Medicina Interna**, Cardiologia
- Michele M. Gulizia — **Cardiologia** Ospedaliera – Fondazione per il Tuo Cuore
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- Marco Metra — **Cardiologia** Universitaria
- Alessandro Mugelli — **Farmacologia** Cardiovascolare
- Carlo Nozzoli — **Medicina Interna** Ospedaliera
- Ugo Oliviero — **Cardiologia** Territoriale
- Giuseppe Rosano — **Cardiologia** Universitaria
- Francesco Rossi — **Farmacologia** Cardiovascolare
- Giorgio Vescovo — **Medicina Interna** Ospedaliera
- Maurizio Volterrani — **Riabilitazione** cardiovascolare
-

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- Maurizio Volterrani — **Riabilitazione** cardiovascolare
-

Trattamento farmacologico dello scompenso cardiaco cronico. Modifiche e sfide principali

G. Rosano, G.F. Gensini

ESC Classes of recommendations

Classes of recommendations	Definition	Suggested wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended/is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	*Weight of evidence/opinion is in favour of usefulness/efficacy.*	Should be considered
Class IIb	*Usefulness/efficacy is less well established by evidence/opinion.*	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

ESC Levels of Evidence

Level of evidence A	**Data derived from multiple randomized clinical trials or meta-analyses.**
Level of evidence B	**Data derived from a single randomized clinical trial or large non-randomized studies.**
Level of evidence C	**Consensus of opinion of the experts and/ or small studies, retrospective studies, registries.**

ESC Heart Failure Guidelines: what is new

Objectives in the management of heart failure

- **Reduce mortality**
- **Improve**
  - clinical status
  - functional capacity
  - quality of life, prevent hospital admission

- **Preventing HF hospitalization and improving functional capacity are important benefits to be considered in chronic heart failure**

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Pharmacological treatments indicated in patients with symptomatic (NYHA Class II-IV) HFrEF

Recommendations	Class [a]	Level [b]
An ACE-I[d] is recommended, in addition to a beta-blocker, for symptomatic patients with HFrEF to reduce the risk of HF hospitalization and death.	I	A
A beta-blocker is recommended, in addition an ACE-I[d], for patients with stable, symptomatic HFrEF to reduce the risk of HF hospitalization and death.	I	A
An MRA is recommended for patients with HFrEF, who remain symptomatic despite treatment with an ACE-I[d] and a beta-blocker, to reduce the risk of HF hospitalization and death.	I	A

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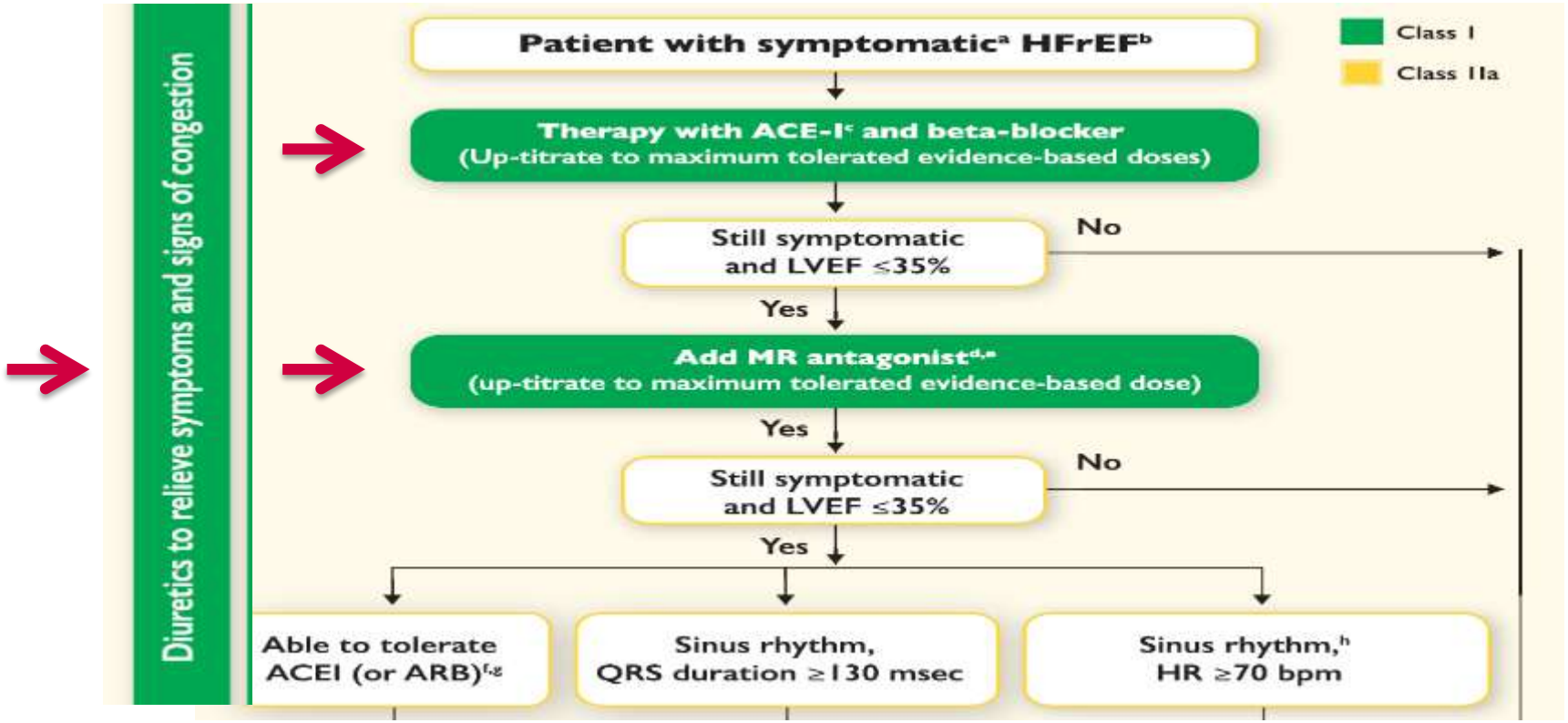
Therapeutic algorithm for a patient with symptomatic HF with reduced ejection fraction.



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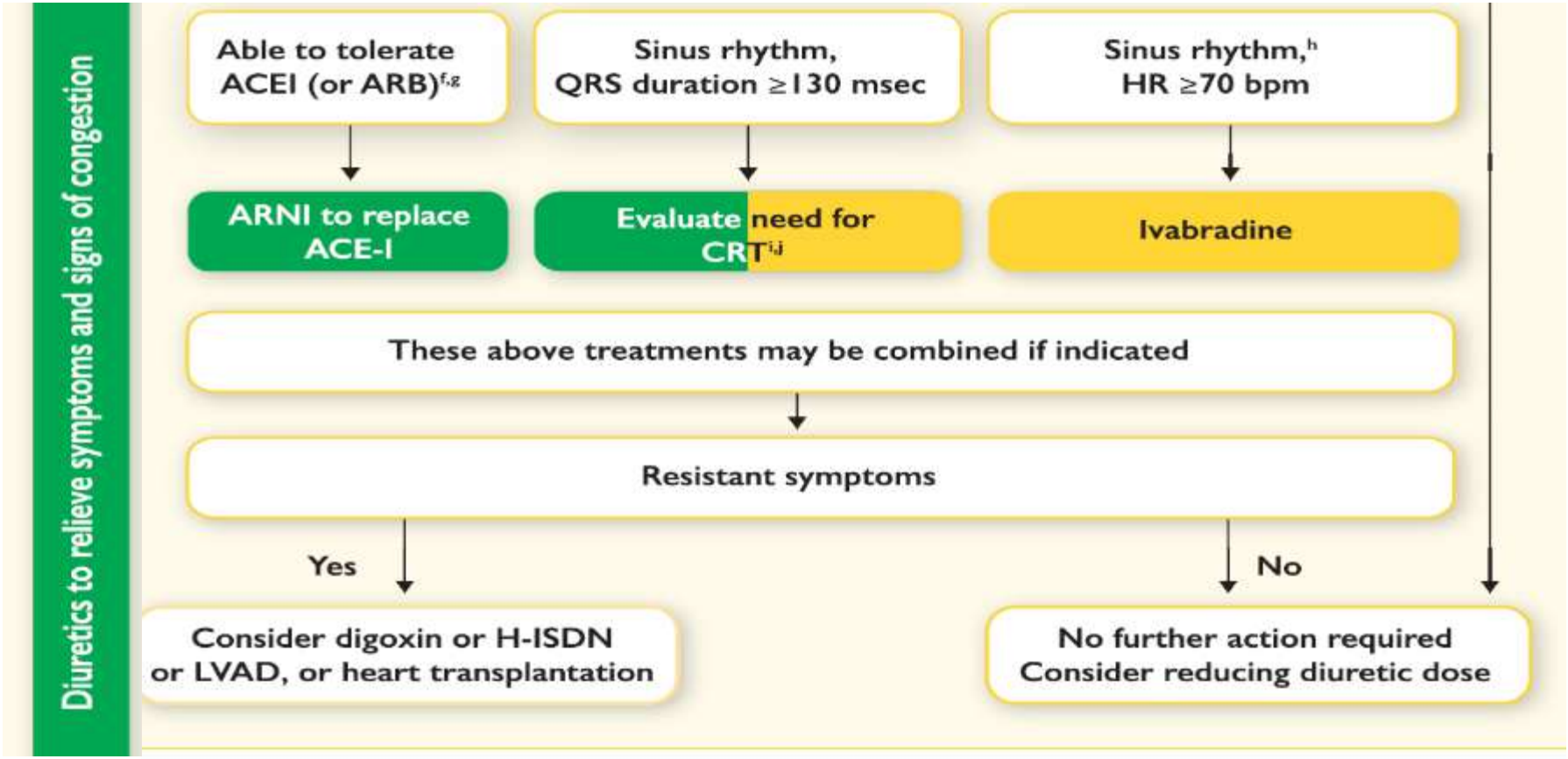
Therapeutic algorithm for a patient with symptomatic HF with reduced ejection fraction. (cont..)



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Angiotensin receptor neprilysin inhibitor (Sacubitril/Valsartan)

- LCZ 696 is indicated in patients with:
  - ambulatory, symptomatic HFrEF
  - LVEF ≤35%
  - elevated plasma NP levels (BNP ≥150 pg/mL or NT-proBNP ≥600 pg/mL)
  - estimated GFR (eGFR) ≥30 mL/min/1.73 m2 of body surface area
  - who are able to tolerate treatment with enalapril (at least 10 mg b.i.d.)

- Some relevant safety issues remain when initiating therapy with this drug in clinical practice:
  - symptomatic hypotension
  - risk of angioedema (ACEI should be withheld for at least 36 h before initiating LCZ696)
  - concerns about its effects on the degradation of beta-amyloid peptide in the brain

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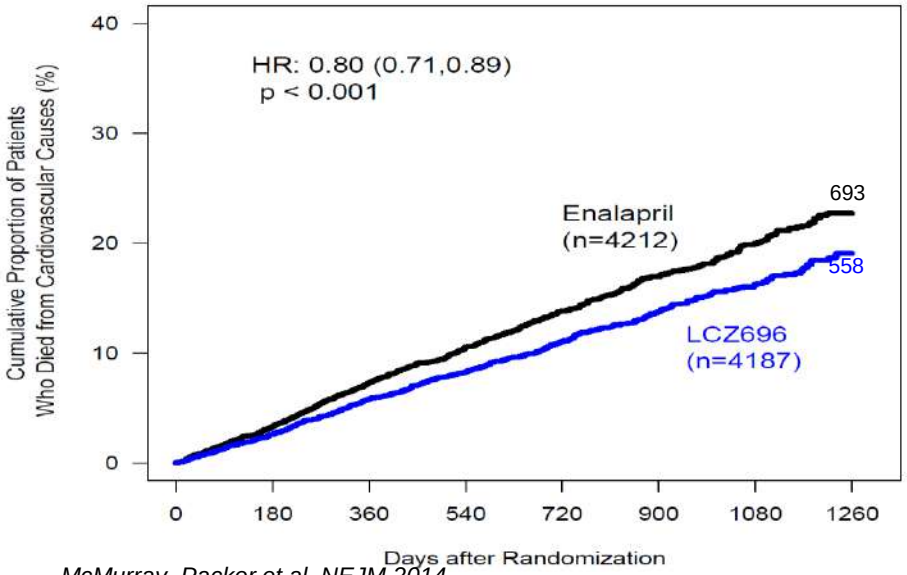
PARADIGM-HF

Prospective comparison of ARNI with ACEI to Determine Impact on Global Mortality and morbidity in Heart Failure trial

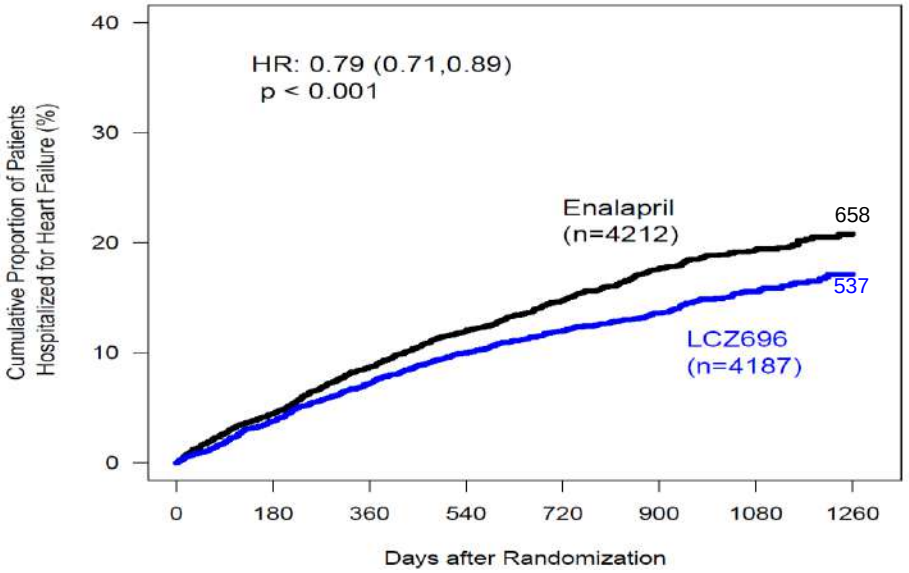
Primary composite outcome
HR: 0.80 (0.73, 0.87)

Death from CV causes



McMurray, Packer et al NEJM 2014

HF hospitalization



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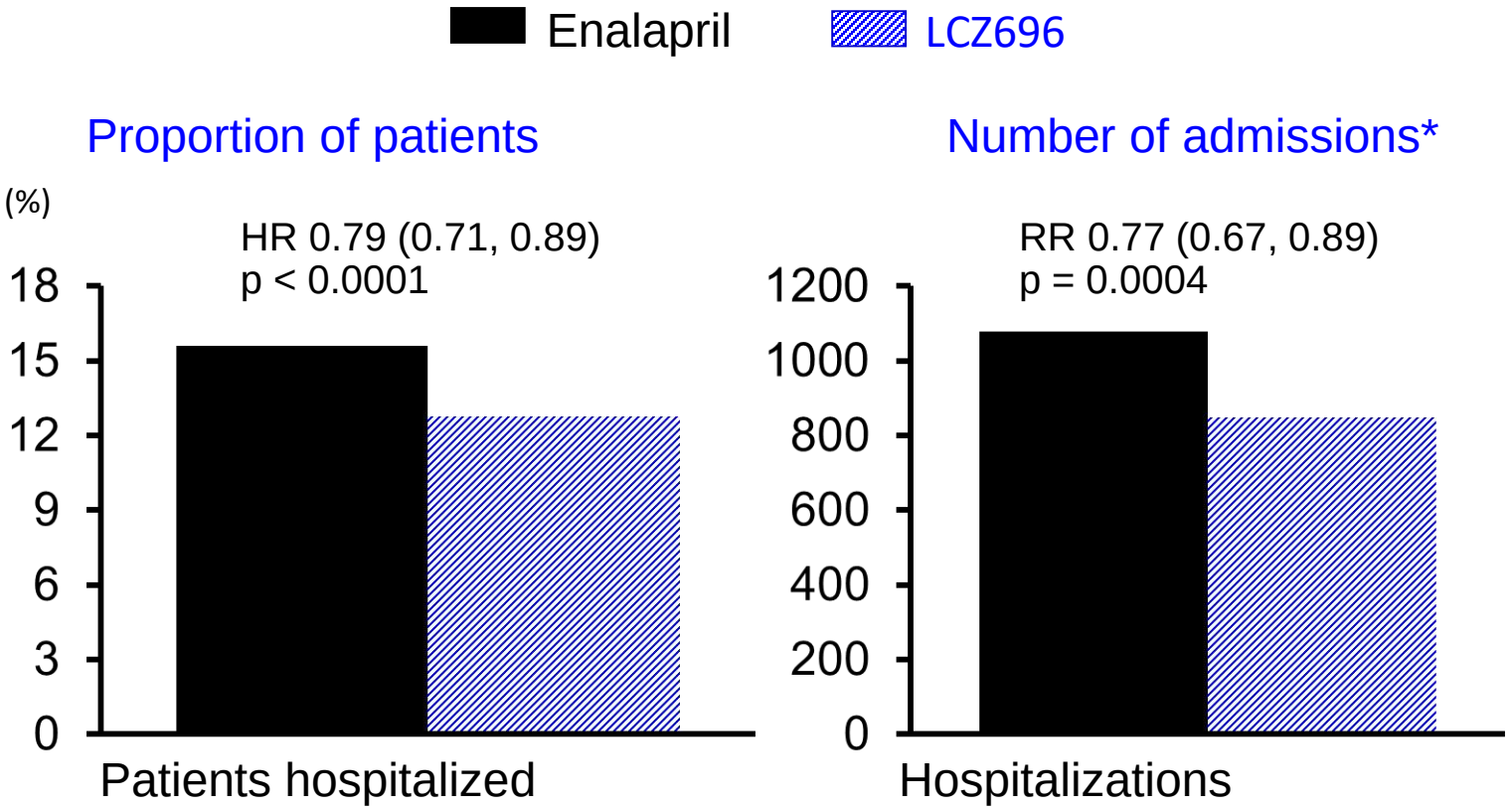
PARADIGM-HF: Hospitalization for heart failure



*Includes repeat episodes

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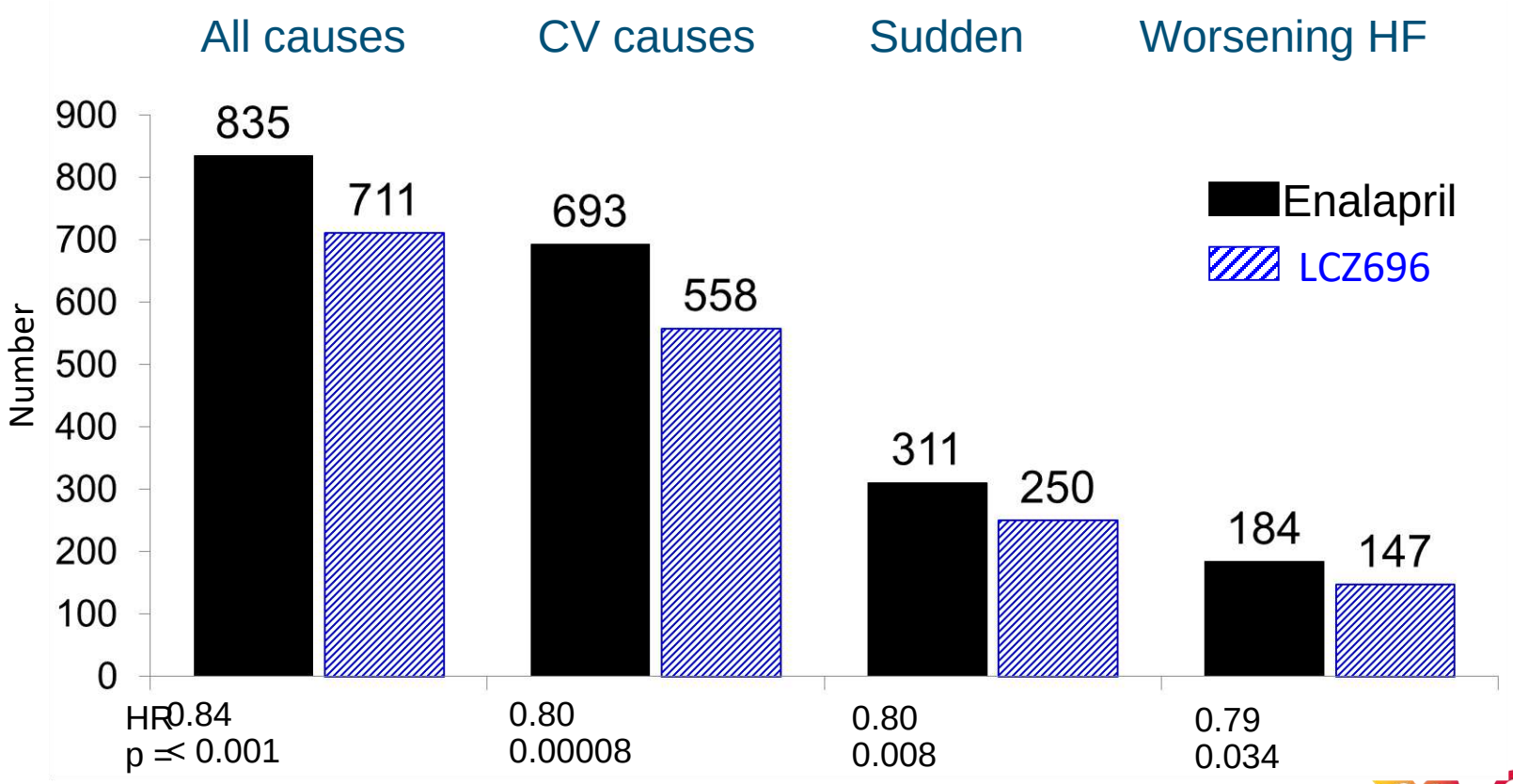
PARADIGM-HF: cause/mode of death



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PARADIGM-HF: Summary of Findings

LCZ696 was *more effective* than enalapril in . . .

- Reducing the risk of CV death and HF hospitalization
- Reducing the risk of CV death
- Reducing the risk of HF hospitalization
- Reducing all-cause mortality

In ambulatory patients with .. .

- Chronic heart failure treated with ACEi – BB - MRAs
- Elevated NP levels
- Able to tolerate ACEi or ARBs
- With no history of angioedema or RAASi induced cough

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Prognostic importance of heart rate, and effect of sacubitril/valsartan according to heart rate, in PARADIGM-HF

	Adjusted hazard ratio		
	Tertile 1 - reference group (≤66 bpm)	Tertile 2 (67-76 bpm)	Tertile 3 (≥ 77 bpm)
Primary endpoint	1.00	1.19 (1.05, 1.35)	1.24 (1.09, 1.43)
CV death	1.00	1.19 (1.01, 1.40)	1.24 (1.04, 1.47)
HF hospitalization	1.00	1.16 (0.99, 1.39)	1.37 (1.15, 1.63)
All-cause mortality	1.00	1.23 (1.07, 1.42)	1.27 (1.08, 1.48)

Association between heart rate and outcome (tertile analysis)

HR is adds incremental prognostic information to other prognostic variables, including NT proBNP.
LCZ696 is equally effective, irrespective of HR (and whether the rhythm is sinus or atrial fibrillation/flutter).

Presented at ESC Congress 2016

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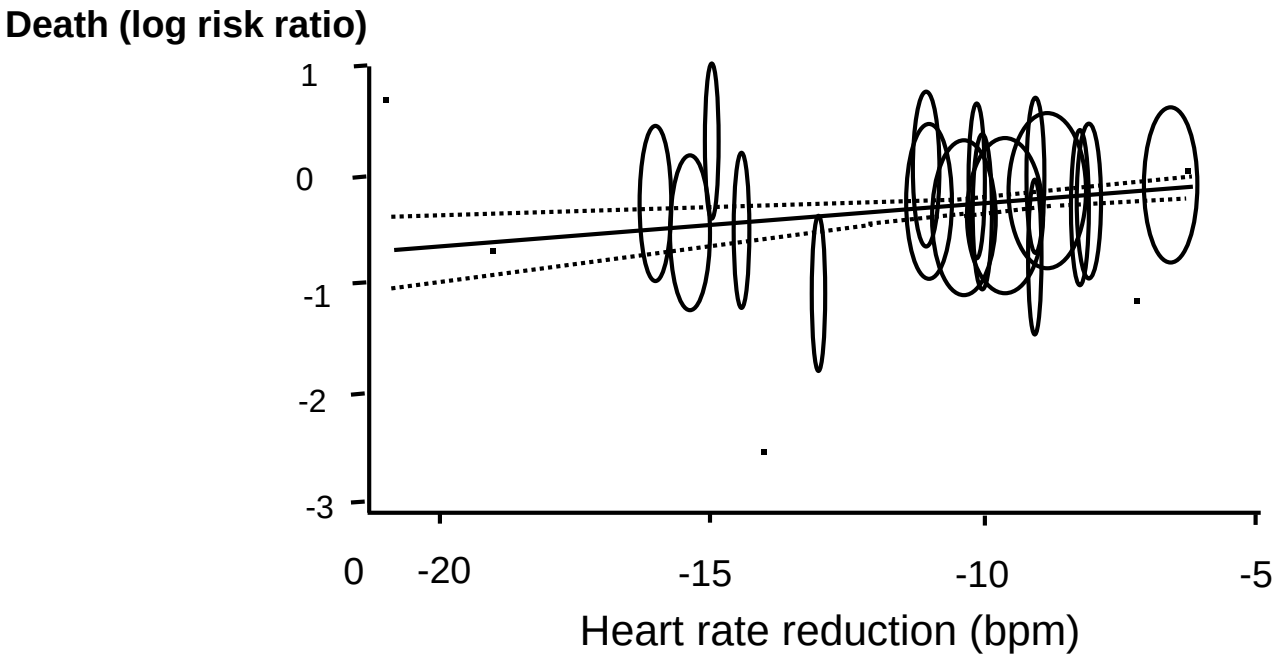
Relation between magnitude of heart rate reduction with beta-blockers and outcomes in heart failure



McAlister FA, et al. *Ann Intern Med.* 2009:150:784-794.

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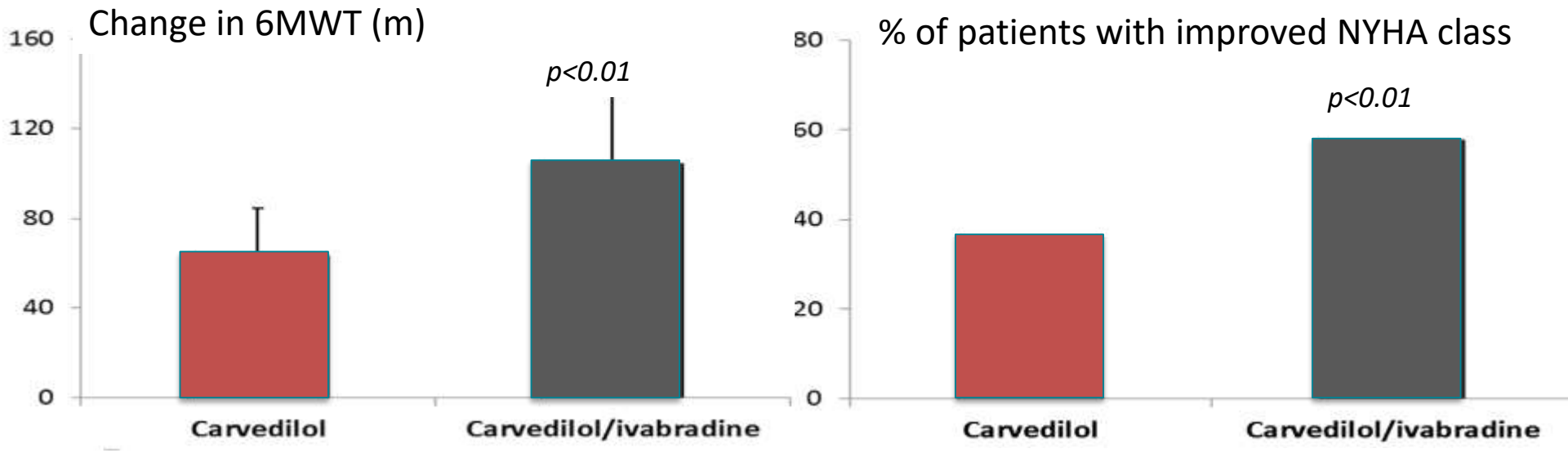
Ivabradine plus carvedilol compared to uptitration of carvedilol on exercise tolerance and symptoms



Bagriy AE, et al Adv Ther. 2015 Feb;32(2):108-19.

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Other pharmacological treatments recommended in selected patients with symptomatic (NYHA Class II-IV) HFrEF

Recommendations	Class [a]	Level [b]
Diuretics		
Diuretics are recommended in order to improve symptoms and exercise capacity in patients with signs and/or symptoms of congestion.	I	B
Diuretics should be considered to reduce the risk of HF hospitalization in patients with signs and/or symptoms of congestion.	IIa	B
Angiotensin receptor neprilysin inhibitor		
Sacubitril/valsartan is recommended as a replacement for an ACE-I to further reduce the risk of HF hospitalization and death in ambulatory patients with HFrEF who remain symptomatic despite optimal treatment with an ACE-I, a beta-blocker and an MRA[d]	I	B
If-channel inhibitor		
Ivabradine should be considered to reduce the risk of HF hospitalization and cardiovascular death in symptomatic patients with LVEF ≤35%, in sinus rhythm and a resting heart rate ≥70 bpm despite treatment with an evidence-based dose of beta-blocker (or maximum tolerated dose below that), ACE-I (or ARB), and an MRA (or ARB).	IIa	B
Ivabradine should be considered to reduce the risk of HF hospitalization and cardiovascular death in symptomatic patients with LVEF ≤35%, in sinus rhythm and a resting heart rate ≥70 bpm who are unable to tolerate or have contra-indications for a beta-blocker. Patients should also receive an ACE-I (or ARB) and an MRA (or ARB).	IIa	C

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Other pharmacological treatments recommended in selected patients with symptomatic (NYHA Class II-IV) heart failure with reduced ejection fraction (cont…)

Hydralazine and isosorbide dinitrate		
Hydralazine and isosorbide dinitrate should be considered in self-identified black patients with LVEF ≤35% or with an LVEF <45% combined with a dilated LV in NYHA Class III–IV despite treatment with an ACE-I a beta-blocker and an MRA to reduce the risk of HF hospitalization and death.	IIa	B
Hydralazine and isosorbide dinitrate may be considered in symptomatic patients with HFrEF who can tolerate neither an ACE-I nor an ARB (or they are contra-indicated) to reduce the risk of death.	IIb	B
Other treatments with less-certain benefits		
Digoxin		
Digoxin may be considered in symptomatic patients in sinus rhythm despite treatment with an ACE-I (or ARB), a beta-blocker and an MRA, to reduce the risk of hospitalization (both all-cause and HF-hospitalizations).	IIb	B
N-3 PUFA		
An n-3 PUFA* preparation may be considered in symptomatic HF patients to reduce the risk of cardiovascular hospitalization and cardiovascular death.	IIb	B

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Other pharmacological treatments recommended in selected patients with symptomatic (NYHA Class II-IV) HFrEF

Angiotensin II type I receptor blockers

- ARBs are recommended only as an alternative in patients intolerant of an ACEI
- The combination of ACEI/ARB should be restricted to symptomatic HFrEF patients receiving a beta-blocker who are unable to tolerate an MRA, and must be used under strict supervision

Combination of hydralazine and isosorbide dinitrate

- There is no clear evidence to suggest the use of this fix-dose combination therapy in all patients with HFrEF
- This combination may be considered in patients who can tolerate neither ACEi nor ARB

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Other treatments with less certain benefit in symptomatic patients with HFrEF

Digoxin and other digitalis glycosides

- Digoxin may be considered in patients in sinus rhythm to reduce the risk of hospitalisation in symptomatic patients with HFrEF
- It is only recommended for the treatment of patients with HFrEF and AF with rapid ventricular rate when other therapeutic options cannot be pursued
  - A resting ventricular rate in the range of 70–90 bpm is recommended, although a resting ventricular rate of up to 110 bpm might still be acceptable
- Digitalis should always be prescribed under specialist supervision. Caution should be exerted in females, in the elderly and in patients with reduced renal function.

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Other pharmacological treatments recommended in selected patients with symptomatic (NYHA Class II-IV) HFrEF and IHD/CAD

Recommendations	Class [a]	Level [b]	Ref [c]
Step 1			
A beta-blocker (in an evidence-based dose or maximum tolerated) is recommended as the preferred first-line treatment to relieve angina because of the associated benefits of this treatment (reducing the risk of HF hospitalization and the risk of premature death).	I	A	167–173
Step 2: on top of beta-blocker or if a beta-blocker is not tolerated			
Ivabradine should be considered as an anti-anginal drug in suitable HFrEF patients (sinus rhythm and HR ≥70 bpm) as per recommended HFrEF management.	IIa	B	180, 410, 411
Step 3: For additional angina symptom relief – except from any combination not recommended			
A short-acting oral or transcutaneous nitrate should be considered (effective anti-anginal treatment, safe in HF).	IIa	A	183, 184, 409
A long acting oral or transcutaneous nitrate should be considered (effective anti-anginal treatment, not extensively studied in HF).	IIa	B	183, 184
Trimetazidine may be considered when angina persists despite treatment with a beta-blocker (or alternative) to relieve angina (effective anti-anginal treatment, safe in HF).	IIb	A	400–403
Amlodipine may be considered in patients unable to tolerate a beta-blocker to relieve angina (effective anti-anginal treatment, safe in HF).	IIb	B	215, 407
Nicorandil may be considered in patients unable to tolerate a beta-blocker to relieve angina (effective anti-anginal treatment, but safety in HF uncertain).	IIb	C	
Ranolazine may be considered in patients unable to tolerate a beta-blocker to relieve angina (effective anti-anginal treatment, but safety in HF uncertain).	IIb	C	
Step 4: Myocardial revascularization			
Myocardial revascularization is recommended when angina persists despite treatment with anti-angina drugs.	I	A	385, 412, 413

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Recommendations	Class [a]	Level [b]
Thiazolidinediones (glitazones) are not recommended in patients with HF, as they increase the risk of HF worsening and HF hospitalization.	III	A
NSAIDs or COX-2 inhibitors are not recommended in patients with HF, as they increase the risk of HF worsening and HF hospitalization.	III	B
Diltiazem or verapamil are not recommended in patients with HFrEF, as they increase the risk of HF worsening and HF hospitalization.	III	C
The addition of an ARB (or renin inhibitor) to the combination of an ACE-I and an MRA is not recommended in patients with HF, because of the increased risk of renal dysfunction and hyperkalaemia.	III	C

Treatments (or combinations of treatments) that may cause harm in patients with symptomatic (NYHA Class II–IV) HFrEF

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European Heart Journal (2017) **38**, 705–711
doi:10.1093/eurheartj/ehw638

CURRENT OPINION

The year in cardiology 2016: heart failure

Aldo Pietro Maggioni[1]* and Frank Ruschitzka[2]

[1]ANMCO Research Center, Via La Marmora 34, 50121 Florence, Italy; and [2]Department of Cardiology, University Heart Center, University Hospital Zurich, Rämistrasse 100, 8091 Zurich, Switzerland

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Aldo Pietro Maggioni, Frank Ruschitzka
The year in cardiology 2016: heart failure
European Heart Journal (2017) 38, 705–711

A revised algorhytm for the treatment of patients with chronic HF has been proposed. All patients with symptomatic HFrEF should receive a combination of an Angiotensin-converting enzyme (ACE)-I [or Angiotensin receptor blocker (ARB) if ACE-I not tolerated], a b-blocker and a mineralocorticoid antagonist (MRA). **If a patient still remains symptomatic ARNI (sacubitril/valsartan) is recommended to replace ACE-I.** Use diuretics in order to improve symptoms and exercise capacity in patients with signs and/or symptoms of congestion. Updated guidelines incorporate the results of the PARADIGM-HF Trial, published in 2014, in the new algorhythm for the treatment of patients with symptomatic HFrEF (Figure 1).

Aldo Pietro Maggioni, Frank Ruschitzka
The year in cardiology 2016: heart failure
European Heart Journal (2017) 38, 705–711

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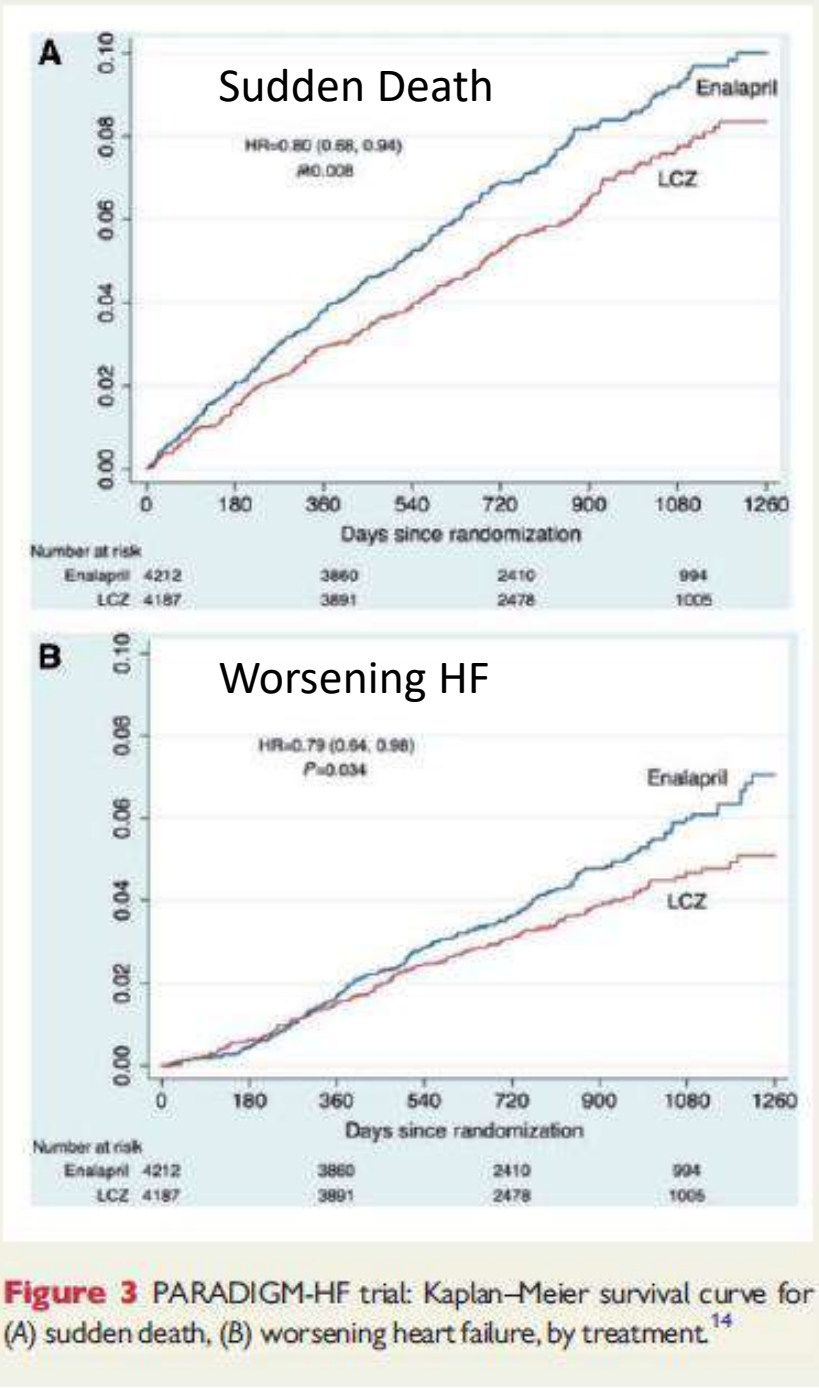

Figure 3 PARADIGM-HF trial: Kaplan–Meier survival curve for (A) sudden death, (B) worsening heart failure, by treatment.[14]

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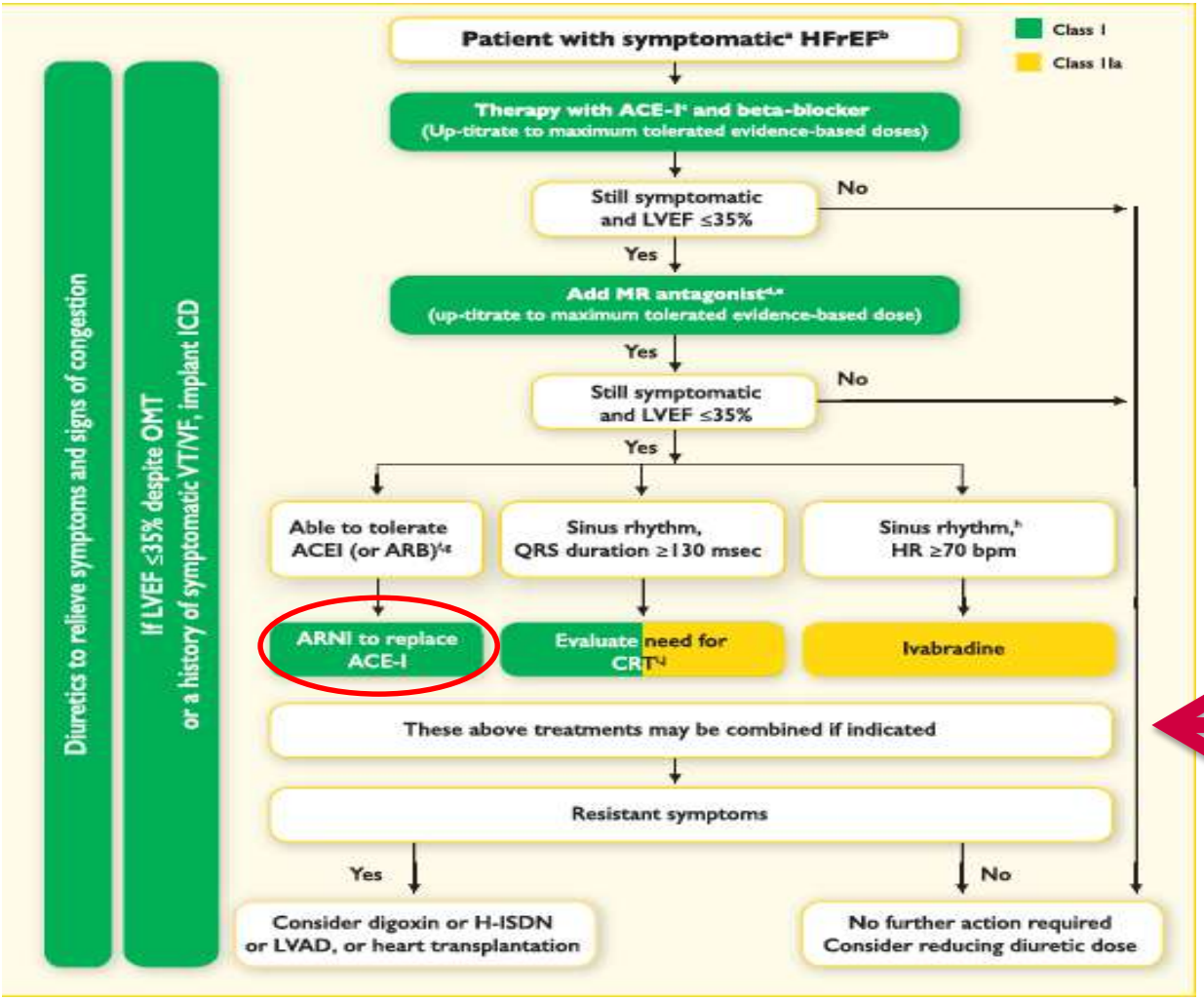

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ARNI (antagonisti della neprilisina e del recettore dell'angiotensina)

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Even more relevant for implementing the general conclusions of the PARADIGM-HF study in clinical practice was **the evaluation of the effects of the drug according to the different levels of risk**, using the MAGGIC or the EMPHASIS-HF stratification models.15 Although most PARADIGM-HF patients had mild symptoms, **the benefit of sacubitril/valsartan over enalapril was apparent across the whole spectrum of risk defined by the MAGGIC and EMPHASIS-HF risk score**, and

even within the large subset of patients in NYHA functional class II.

Aldo Pietro Maggioni, Frank Ruschitzka
The year in cardiology 2016: heart failure *Speaker*
European Heart Journal (2017) 38, 705–711

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Finally, a practical open question was related to the **potential risk** of **combining the more potent sacubitril/valsartan with a MRA**.

The benefit of sacubitril/valsartan over enalapril was consistent for the primary composite outcome of cardiovascular death or HF hospitalization, and cardiovascular death alone, irrespective of the background therapy.

In other terms, the superiority of the new drug compared with the traditional one was present in both patients receiving or not MRAs.