Outcome funzionali nell'anziano con scompenso cardiaco

Angelo Scuteri

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University of Sassari -Sassari (Italy)

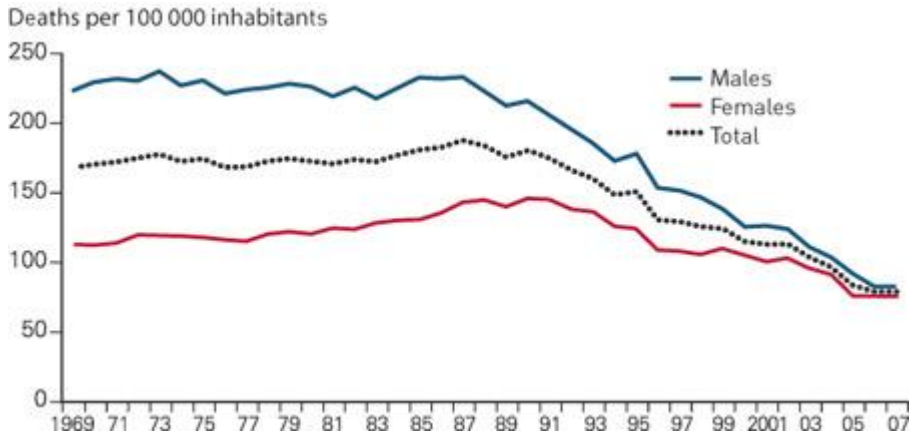
Tunstall-Pedoe H et al.

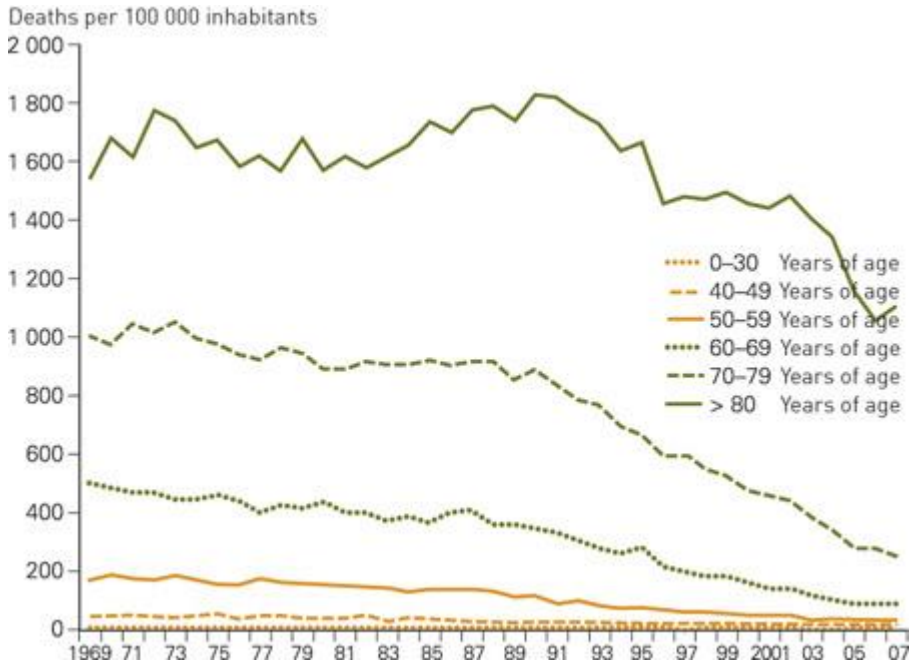
Lancet. 2000; 355: 688-700

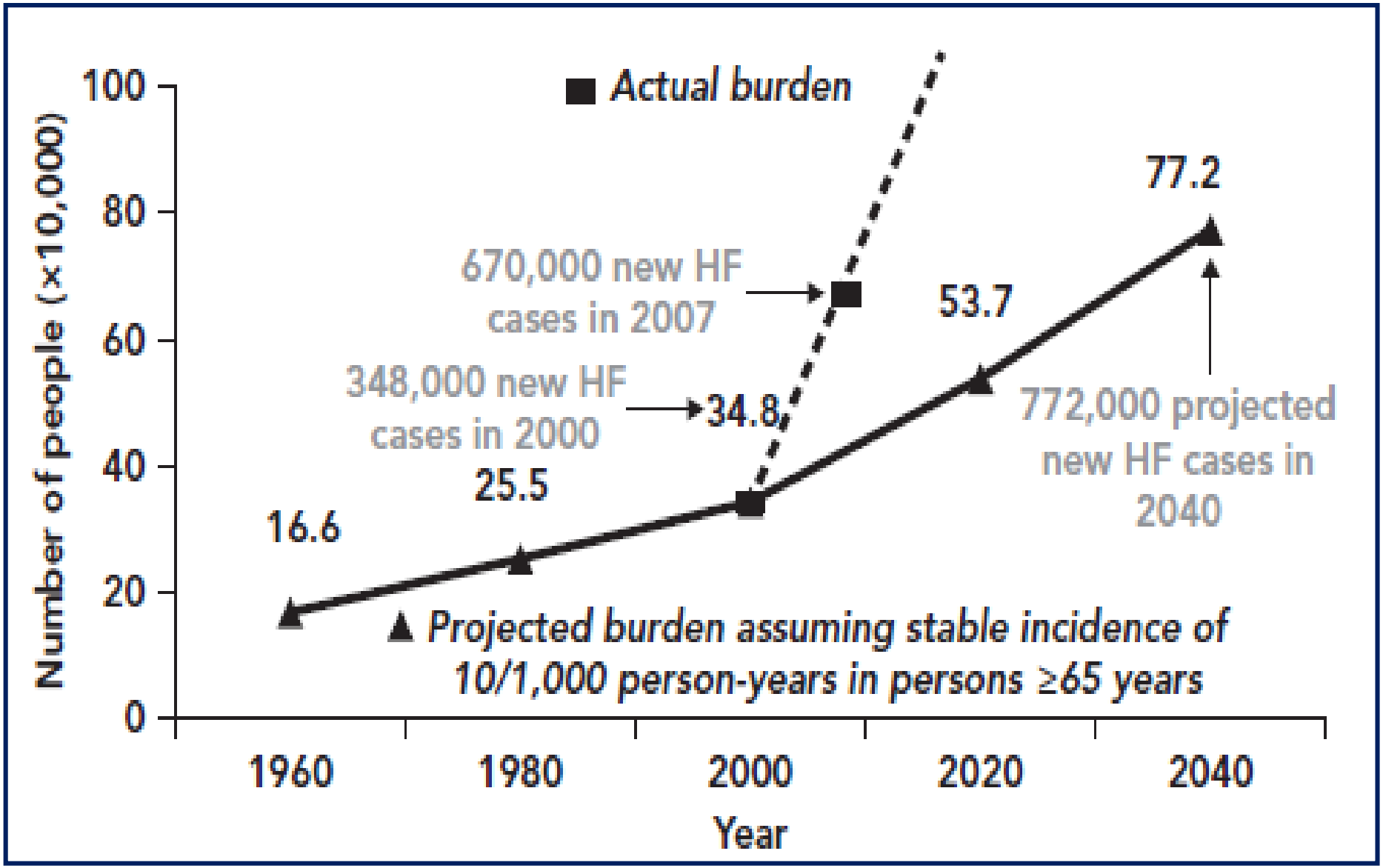
Case fatality, coronary-event rates, and CHD mortality in M and F, aged 35-64 yrs, in two separate 3-4-year periods

	M	F
Case fatality	-19%	-16%
CHD rates	-25%	-23%
CHD mortality	-42%	-34%

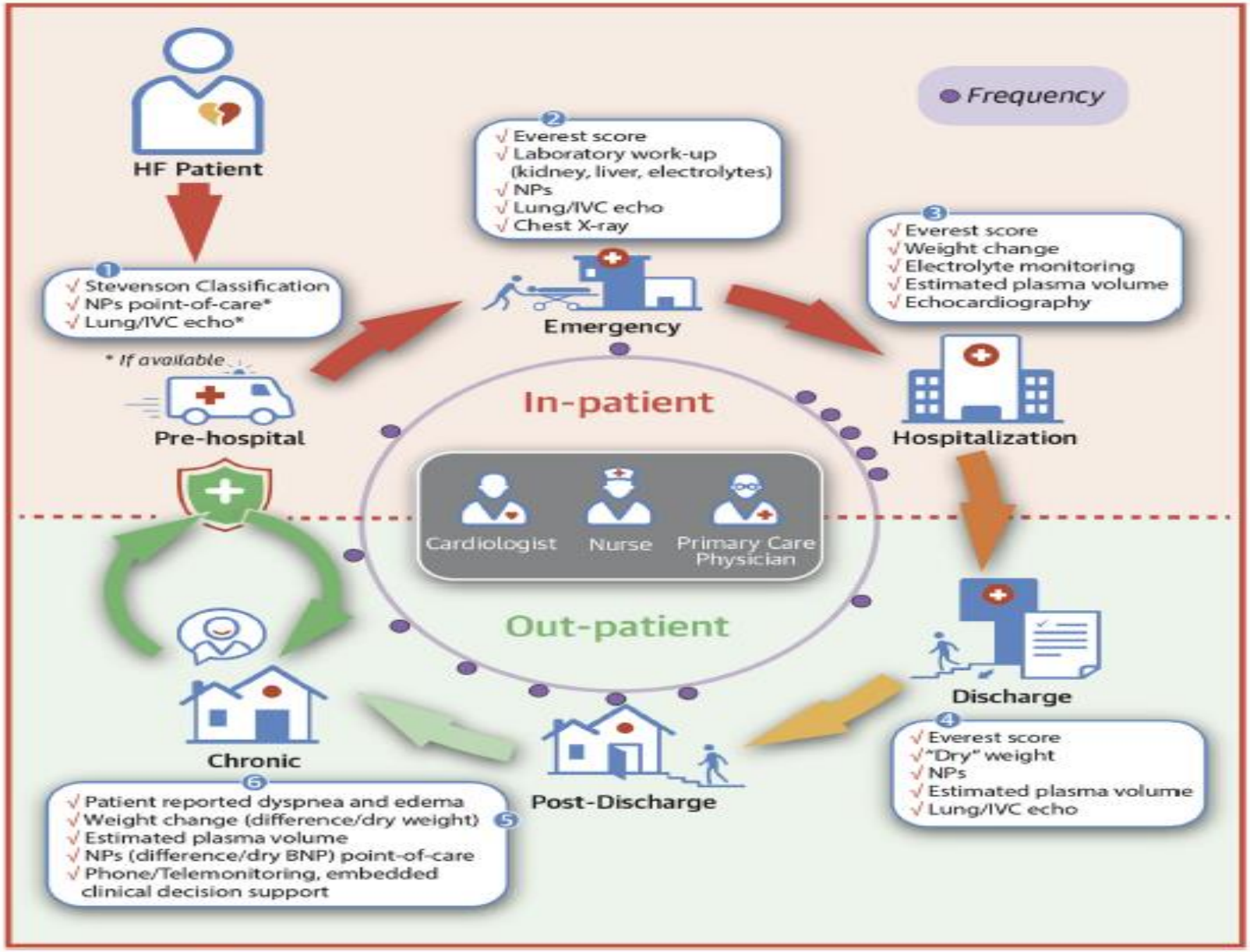
Mortality rates for myocardial infarction (deaths per 100 000 inhabitants) 1969–2007






Actual burden
77.2
670,000 new HF cases in 2007
53.7
348,000 new HF cases in 2000
34.8
772,000 projected new HF cases in 2040
25.5
16.6
Projected burden assuming stable incidence of 10/1,000 person-years in persons ≥65 years
Number of people (x10,000)
100
80
60
40
20
0
1960
1980
2000
2020
2040
Year

CENTRAL ILLUSTRATION Congestion Assessment in HF Patient Journey



Girerd, N. et al. J Am Coll Cardiol HF. 2018;6(4):273–85.

BNP = B-type natriuretic peptide; HF = heart failure; IVC = inferior vena cava; NP = natriuretic peptide.

ESC European Society of Cardiology

European Heart Journal (2019) **40**, 3626–3644
doi:10.1093/eurheartj/ehy600

SPECIAL ARTICLE
Heart failure/cardiomyopathy

Treatments targeting inotropy

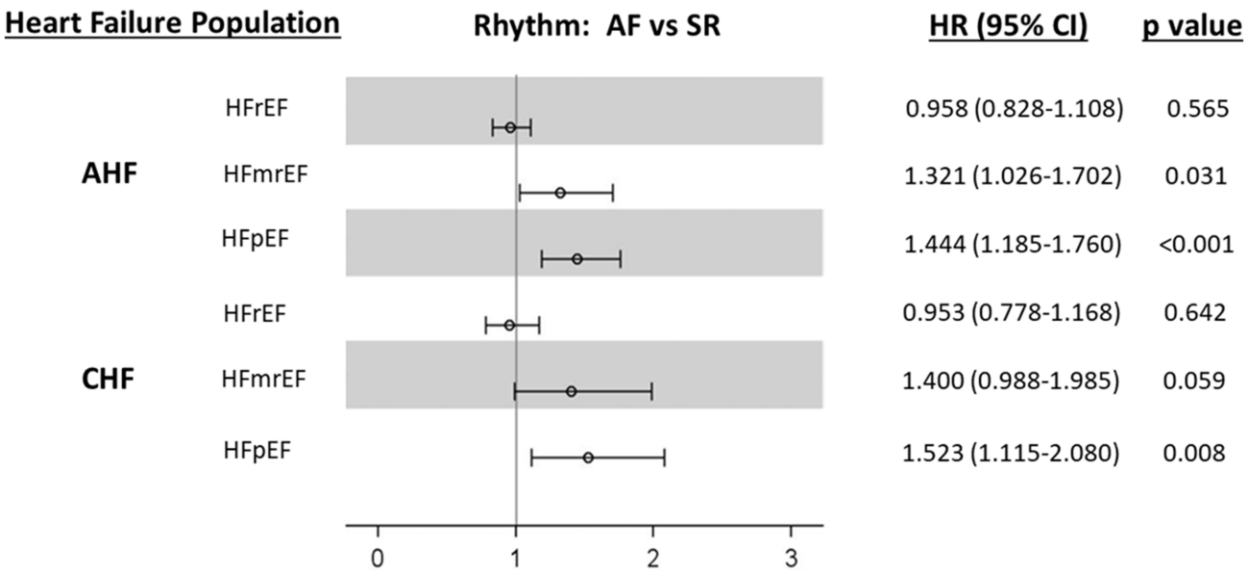
A position paper of the Committees on Translational Research and Acute Heart Failure of the Heart Failure Association of the European Society of Cardiology

Christoph Maack[1]*, Thomas Eschenhagen[2,3], Nazha Hamdani[4], Frank R. Heinzel[5], Alexander R. Lyon[6], Dietmar J. Manstein[7,8], Joseph Metzger[9], Zoltán Papp[10], Carlo G. Tocchetti[11], M. Birhan Yilmaz[12], Stefan D. Anker[13,14], Jean-Luc Balligand[15], Johann Bauersachs[16], Dirk Brutsaert[17], Lucie Carrier[2,3], Stefan Chlopicki[18], John G. Cleland[19,20], Rudolf A. de Boer[21], Alexander Dietl[22], Rodolphe Fischmeister[23], Veli-Pekka Harjola[24], Stephane Heymans[25], Denise Hilfiker-Kleiner[26], Johannes Holzmeister[27], Gilles de Keulenaer[28], Giuseppe Limongelli[29], Wolfgang A. Linke[30], Lars H. Lund[31], Josep Masip[32], Marco Metra[33], Christian Mueller[34], Burkert Pieske[35,36], Piotr Ponikowski[37], Arsen Ristić[38], Frank Ruschitzka[39], Petar M. Seferović[40], Hadi Skouri[41], Wolfram H. Zimmermann[42,43], and Alexandre Mebazaa[44]

Gittata **Consumo O_2**

Acute heart failure (HF) and in particular, cardiogenic shock are associated with high morbidity and mortality. A therapeutic dilemma is that the use of positive inotropic agents, such as catecholamines or phosphodiesterase-inhibitors, is associated with increased mortality. Newer drugs, such as levosimendan or omecamtiv mecarbil, target sarcomeres to improve systolic function putatively without elevating intracellular Ca^{2+}. Although meta-analyses of smaller trials suggested that levosimendan is associated with a better outcome than dobutamine, larger comparative trials failed to confirm this observation. For omecamtiv mecarbil, Phase II clinical trials suggest a favourable haemodynamic profile in patients with acute and chronic HF, and a Phase III morbidity/mortality trial in patients with chronic HF has recently begun. Here, we review the pathophysiological basis of systolic dysfunction in patients with HF and the mechanisms through which different inotropic agents improve cardiac function. Since adenosine triphosphate and reactive oxygen species production in mitochondria are intimately linked to the processes of excitation–contraction coupling, we also discuss the impact of inotropic agents on mitochondrial bioenergetics and redox regulation. Therefore, this position paper should help identify novel targets for treatments that could not only safely improve systolic and diastolic function acutely, but potentially also myocardial structure and function over a longer-term.

Figure 4 Multivariable hazards ratios for long-term total mortality or heart failure hospitalizations associated with ...



European Heart Journal, Volume 39, Issue 48, 21 December 2018, Pages 4277–4284, https://doi.org/10.1093/eurheartj/ehy626

ESC European Society of Cardiology
European Heart Journal (2019) **40**, 3651–3652
doi:10.1093/eurheartj/ehz655

DISCUSSION FORUM

Conversion to and maintenance of sinus rhythm do not yield a significant increase in stroke-volume in HFREF patients, whose heart works on the flat branch of Frank–Starling curve, thereby making the retrieval of the atrial mechanical contribution in this subset a substantially futile choice

Renato De Vecchis * and Carmelina Ariano

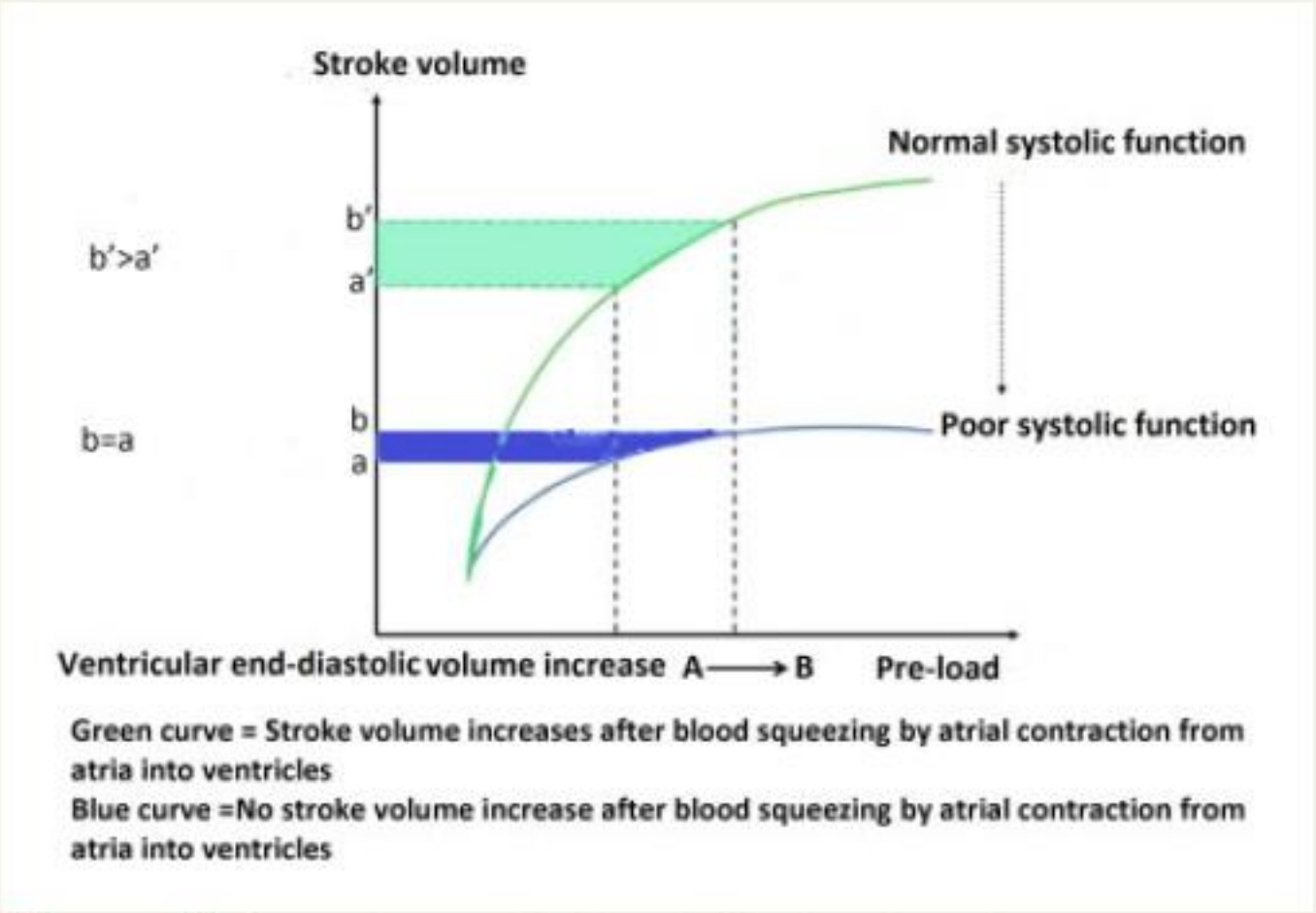


Figure 1 According to the Frank–Starling law, the augmentation of end-diastolic ventricular volume, induced by atrial contraction, is able to increase the force of contraction of myocardial fibres when it occurs in the presence of normal systolic function, but does not induce any detectable increase in the presence of poor systolic function (flat branch of the curve).

ESC European Society of Cardiology

European Heart Journal (2019) **40**, 3605–3612
doi:10.1093/eurheartj/ehz554

FASTTRACK CLINICAL RESEARCH
Heart failure/cardiomyopathy

Short-term diuretic withdrawal in stable outpatients with mild heart failure and no fluid retention receiving optimal therapy: a double-blind, multicentre, randomized trial

Luis E. Rohde [1,2]*, Marciane M. Rover [3], Jose A. Figueiredo Neto[4], Luiz C. Danzmann[5,6], Eduardo G. Bertoldi [7], Marcus V. Simões[8], Odilson M. Silvestre [9], Antonio L. P. Ribeiro[10], Lidia Zytynski Moura[11], Luis Beck-da-Silva [1,2], Debora Prado [10], Roberto T. Sant'Anna[3], Leonardo H. Bridi[3], André Zimerman[1], Priscila Raupp da Rosa[6], and Andréia Biolo[1]

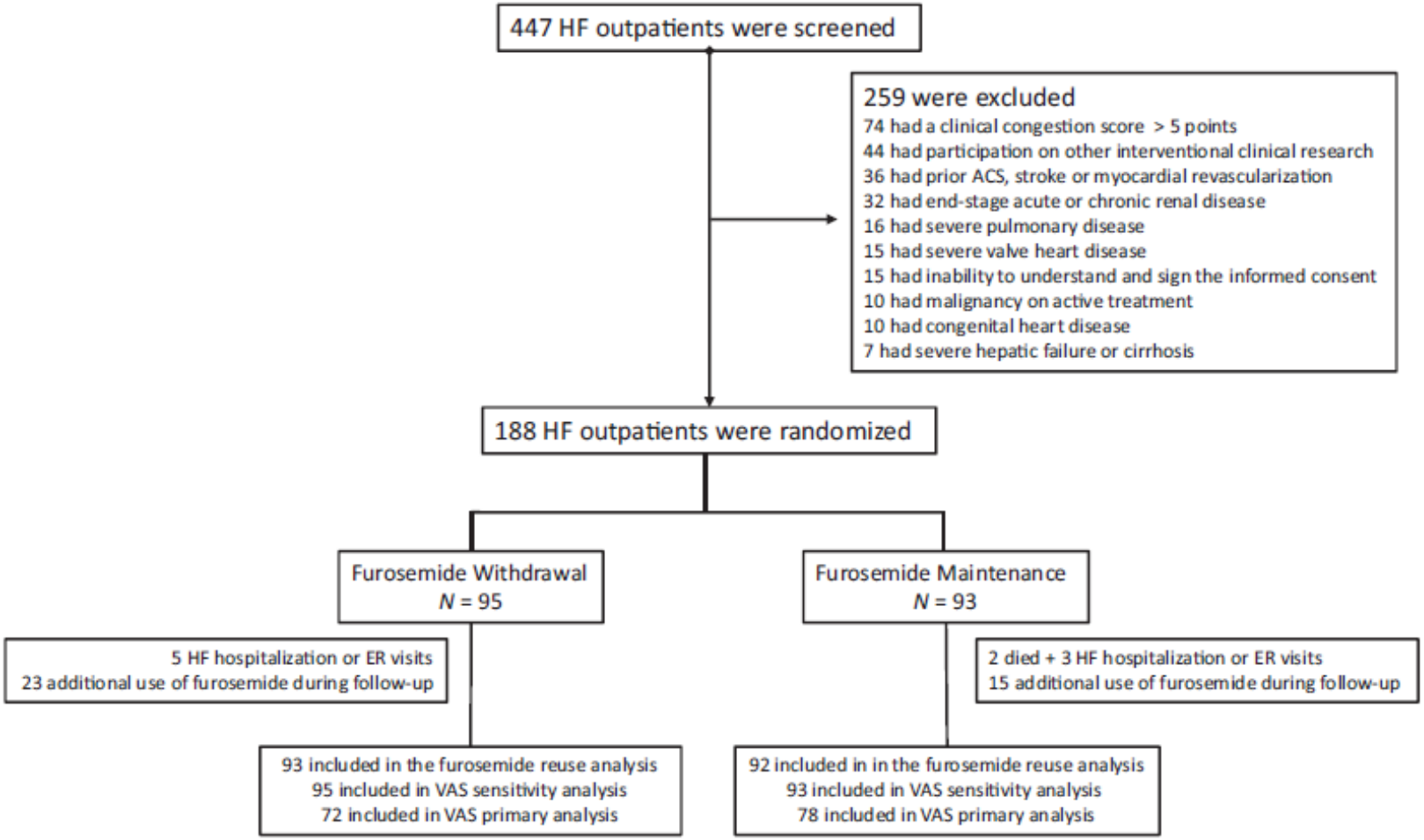


Figure 1 Consort diagram (screening, exclusions, randomization and analysis). ACS, acute coronary syndrome; ER, emergency room; HF, heart failure; VAS, visual-analogue scale.

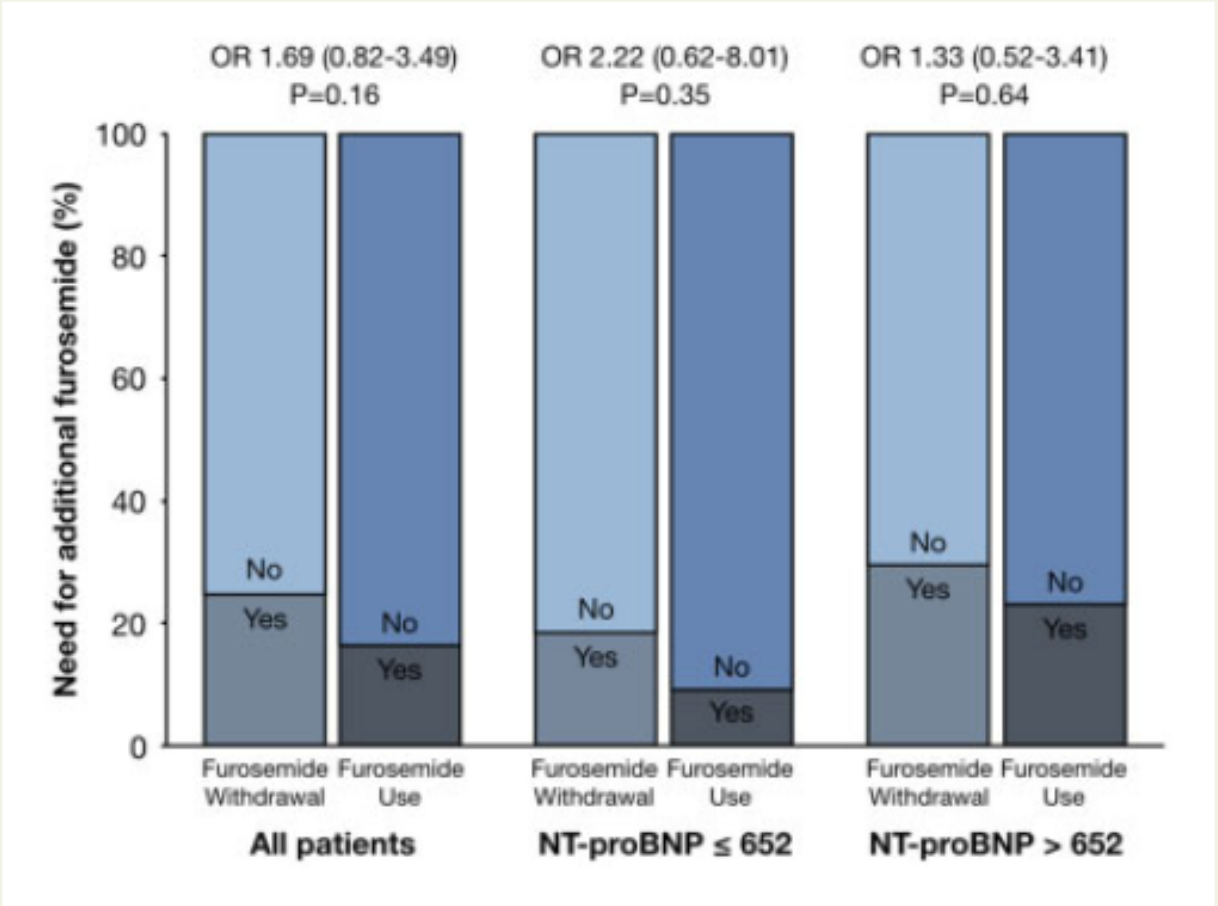


Figure 3 Proportion of patients free from (No) and in need of (Yes) additional furosemide use during the 90-days study period. 95% confidence intervals are described in parenthesis. NT-proBNP, N-terminal pro-brain natriuretic peptide levels and is expressed in pg/mL; OR, odds ratio for additional furosemide use in the withdrawal group.

Conclusion

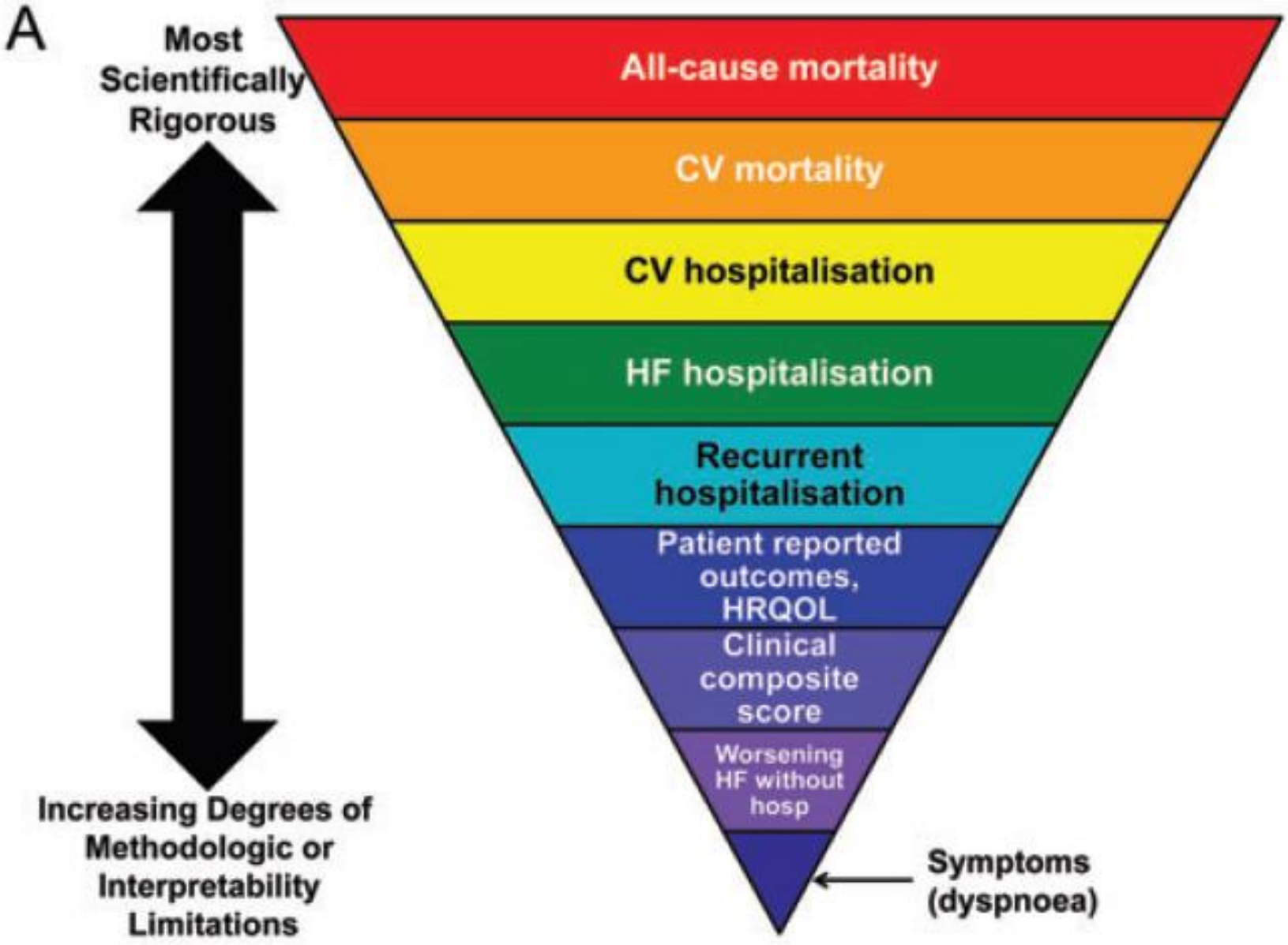
The ReBIC-1 trial demonstrated that in outpatients with stable HF furosemide withdrawal did not change the self-perception of dyspnoea and was not associated with increased reuse of additional diuretics (*Take home figure*). Therefore, furosemide discontinuation might be a safe strategy that deserves consideration for selected a subgroup of HF patients in the outpatient setting, with cautious follow-up. These results apply only to relatively young patients with mild and stable symptoms, no or minimal clinical signs of congestion, a reduced LVEF, receiving optimal medical therapy.

European Journal of Heart Failure (2013) **15**, 1082–1094
doi:10.1093/eurjhf/hft095

REVIEW

Clinical outcome endpoints in heart failure trials: a European Society of Cardiology Heart Failure Association consensus document

Faiez Zannad[1]*, Angeles Alonso Garcia[2], Stefan D. Anker[3], Paul W. Armstrong[4],


A
Most Scientifically Rigorous
Increasing Degrees of Methodologic or Interpretability Limitations
All-cause mortality
CV mortality
CV hospitalisation
HF hospitalisation
Recurrent hospitalisation
Patient reported outcomes, HRQOL
Clinical composite score
Worsening HF without hosp
Symptoms (dyspnoea)

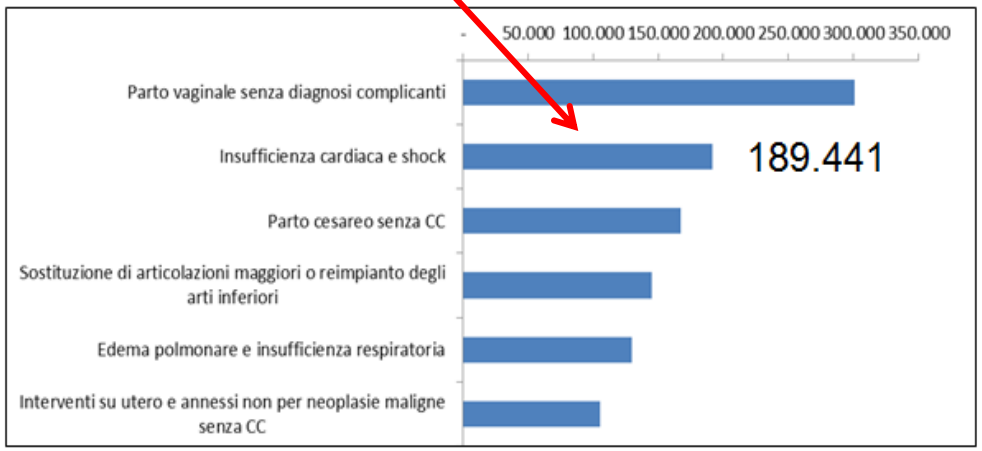
DRG 127- Scompenso Cardiaco

2014

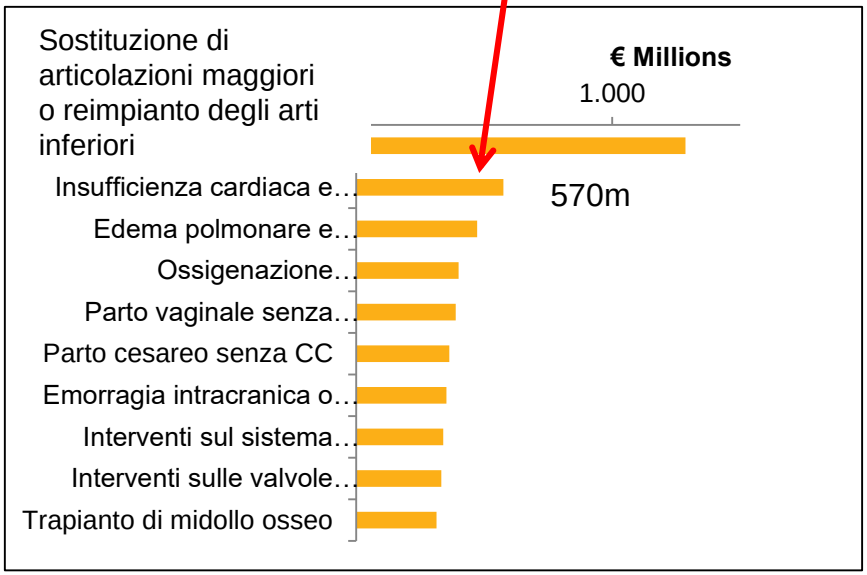
RANGO			DRG	GIORNATE	%
1	373	M	Parto vaginale senza diagnosi complicanti	1.013.516	2,3
2	127	M	Insufficienza cardiaca e shock	1.727.378	4,0
3	371	C	Parto cesareo senza CC	750.273	1,7
4	544	C	Sostituzione di articolazioni maggiori o reimpianto degli arti inferiori	1.356.965	3,1
5	087	M	Edema polmonare e insufficienza respiratoria	1.308.583	3,0

1.727.378 giornate di ricovero (4%) → Al primo posto tra tutti i DRG

Secondo posto tra i primi 30 DRG ospedalieri per **numerosità** (primo per patologia)



€ 569.861.824 → **2,4%** sul costo totale dei DRG ospedalieri



Fonte: Rapporto SDO 2014

Riammissioni ospedaliere:

Non evitabili

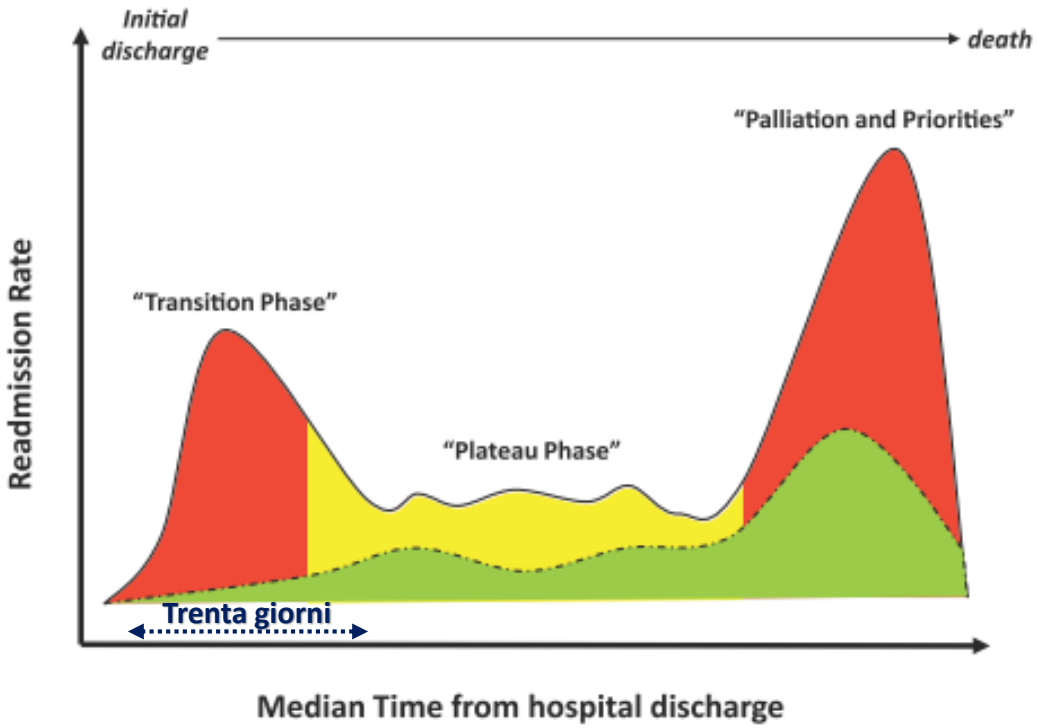
Evitabili – ‘’Inappropriate’’

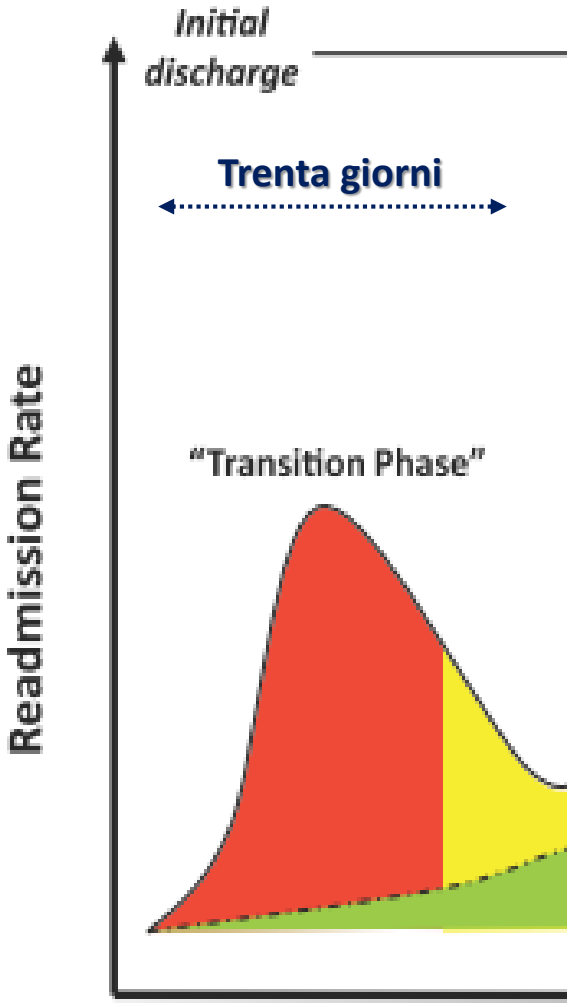
Circulation 2012

Special Report

Rehospitalization for Heart Failure
Predict or Prevent?

Akshay S. Desai, MD, MPH; Lynne W. Stevenson, MD





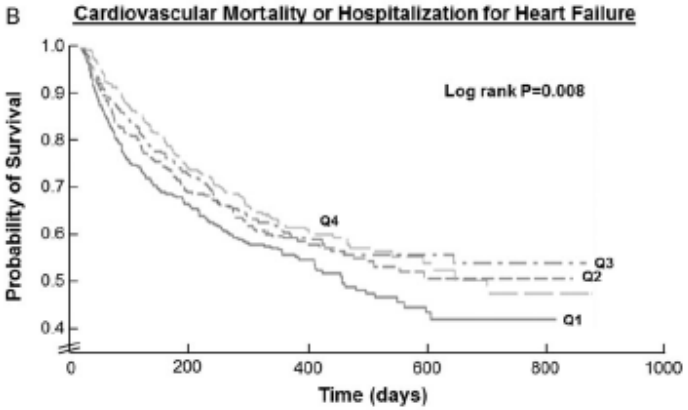
Incompleta decongestione intraospedaliera

Cause infettive o peggioramento funz. renale

European Journal of Heart Failure (2013) 15, 1401–1411
doi:10.1093/eurjhf/hft110

Haemoconcentration, renal function, and post-discharge outcomes among patients hospitalized for heart failure with reduced ejection fraction: insights from the EVEREST trial

Q1	Q2	Q3	Q4
△ -17 -2%	△ -1-0 %	△ 1-2 %	△ 3-16 %



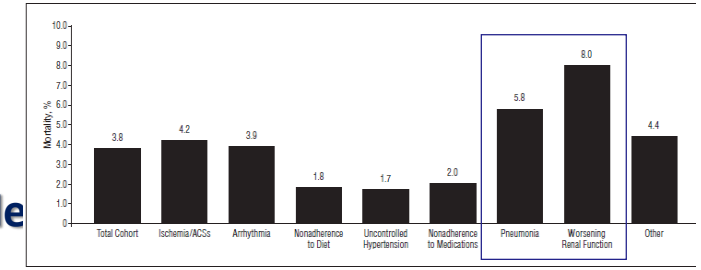
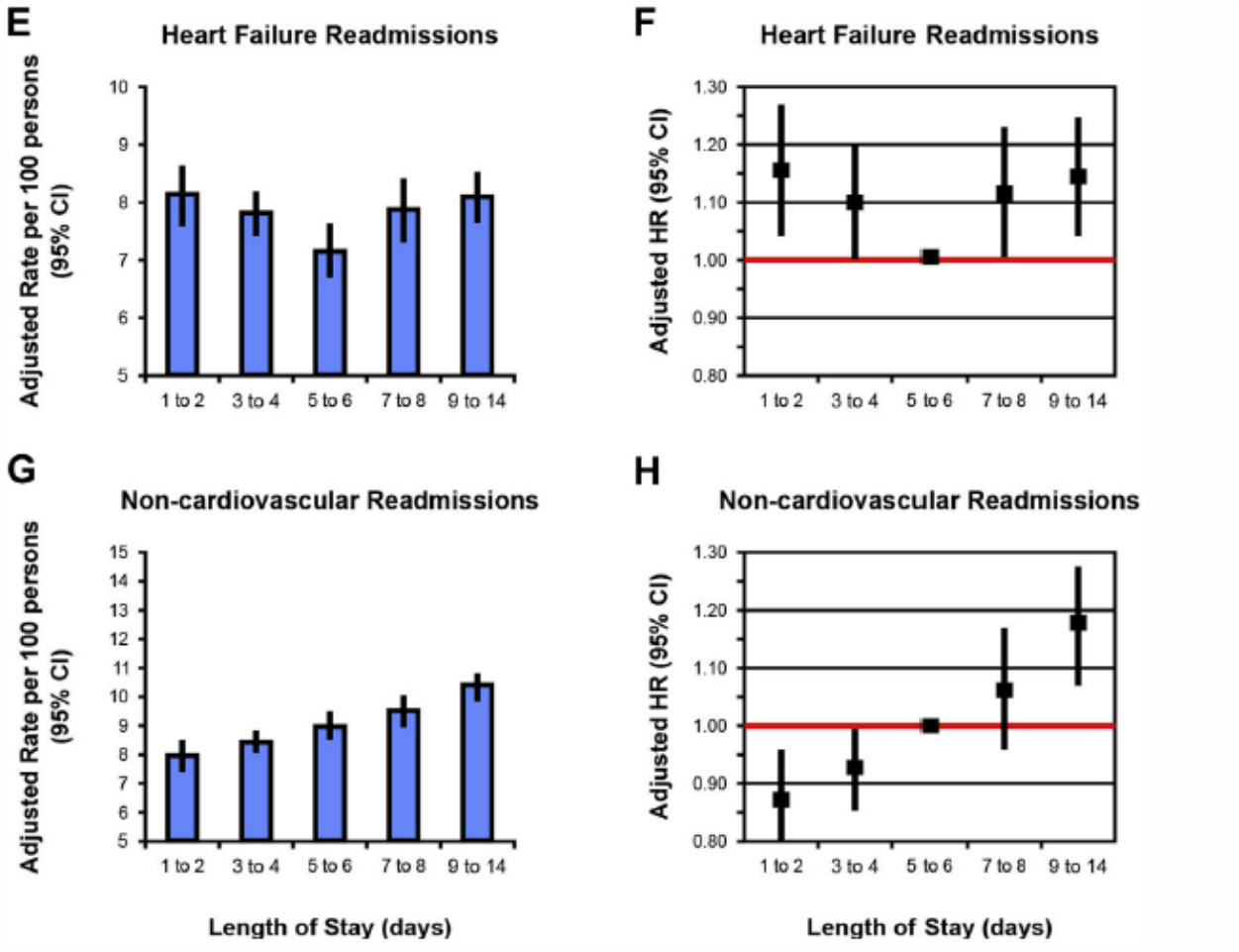


Figure. Unadjusted in-hospital mortality rates by precipitating factors for heart failure admission. ACSs indicates acute coronary syndromes.

Arch Intern Med. 2008;168(8):847-854

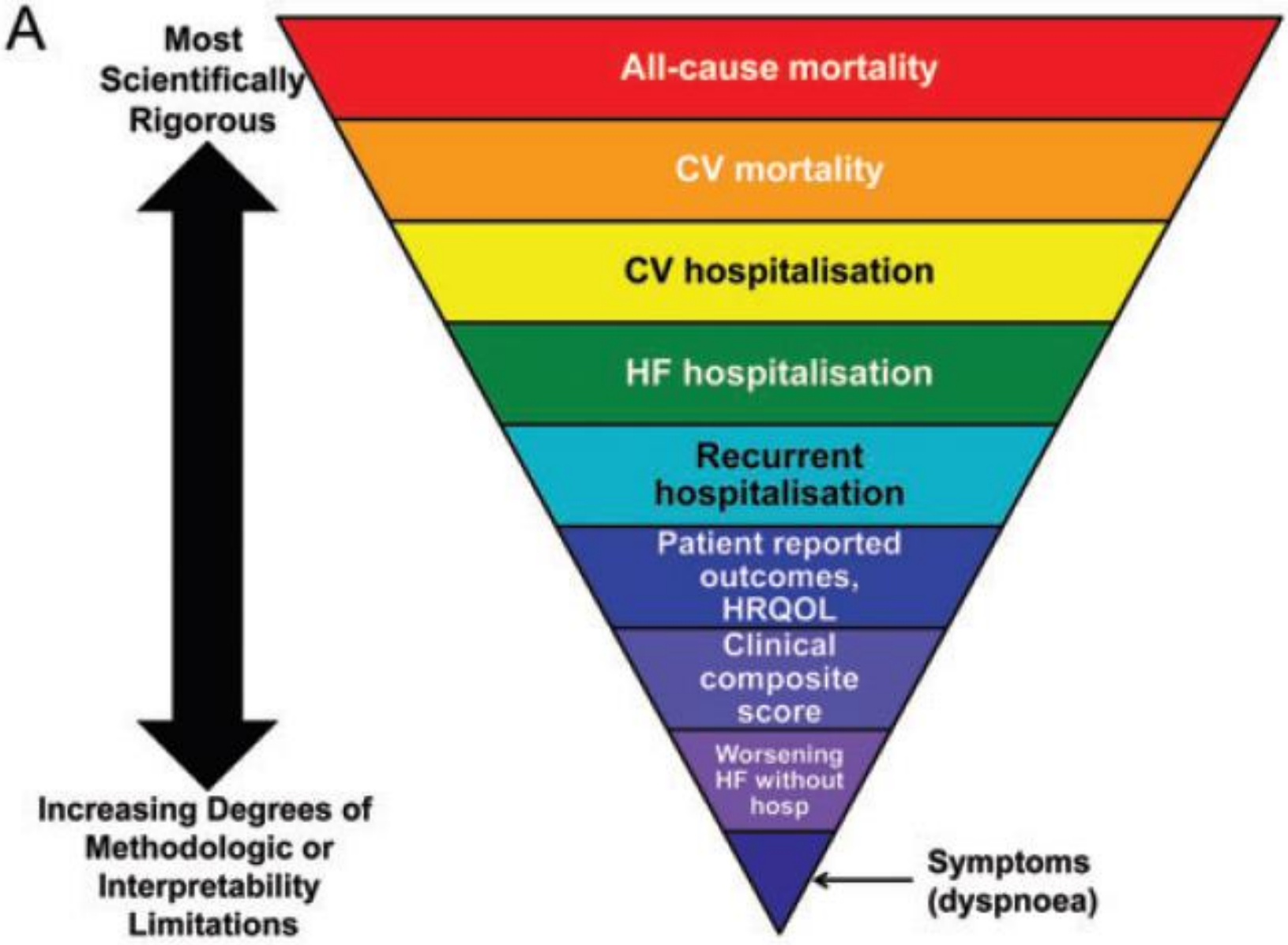
Associations Between Short or Long Length of Stay and 30-Day Readmission and Mortality in Hospitalized Patients With Heart Failure



PERSPECTIVES

COMPETENCY IN PATIENT CARE: In older patients hospitalized with acute HF, LOS is an important metric that demonstrates a U-shaped relationship with 30-day cardiovascular and HF readmissions but a linear relationship with 30-day noncardiovascular readmissions. Furthermore, a shorter LOS (1 to 2 days) was associated with a reduced risk of 30-day noncardiovascular readmissions, at the expense of an increased risk of 30-day cardiovascular and HF readmissions.

TRANSLATIONAL OUTLOOK: Future studies should evaluate the impact of post-discharge strategies such as early physician follow-up and transitional care in reducing cardiovascular and HF readmissions after a short LOS.


A
Most Scientifically Rigorous
Increasing Degrees of Methodologic or Interpretability Limitations
All-cause mortality
CV mortality
CV hospitalisation
HF hospitalisation
Recurrent hospitalisation
Patient reported outcomes, HRQOL
Clinical composite score
Worsening HF without hosp
Symptoms (dyspnoea)

Endpoints other than hospitalization	(1) More research is needed to develop robust methods for capturing heart failure events other than hospitalization or death. (2) Careful consideration needs to be given to defining these events to avoid capturing non-heart failure events.
Symptom and patient-reported health outcomes	(1) Dyspnoea is an important outcome to measure in clinical trials focusing on acute heart failure. (2) Consistent measures (e.g. instruments) and standardized methods (e.g. sitting vs. supine, or specifying degree of head elevation for orthopnoea evaluation) of dyspnoea assessment need to be developed, adopted, and used consistently within the heart failure research community. (3) Repeated assessments of dyspnoea provide more information and are more relevant to patients than measurement at a single time point. Trials should integrate measurements of the severity of dyspnoea over time as an endpoint.[10,70,110,111] (4) Patient-reported outcomes are independent endpoints, not surrogates for mortality. (5) Unless the regulatory environment changes and assessment instruments improve, it is unlikely that patient-reported outcome endpoints (quality of life) will be acceptable as the only basis for approval. (6) Other patient-reported outcomes focusing on symptoms in acute heart failure (e.g. dyspnoea) may be acceptable for approval, provided safety is adequately demonstrated. (7) Instruments should be self-administered when possible. When patients are unable to self-administer, the instruments should be administered by personnel not involved with the clinical trial or who are blinded to clinical and trial data to minimize bias.
Clinical composite endpoints	(1) Multiple components should not be added to composites only for the purpose of enriching the event rate, particularly if compelling evidence is lacking to suggest the treatment will influence the components similarly. (2) Individual components of the composite should be reported separately to allow for observation of divergent effects or situations where one component drives the overall composite. (3) Components of a unconventional composite endpoint should have a predictable (reproducible) response to the treatment.

European Journal of Heart Failure (2013) **15**, 1113–1121
doi:10.1093/eurjhf/hft071

Preferences of heart failure patients in daily clinical practice: quality of life or longevity?

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[1]Department of Cardiology, University Medical Center Groningen, University of Groningen, The Netherlands; [2]Department of Epidemiology, University Medical Center Groningen, University of Groningen, The Netherlands; [3]Hanze University of Applied Sciences Groningen, School of Nursing, The Netherlands; and [4]Department of Social and Welfare Studies, Faculty of Health Sciences Linköping University, Linköping, Sweden

Received 22 January 2013; revised 20 March 2013; accepted 10 April 2013; online publish-ahead-of-print 5 May 2013

Aims Knowledge of patient preferences is vital for delivering optimal healthcare. This study uses utility measurement to assess the preferences of heart failure (HF) patients regarding quality of life or longevity. The utility approach represents the perspective of a patient; facilitates the combination of mortality, morbidity, and treatment regimen into a single score; and makes it possible to compare the effects of different interventions in healthcare.

Methods and results Patient preferences of 100 patients with HF were assessed in interviews using the time trade-off (TTO) approach. Health-related quality of life (HR-QoL) was assessed with the EQ-5D and the Minnesota Living with Heart Failure Questionnaire (MLHFQ). Patients' own estimation of life expectancy was assessed with a visual analogue scale (VAS). Of the 100 patients (mean age 70 $\pm$ 9 years; 71% male), 61% attach more weight to quality of life over longevity; while 9% and 14% were willing to trade 6 and 12 months, respectively, for perfect health and attach more weight to quality of life. Patients willing to trade time had a significantly higher level of NT-proBNP and reported significantly more dyspnoea during exertion. Predictors of willingness to trade time were higher NT-proBNP and lower EQ VAS.

Conclusion The majority of HF patients attach more weight to quality of life over longevity. There was no difference between both groups with respect to life expectancy described by the patients. These insights enable open and personalized discussions of patients' preferences in treatment and care decisions, and could guide the future development of more patient-centred care.

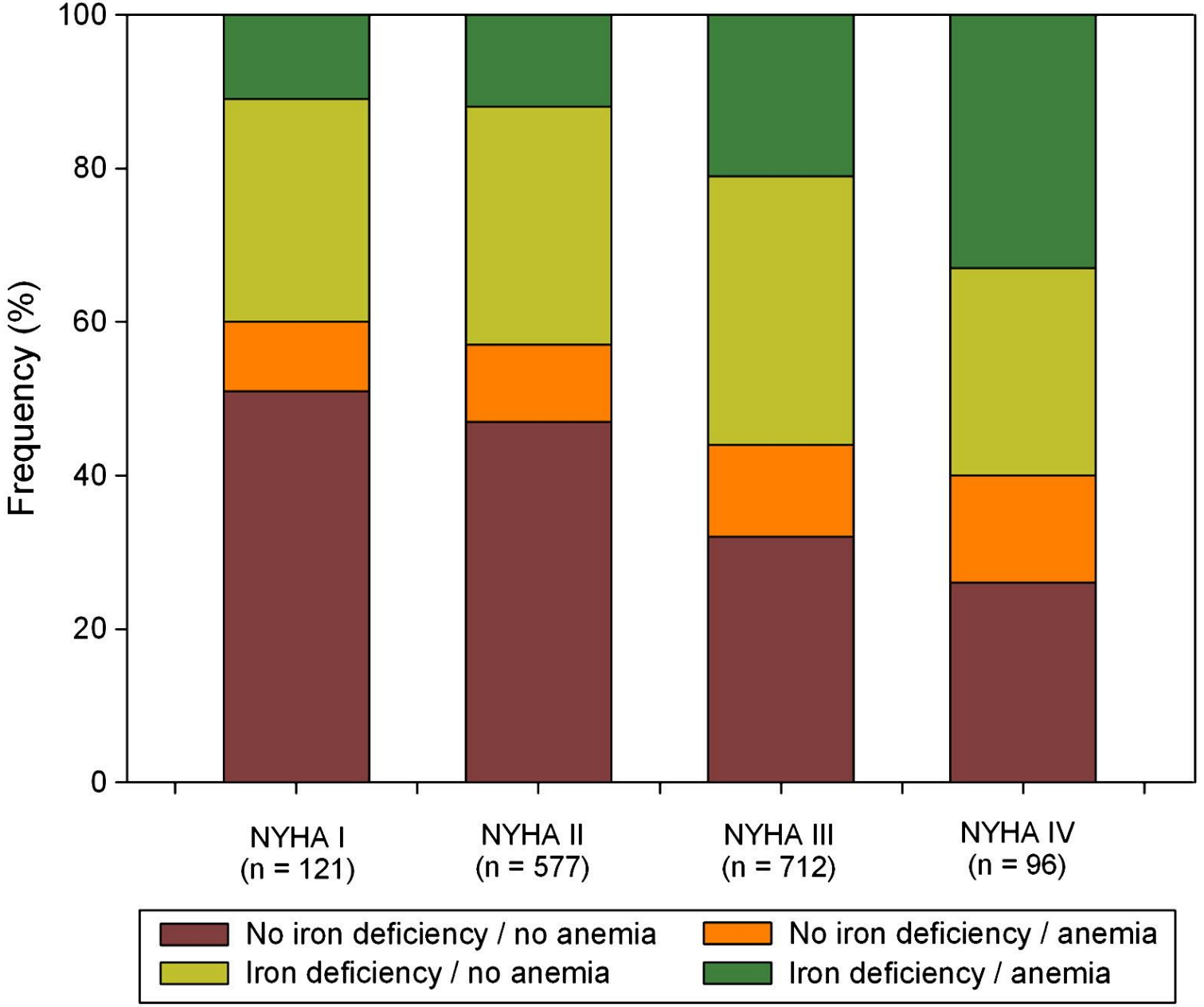
ESC European Society of Cardiology

European Heart Journal (2019) **40**, 3616–3625
doi:10.1093/eurheartj/ehz680

CLINICAL RESEARCH
Heart failure/cardiomyopathy

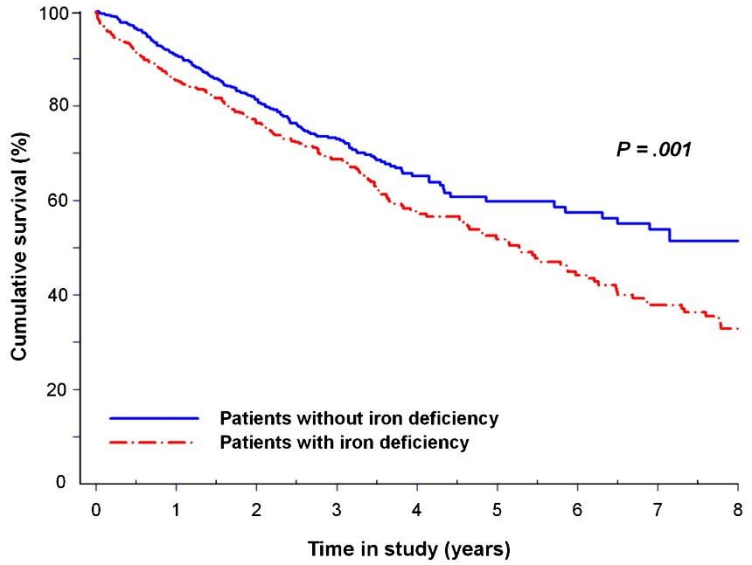
Iron deficiency in worsening heart failure is associated with reduced estimated protein intake, fluid retention, inflammation, and antiplatelet use

Haye H. van der Wal[1], Niels Grote Beverborg [1], Kenneth Dickstein[2,3], Stefan D. Anker [4], Chim C. Lang[5], Leong L. Ng [6,7], Dirk J. van Veldhuisen[1], Adriaan A. Voors[1], and Peter van der Meer[1]*



Am Heart J 2013; 165: 575-582

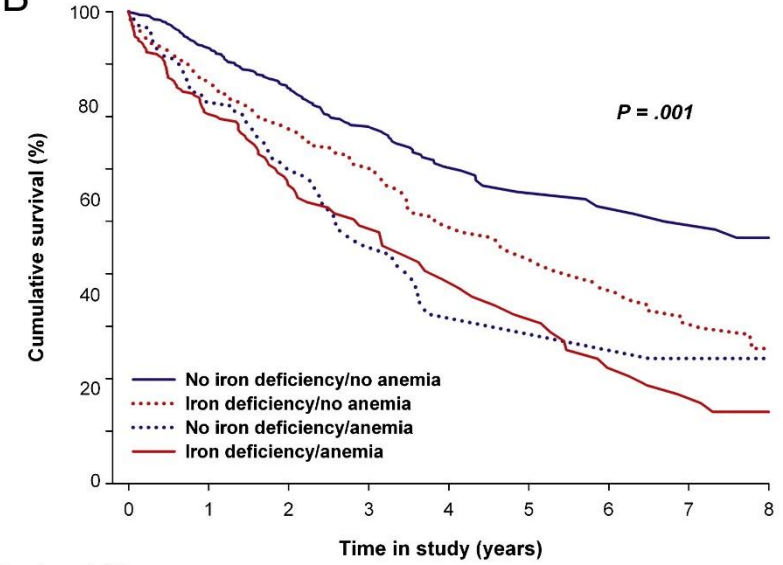
A



Numbers at risk:

ID absent	753	386	104	63	40
ID present	753	343	100	49	33

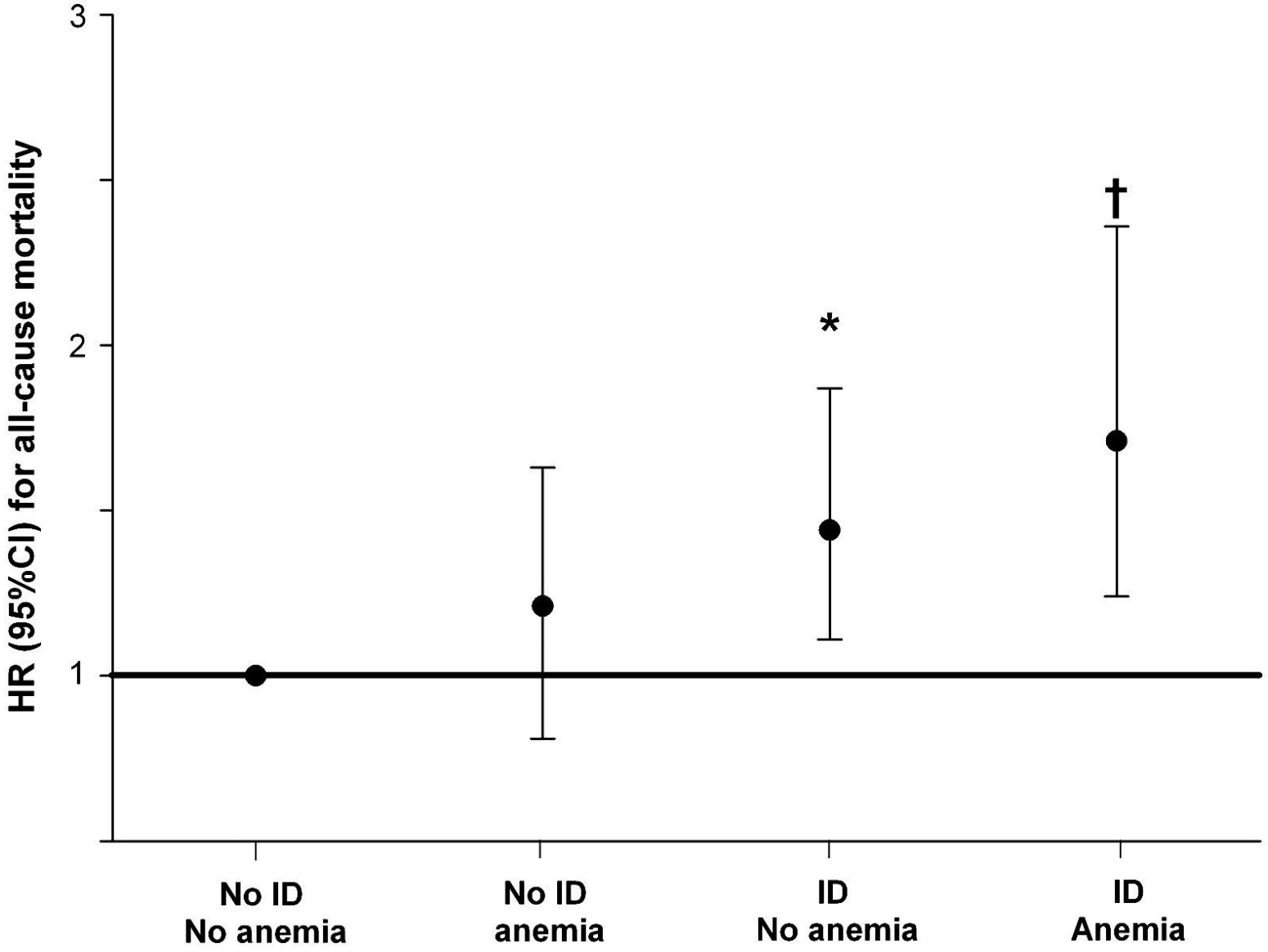
B



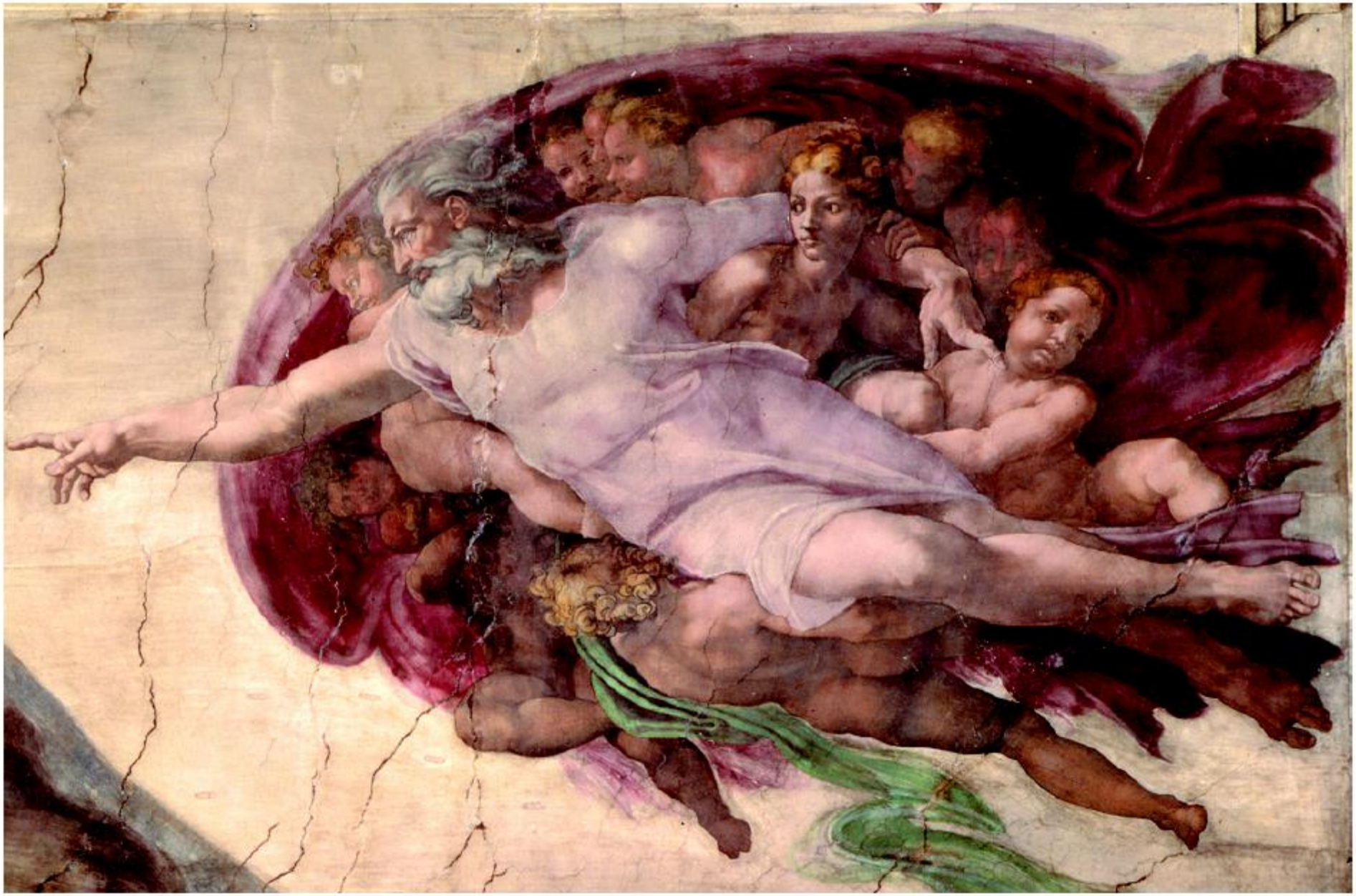
Numbers at risk:

No ID/no anemia	589	328	86	38	31
ID/no anemia	492	256	76	50	26
No ID/anemia	164	58	18	11	9
ID/anemia	261	87	24	13	7

Am Heart J 2013; 165: 575-582



Am Heart J 2013; 165: 575-582



ORIGINAL ARTICLE

Long-Term Cognitive Decline After Newly Diagnosed Heart Failure

Longitudinal Analysis in the CHS (Cardiovascular Health Study)

Table 2. Model-Predicted 5-y Declines in Mean 3MSE Score, by Age and Incident HF

HF*	Predicted 5-y Decline (95% Confidence Interval)†			
	70–75 y of Age	75–80 y of Age	80–85 y of Age	85–90 y of Age
No HF diagnosed before or during the 5-y interval	0.3 (0.0–0.6)	3.0 (2.8–3.3)	5.8 (5.3–6.2)	8.5 (7.7–9.2)
Incident HF diagnosed at beginning of the 5-y interval	2.8 (0.7–4.9)	6.1 (4.6–7.5)	10.2 (8.6–11.8)	15.2 (13.1–17.4)
Difference (incident HF minus no HF)	2.5 (0.4–4.6)	3.0 (1.6–4.4)	4.4 (2.8–6.0)	6.7 (4.6–8.8)

3MSE indicates Modified Mini-Mental State Examination; and HF, heart failure.

*F test P=0.011 for whether 3MSE trajectory across age differed by incident HF.

†Adjusted for birth year, sex, race, education, cigarette smoking, alcohol use, β-blocker use, angiotensin-converting enzyme inhibitor use, systolic blood pressure, body mass index, chronic kidney disease, chronic obstructive pulmonary disease, anemia, diabetes mellitus, hypertension, coronary heart disease, and AF. Participants were censored at the development of clinically recognized stroke.

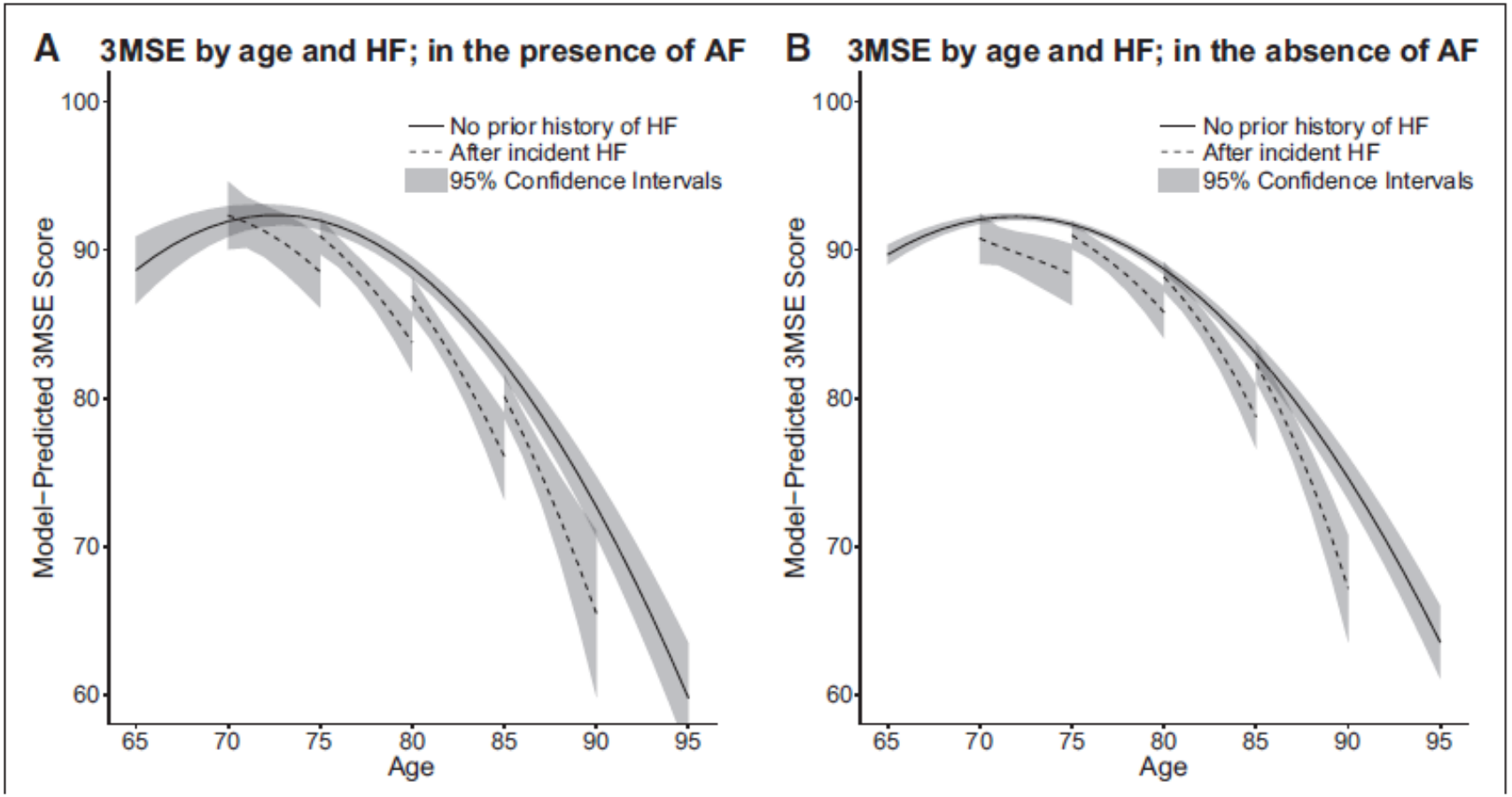

A
3MSE by age and HF; in the presence of AF
Model−Predicted 3MSE Score
100
90
80
70
60
No prior history of HF
After incident HF
95% Confidence Intervals
65
70
75
80
85
90
95
Age
B
3MSE by age and HF; in the absence of AF
Model−Predicted 3MSE Score
100
90
80
70
60
No prior history of HF
After incident HF
95% Confidence Intervals
65
70
75
80
85
90
95
Age

Table 5. Model-Predicted 5-y Decline in Mean 3MSE Score and DSST Score After Incident HF Diagnosis, by Left Ventricular EF Category

EF Category	Predicted 5-y Decline (95% Confidence Interval)*	
	3MSE Analysis†	DSST Analysis‡
Reduced EF	5.8 (2.3–9.3)	4.6 (1.7–7.6)
Preserved EF	7.7 (4.6–10.8)	4.9 (2.1–7.6)
Unknown EF	6.8 (4.2–9.5)	7.3 (4.9–9.8)

3MSE indicates Modified Mini-Mental State Examination; DSST, Digit Symbol Substitution Test; EF, ejection fraction; and HF, heart failure.

*Adjusted for age at incident HF diagnosis, sex, race, and education.

†*F* test *P*=0.734 for the difference in 3MSE trajectories by EF category.

‡*F* test *P*=0.280 for the difference in DSST trajectories by EF category.

WHAT IS NEW?

- Global cognitive ability declined significantly faster after newly diagnosed (incident) heart failure (HF) relative to no history of HF, in the absence of clinical stroke.
- The faster rate of decline after incident HF was evident across all ages between 70 and 90 years and was significantly more pronounced at older ages.
- The association of incident HF with more rapid cognitive decline did not differ significantly by whether participants had concomitant atrial fibrillation.
- The rate of cognitive decline after incident HF did not differ significantly by whether ejection fraction was reduced or preserved.

WHAT ARE THE CLINICAL IMPLICATIONS?

- Clinicians may use our estimates of cognitive trajectories to anticipate average rates of cognitive decline that may occur in their populations of patients who have newly diagnosed HF.

Circ Heart Fail. 2018;11:e004476. DOI: 10.1161/CIRCHEARTFAILURE.117.004476

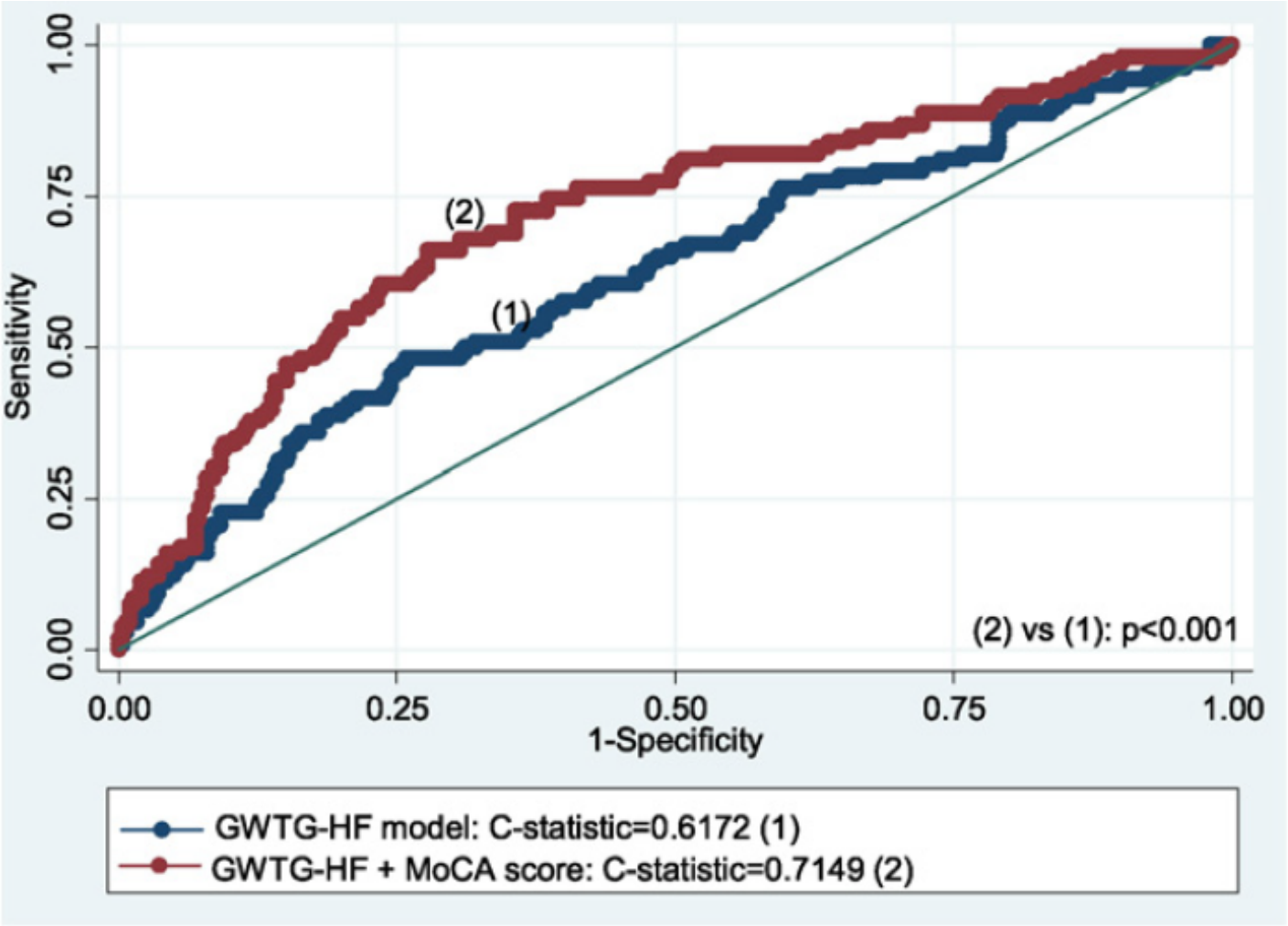
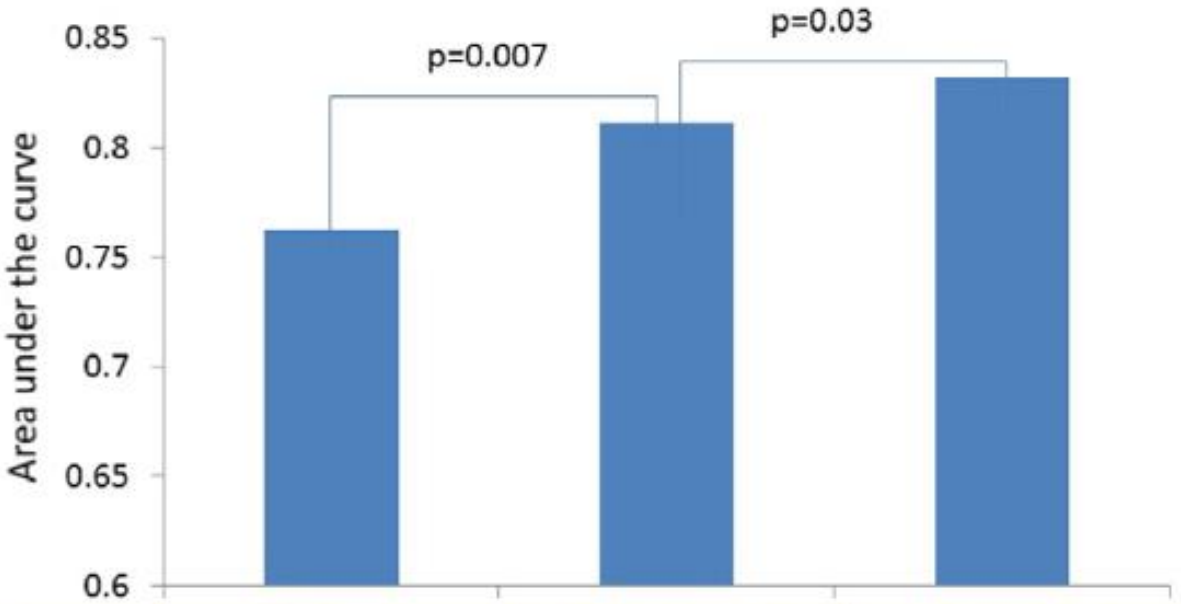


Fig. 1. Comparing area under the curve of the Get With The Guidelines-Heart Failure (GWTG-HF) predictive model with and without the addition of MoCA score.



Prediction model	Clinical	Physiological	Cognitive
Predictors	Basic clinical and non-clinical	Basic + echo	Basic + echo + MoCA
Change of deviance (G)	99.41	125.91	137.58
C-statistic	0.76 (0.71, 0.80)	0.81 (0.77, 0.86)	0.83 (0.78, 0.87)
Integrated discrimination improvement		Physiological vs. Clinical p<0.001	Cognitive vs. Physiological p<0.001

Fig. 2. Incremental values of echocardiographic measures and MoCA in predicting 30-day readmission or death.

Table 2. Prevalence of cognitive impairment according to patients' anemic status (n = 181).

Cognitive Function	Total (n = 181)	Anemia (n = 64)	Non-anemia (n = 117)	χ^2 or t	*p* Value
	n (%) or Mean ± SD	n (%) or Mean ± SD	n (%) or Mean ± SD		
3MS score	84.49 ± 9.90	78.64 ± 11.61	86.13±7.68	23.052	<0.001
< 80 (Impairment)	64 (35.4)	39 (60.9)	29 (24.8)	4.635	<0.0001
≥ 80 (Normal)	117 (64.6)	25 (39.1)	88 (75.2)		

3MS: The Modified Mini-Mental State

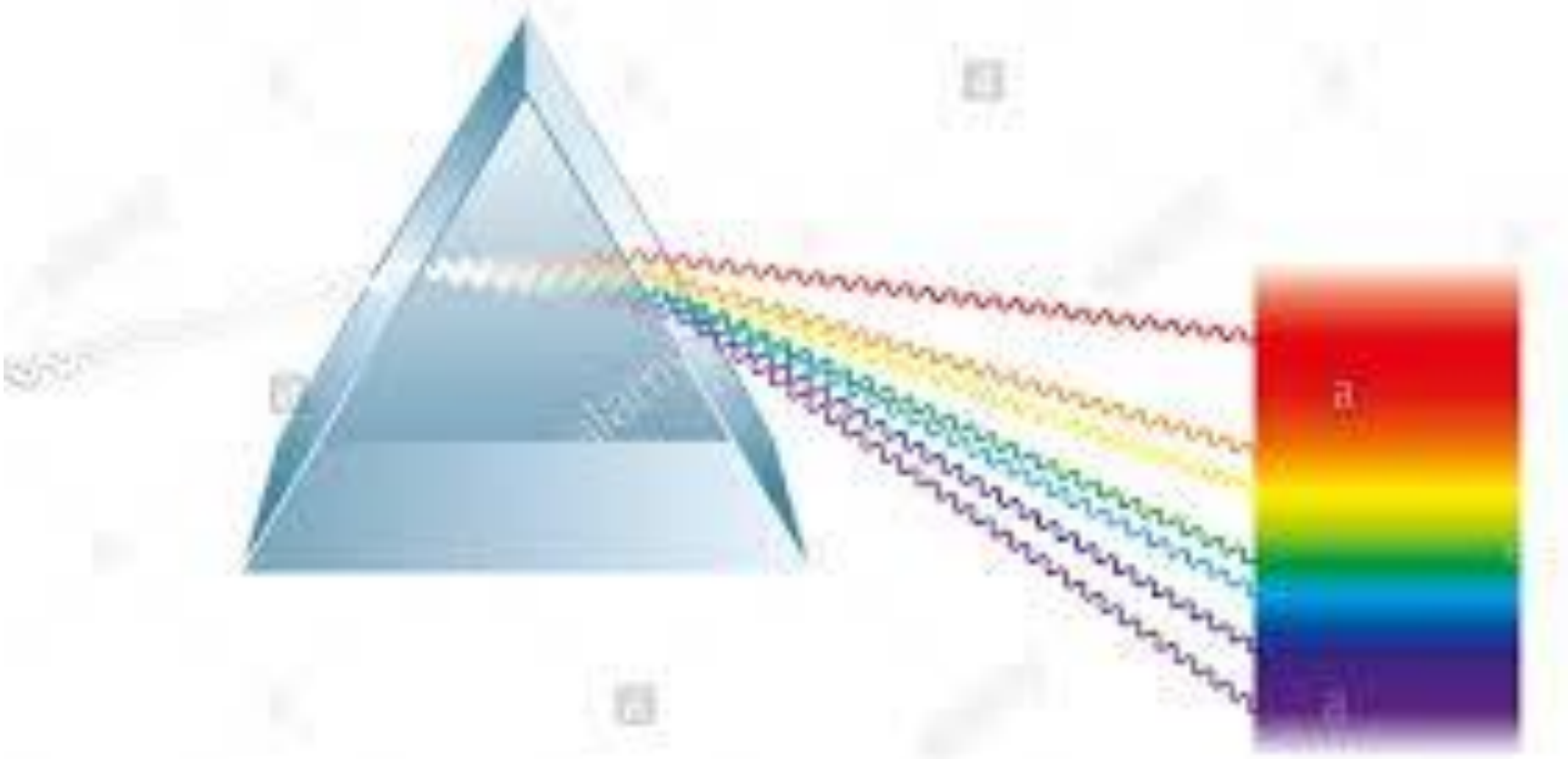
Table 3. Multiple logistic regression analysis of cognitive impairment among older adults with heart failure (*n* = 181).

Variables	Categories	Unadjusted Model		Adjusted Model	
		OR (95% CI)	*p* Value	OR (95% CI)	*p* Value
Age (yrs)	≤ 79	1	< 0.001	1	0.041
	≥ 80	9.115 (3.477–23.891)		3.208 (1.048–9.818)	
Gender	Men	1	0.005	1	0.684
	Women	2.703 (1.356–5.391)		1.194 (0.508–2.809)	
Education	≥ Middle School	1	< 0.001	1	< 0.001
	≤ Elementary school	7.935 (3.992–15.775)		4.918 (2.195–11.020)	
Monthly Income (KRW)	≥ 1,000,000	1	< 0.001	1	0.239
	< 1,000,000	4.425 (2.145–9.132)		1.703 (0.702–4.130)	
Anemic status	Non-anemia	1	< 0.001	1	< 0.001
	Anemia	4.734 (2.460–9.108)		4.268 (1.898–9.593)	

OR: Odds Ratio; CI: Confidence Interval; 3MS: The Modified Mini-Mental State

	Male (n = 70)				Female (n = 49)			
Variables	**β**	***t* Statistics**	***P***	**95% CI**	**β**	***t* Statistics**	***P***	**95% CI**
Comorbidities	0.190	2.715	.008	0.404–2.652				
Diuretics	–0.166	–2.225	.030	–7.047 to –0.381				
Depressive symptoms	0.686	8.805	< .001	1.329–2.109	0.828	10.017	< .001	1.743–2.620
Perceived control	–0.231	–2.775	.007	–0.943 to –0.154				
Model statistics	F statistics = 35.852 R^2 = 0.688 Adjusted R^2 = 0.669 P < .001				F statistics = 100.345 R^2 = 0.686 Adjusted R^2 = 0.679 P < .001			

CONCLUSIONI



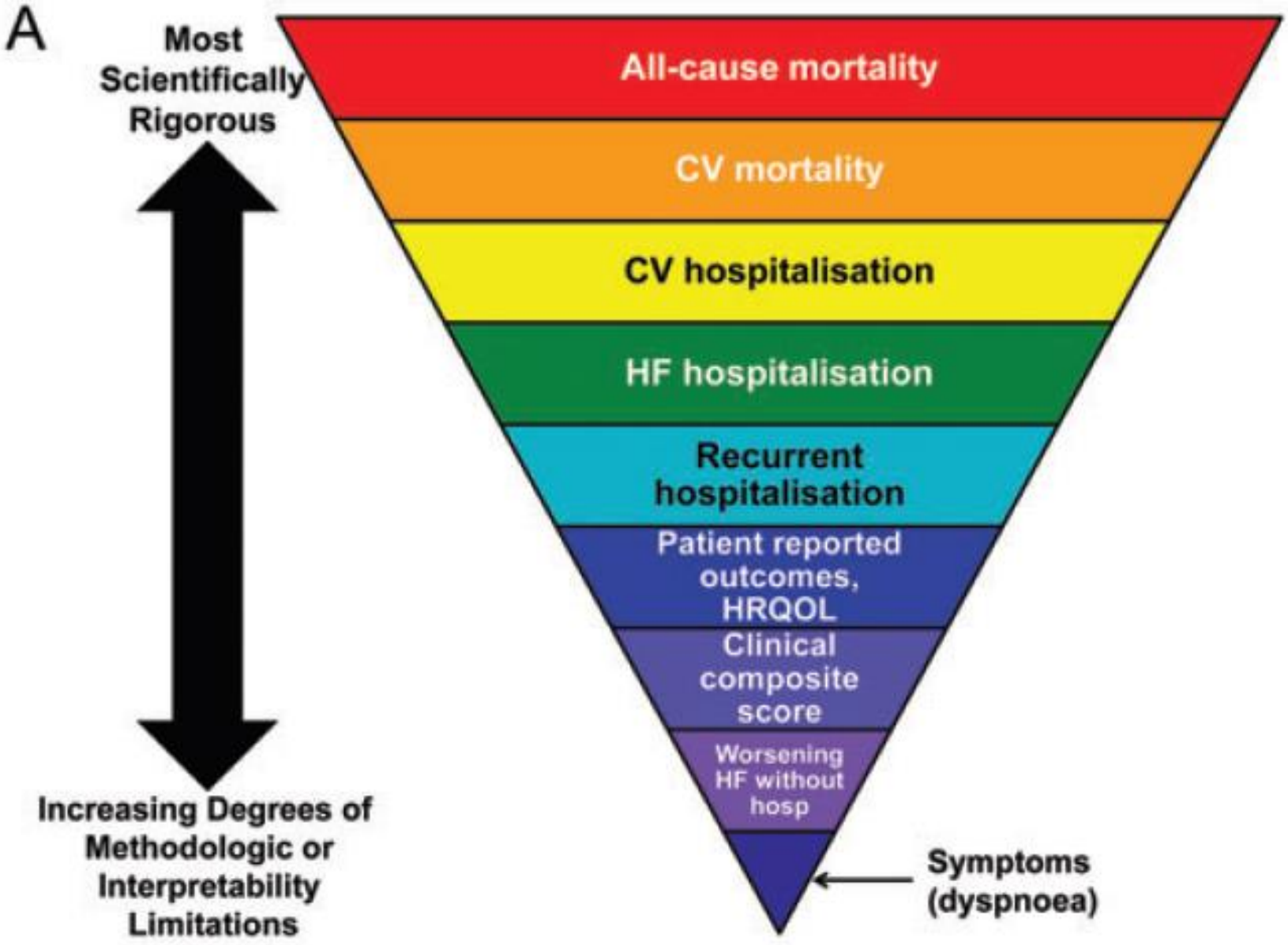

A
Most Scientifically Rigorous
Increasing Degrees of Methodologic or Interpretability Limitations
All-cause mortality
CV mortality
CV hospitalisation
HF hospitalisation
Recurrent hospitalisation
Patient reported outcomes, HRQOL
Clinical composite score
Worsening HF without hosp
Symptoms (dyspnoea)

Figure 1 Schematic of potential endpoints for phase III pivotal chronic heart failure trials (*A*) or acute heart failure trials (*B*). The hierarchy (or order ranking) of the endpoint options to measure efficacy is not definitive. Different hierarchies may be appropriate depending on the endpoint's relevance to a specific patient population, the ability to measure the endpoint objectively in a given study, and the possibility of standardizing the endpoint measurement through accurate and reliable instruments. CV, cardiovascular; HF, heart failure; HRQOL, health-related quality of life.