Management of elderly patients with acute heart failure

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Heart failure in the elderly

- Heart failure (HF) incidence and prevalence increases with age
- As populations age frequency of presentation with HF increases
- High morbidity and mortality
- Demographics of older patients different to younger patients
- More preserved systolic function and co-morbidities
- Evidence base for most management strategies for older patients with HF is poor

What is the target population?

- Defining the HF population provides a challenge
- Depends on selection criteria: acute admission, outpatient, general medical ward or cardiology
- We know that older patients with HF are more likely to be female, have higher BP and preserved EF
- RICA registry: HF admissions to internal medicine in 52 centres in Spain 2008- (1)
- AHA Get With the Guidelines registry admissions to 281 hospitals in United States 2005- (2)
- SENIORS: Randomised trial of ambulatory HF ≥ 70 years 2001-2003, EF≤ 35% or prior HF admission (3)

1. *Pérez-Calvo JI, Montero-Pérez-Barquero M, Camafort-Babkowski M, Conthe-Gutiérrez P, Formiga F, Aramburu-Bodas O, Romero-Requena JM; RICA Investigators. QJM 2011; 104:325-33.*
2. *Steinberg et al Circulation. 2012;126:65-75*
3. *Flather et al Eur Heart J 2005; 26:215-25.*

Age of Patients in Major Trials of β-blockers in HF

Trial	β-blocker	N	Mean Age	% Females	EF (%)
COPERNICUS	Carvedilol*	2289	63	21	19.9
MERIT-HF	Metoprolol*	3991	64	23	28.0
US Carvedilol	Carvedilol*	1094	58	22	22.6
CIBIS-II	Bisoprolol	2647	61	20	27.5
Mean			*61*	*21.5%*	*24.9*
SENIORS	Nebivolol	2135	76	37	36
US Heart Failure Population			77	50	>50%**

- **Agents approved for the treatment of HF in the US.**
- **** Percentage of US population with preserved ejection fraction**

MERIT-HF Study Group. *Lancet.* 1999;353:2001-2007; Packer *N Engl J Med.* 2001;344:1651-1658; Colucci WS. *Circulation*. 1996;94:2800-2806; CIBIS Investigations and Committees. *Lancet* 1999;353:9-13; The Beta-Blocker Evaluation of Survival Trial Investigators. *N Engl J Med*. 2001;344:1659-1667; Heiat et al. *Arch Intern Med*. 2002;162:1682-1688.

Demographics of HF populations

Variable	RICA n=1000	AHA GWTG N=110,000	SENIORS N=2100
Age (years)	78	74	76
Gender %	53	47	37
Hypertension %	86	76	63
Diabetes %	47	43	27
Prior MI %	21	CAD 50%	44
Atrial fibrillation %	54	31	35
NYHA 2 %	54		57
NYHA 3 %	34		39
Systolic BP mmHg	142	138	140
Heart rate (bts/min)	90	82	80
Ejection fraction %	51	40	36

Medications and outcomes in HF populations

Variable	RICA n=1000	AHA GWTG N=110,000	SENIORS N=2100
ACE-I/ARB %	87	66	76
Beta blocker %	64	81	49*
Aldosterone antag %	33	18	28
Diuretic %	89		83
Digoxin %	26		41
Anticoagulant %	55	65	23
Length of stay days	10	4 (median)	--
Mortality 12 months %	20	3% in hosp	10
Mortality/ CV admission	32		23

* Randomised treatment

American Heart Association Get With The Guidelines Registry: in hospital mortality by EF and year

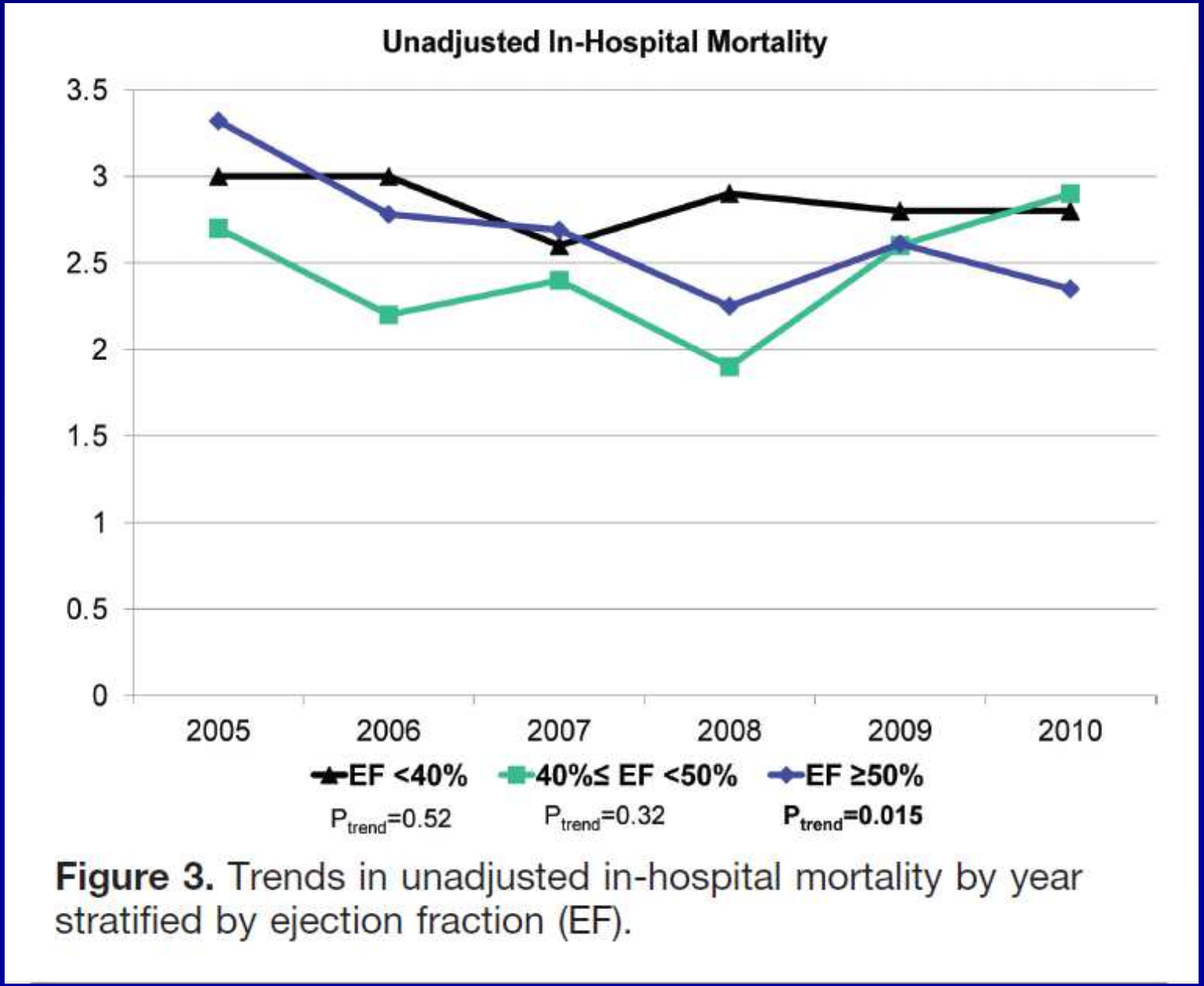
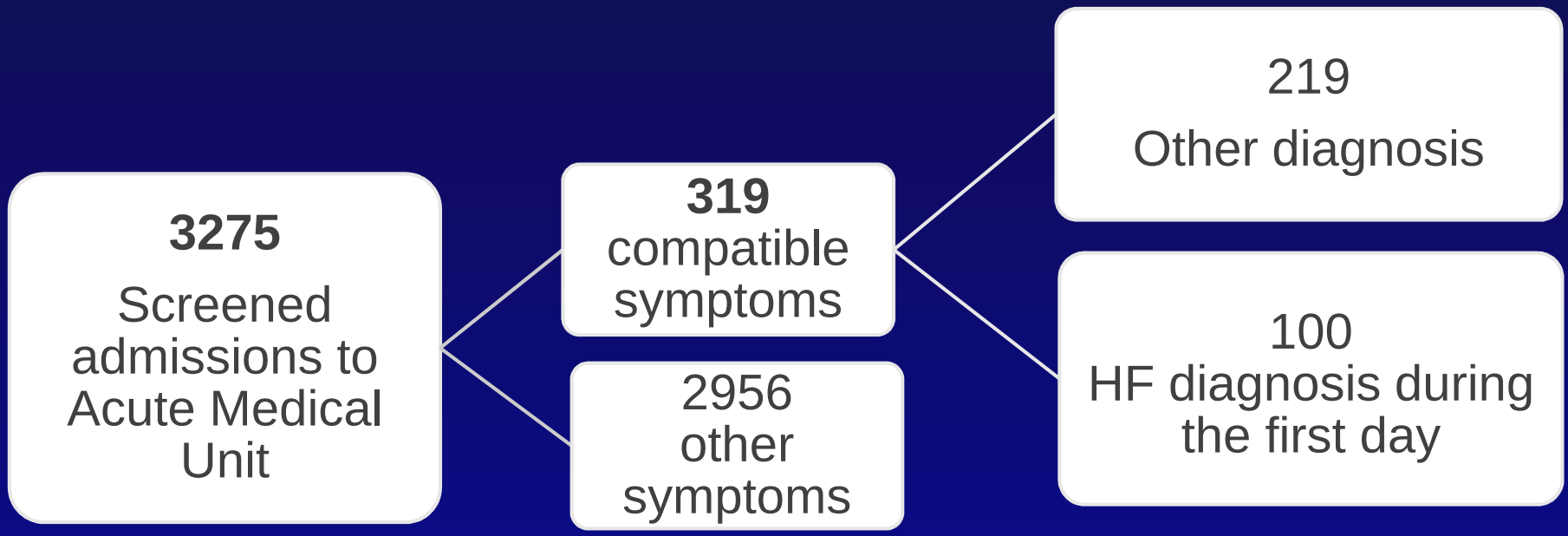


Figure 3. Trends in unadjusted in-hospital mortality by year stratified by ejection fraction (EF).

Steinberg et al Circulation. 2012;126:65-75.

Norlfolk and Norwich University Hospital local Heart Failure audit 2013: Screening over 6 weeks



Limitations

- Review by initial symptom
- Diagnosis of HF during the first day: later development of HF not included
- Direct admissions to ward (e.g. to cardiology) can be missed: cross validation with Cardiology records

Raul Antonio Ruiz Ortega, Joanna Ford, Marcus Flather et al

Norwich HF audit: demographics by specialty

	CARDIO (24)	Medicine* (56)	OTHER (20)	p
Age (years)	71	87	67	<0.005
Male %	67%	36%	65%	0.01
Previous HF %	29%	43%	40%	0.5
AF	25%	38%	10%	0.059
Previous MI	38%	25%	15%	0.23
Hypertension	38%	63%	30%	0.017
Diabetes	21%	25%	25%	0.9
Systolic BP mmHg	130	141	149	
LVEF % **	29	57	56	

* Mainly care of the elderly ** data incomplete

Norwich Audit: Management and outcomes

	CARDIO Adm/disch	Medicine Adm/disch	OTHER Adm/disch
Beta-blockers	38/71	39/46	45/50
Aldosterone antag %	25/71	13/13	20/25
ACE/ ARB %	44/83	41/36	35/40
Loop diuretic %	42/55	48/88	40/80
Length of stay days	11	9	8
Death in hospital %	4	21	5

What is the real world: patient selection and the “Russian doll” effect

Flather et al Clinical Trials 2006;3(6):508-12.

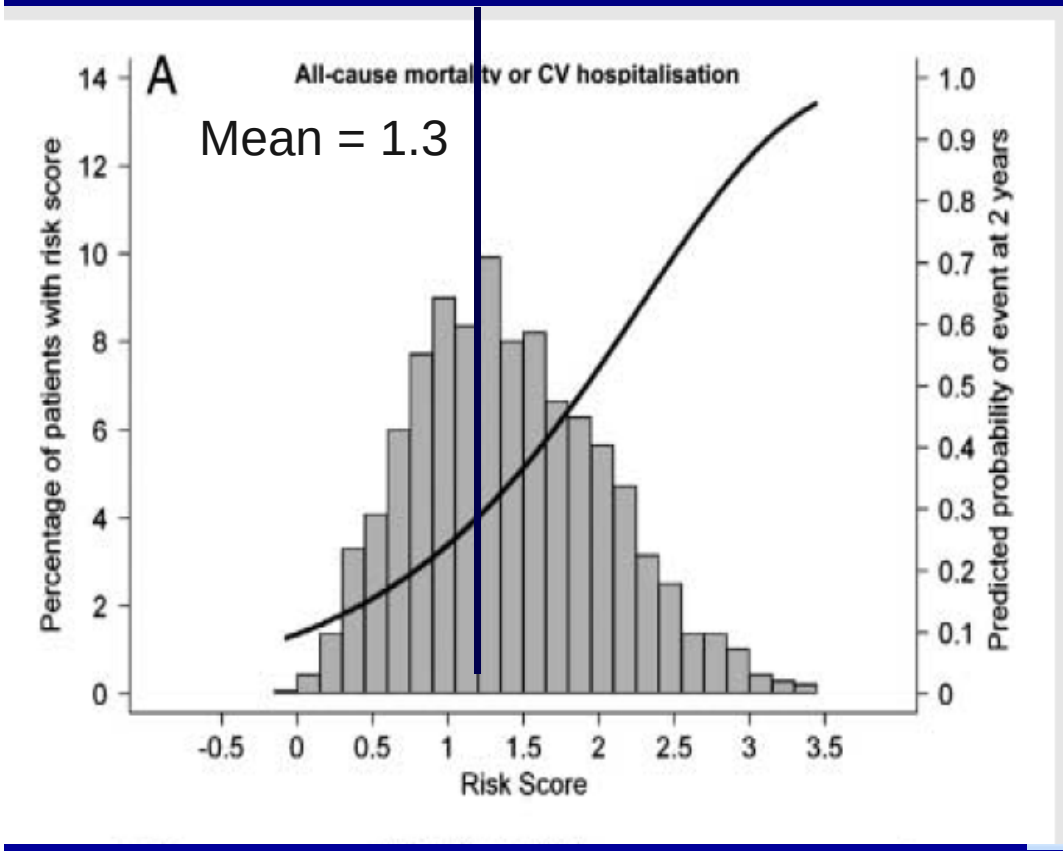
SENIORS risk model applied to RICA

- We previously developed a risk model in elderly HF patients from the SENIORS clinical trial
- Multivariable bootstrap model with internal validation
- For death/ CV hospital admission NYHA class, prior MI, LA dimension, uric acid, BMI, peripheral arterial disease, right bundle branch block and diabetes mellitus were retained in the model
- Risk model applied to RICA
- Risk coefficient adjusted for RICA

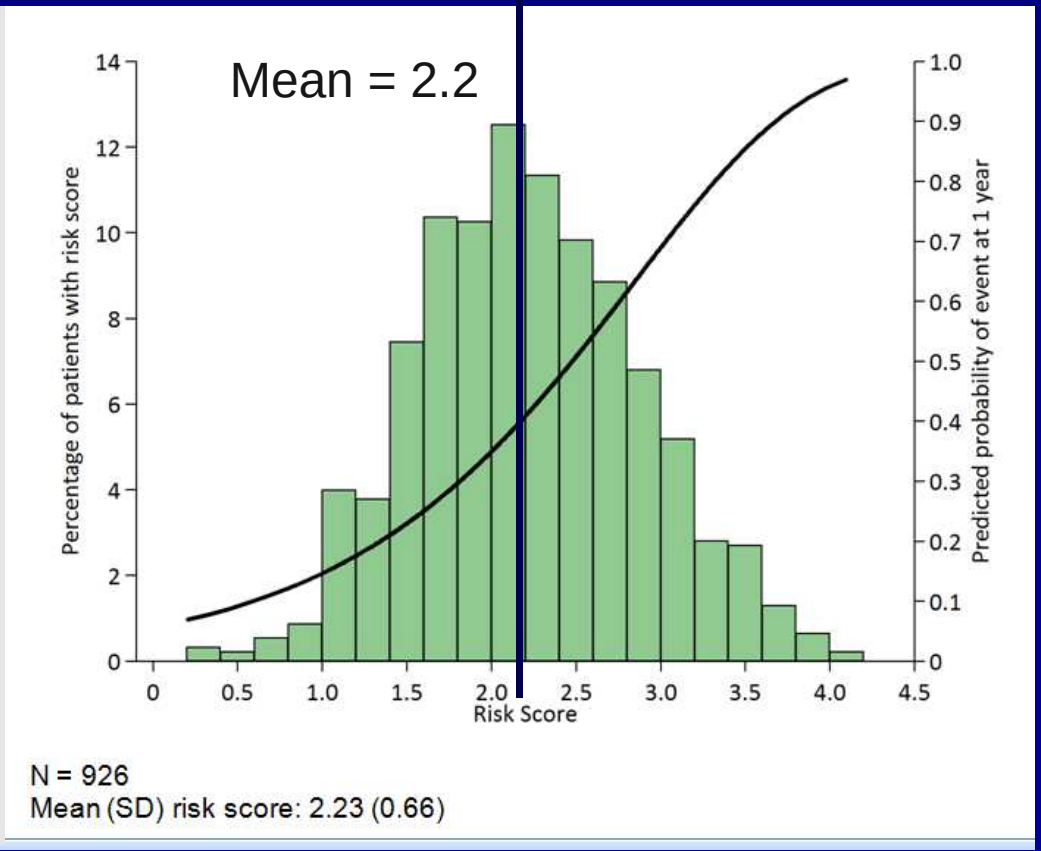
Manzano et al , Eur J Heart Fail 2011; 13:528-36

Risk score distributions for All cause mortality or CV hospitalisation

SENIORS

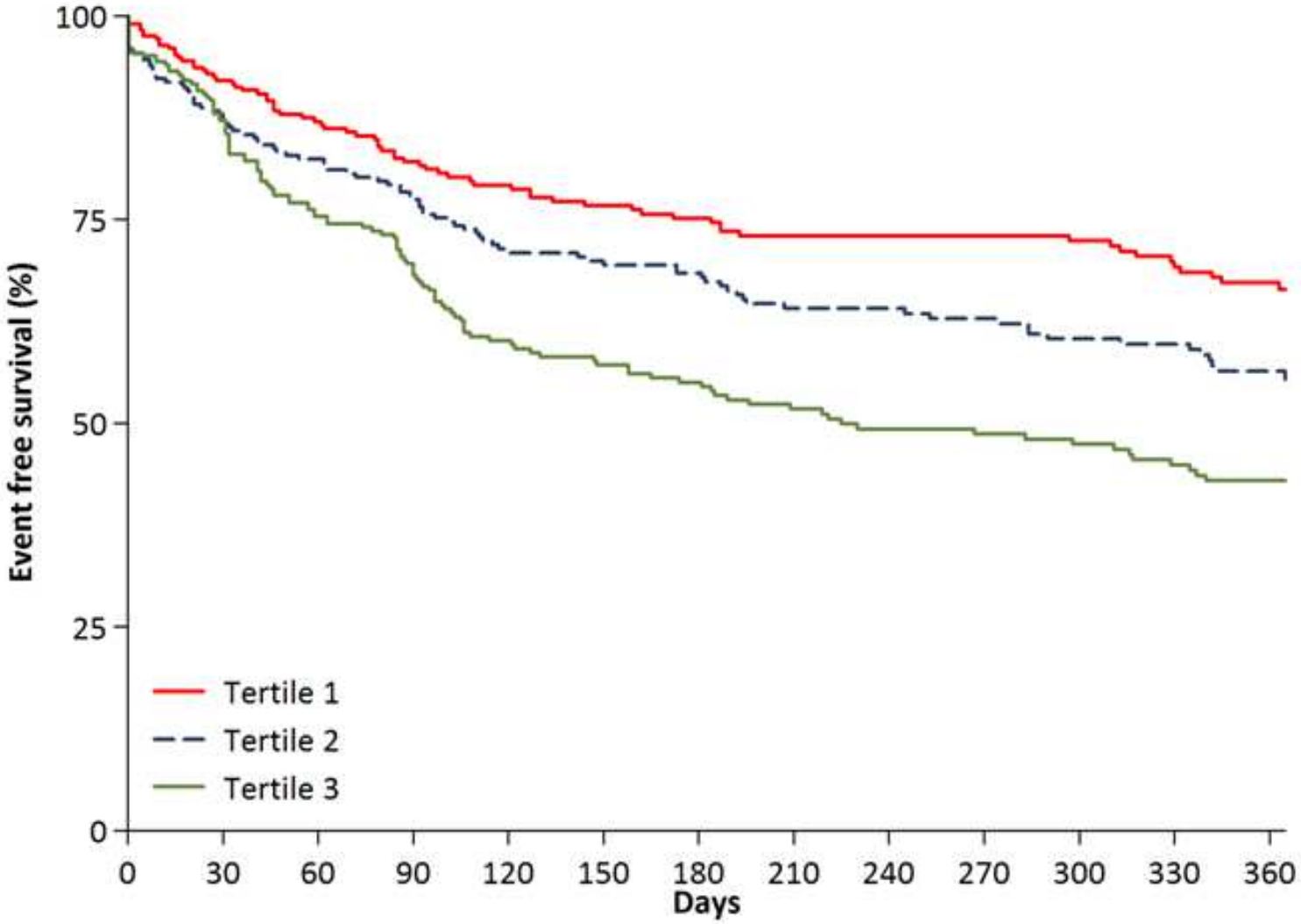


RICA



Montero, Manzano, Flather 2014 et al submitted

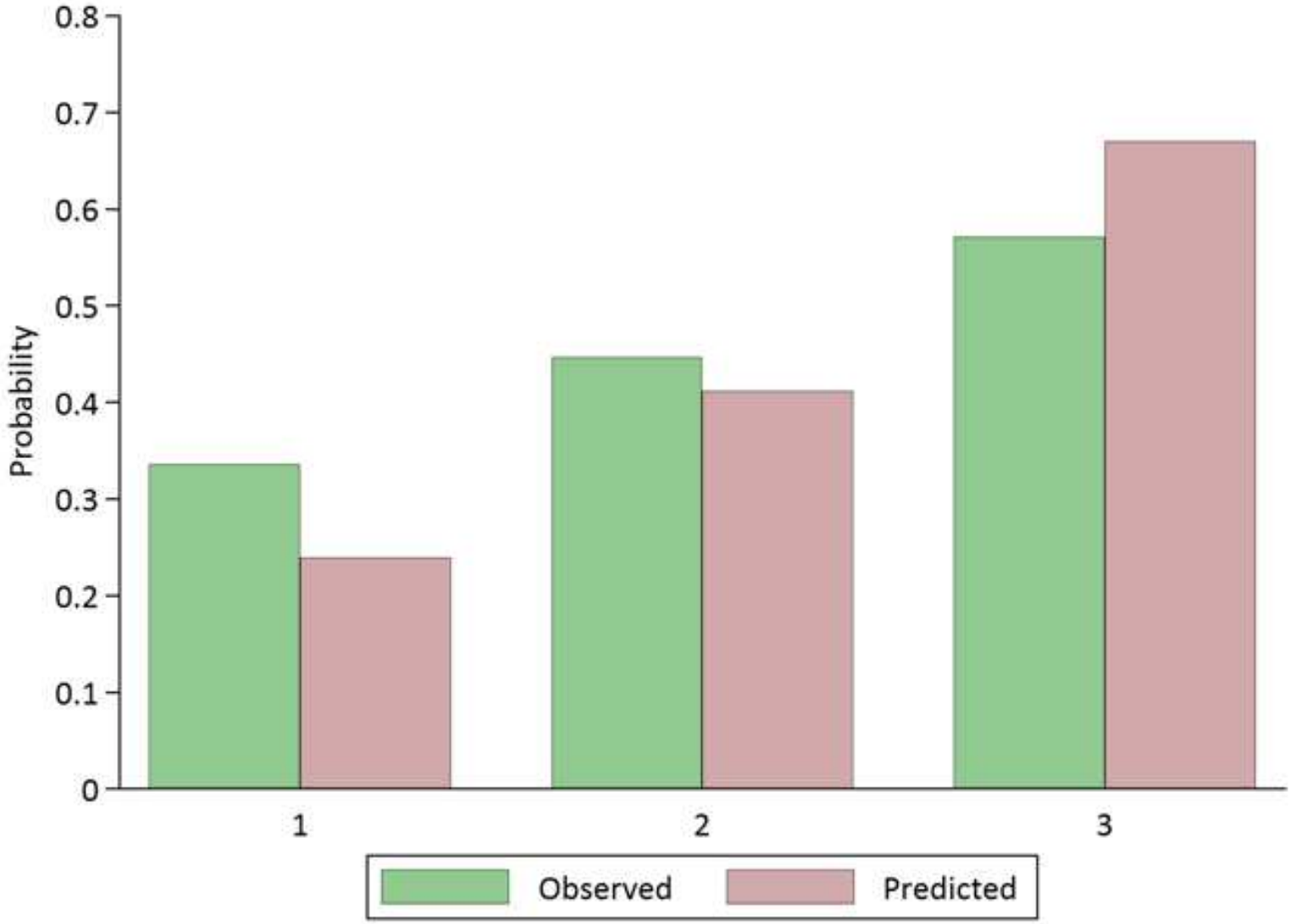
All cause mortality or CV hospitalisation in RICA stratified by tertiles using the SENIORS risk model



p < 0.001, test long rank.

Montero, Manzano, Flather 2014 et al submitted

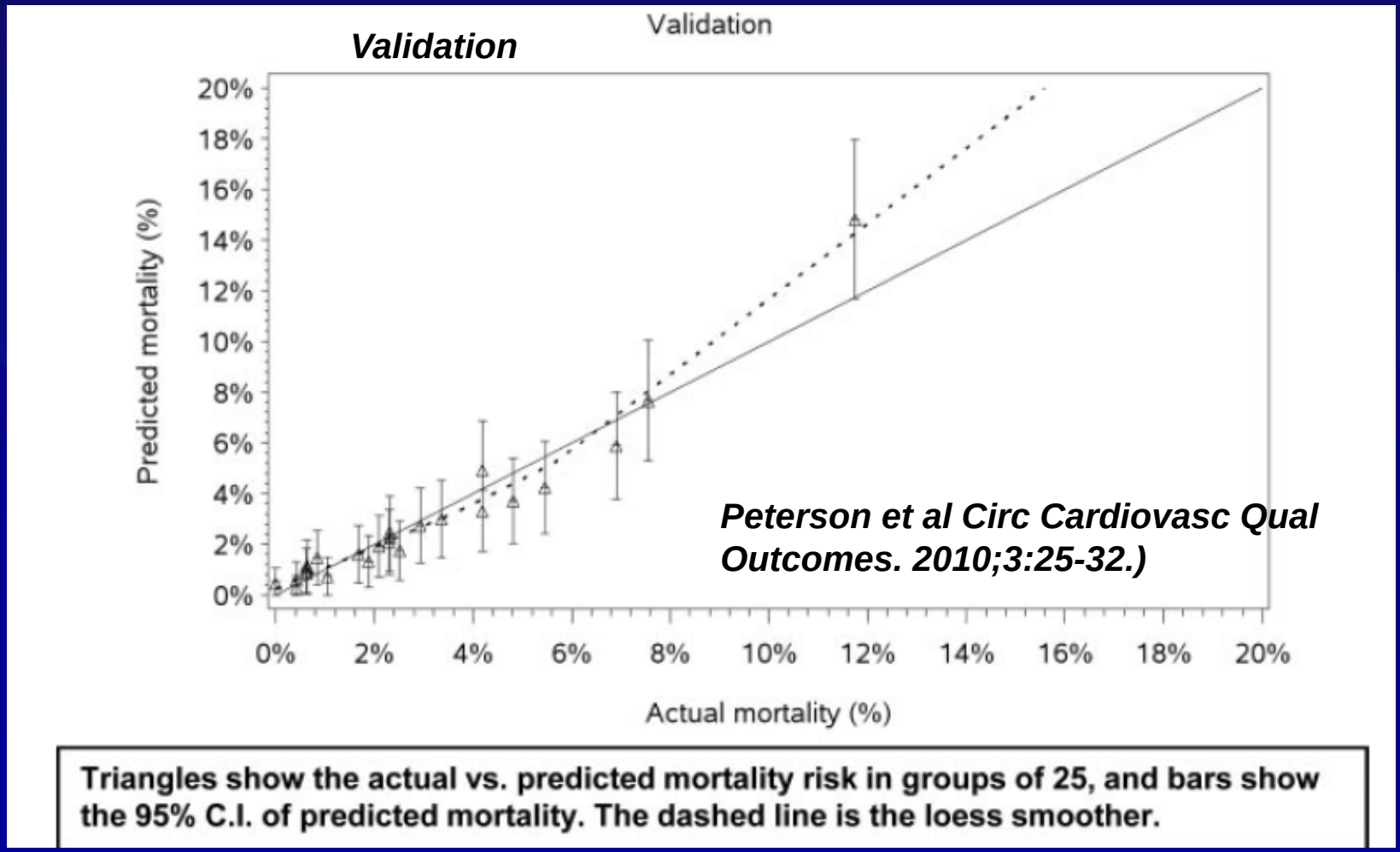
Prediction of all cause mortality or CV hospitalisation in RICA using SENIORS risk model



Montero, Manzano, Flather 2014 et al submitted

Heart failure risk models

- Many HF models have been developed
- AHA GWTG model showed age, systolic blood pressure, creatinine, heart rate, sodium, chronic obstructive pulmonary disease, and nonblack race were predictive of in-hospital mortality
- Other models also retain different variables: the actual variables may not be so important in determining risk



Variables associated with length of stay in RICA

VARIABLES	< 7 days	≥ 7 days	P value
Mean length of stay, days (SD)	4	13	<0.001
Age, years (SD)	80	78	<0.001
HF previous, n (%)	70	67	0.038
COPD, n (%)	22	28	<0.001
NYHA Class II, n (%)	57	50	<0.001
NYHA Class III, n (%)	31	37	0.001
SBP (mmHg)	142	137	<0.001
LVEF	51	50	
Creatinine (mg/dl)	1.3	1.4	0.002
Left ventricular hypertrophy, n (%)	24	29	0.003
Hospital acquired infection	17	27	0.009
Mortality at year %	27	37	<0.001
Readmissions at one year %	28	28	

R. Ruiz-Ortega, M. Montero Perez Barquero, L. Manzano, A. Conde Martel, A. Urrutia De Diego, O. Aramburu-Bodas, JC. Trullas-Vila, A. Muela-Molinero, R. Quiros-Lopez, M. Flather 2014 ESC submitted

What are clinical trials and guidelines telling us about elderly HF with preserved systolic function?

- SENIORS enrolled elderly patients with about 25% EF>45%: no apparent interaction of EF with effect of nebivolol on death/ CV hospitalisation
- PEP-CHF, CHARM preserved and I-Preserve randomised HF patients with preserved EF to ACE-I/ ARB or placebo: no evidence of clinical benefit
- Aldosterone antagonists not tested?
- Guidelines (European, American and NICE (UK)) do not provide advice on use of ACE-I/ARB, beta blockers or aldosterone antagonists for routine use in elderly with preserved EF
- Clinically ACE-I/ARB, BB and diuretics used for BP and heart rate control and fluid overload

I-PRESERVE: Patient Characteristics

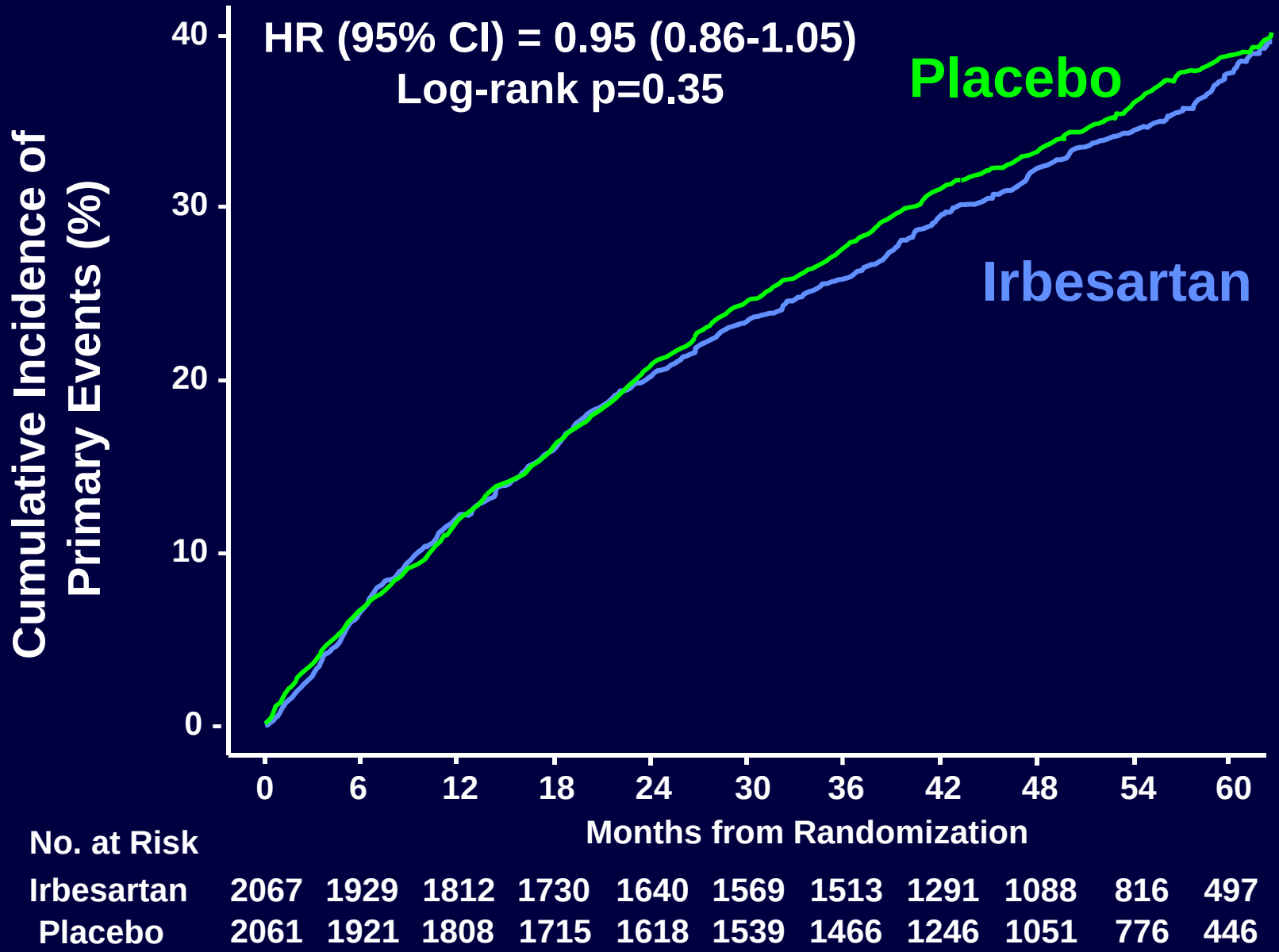
	Cohort & Epidemiological Studies	I-PRESERVE (n=4,128)
Age, yr	75	72
Women	65-70%	60%
EF	60%	59%
Hypertension	80-90%	88%
Prior MI	<20%	23%
Atrial fibrillation	20-30%	29%
Diabetes	20-30%	27%

Massie et al: N Engl J Med 2008 Dec 4;359(23):2456-67.

I-PRESERVE: Primary Endpoint

Death or protocol specified CV hospitalization

Massie et al: N Engl J Med 2008 Dec 4;359(23):2456-67.



Conclusions and recommendations

- Identifying “real world” populations is a challenge and depends on question and selection criteria
- HF in the elderly is a rapidly growing problem with human health and health resource implications
- These patients are mostly women with preserved EF
- High risk of mortality and readmission
- Risk stratification models could help target treatment and feasibility studies should be done
- More evidence is needed on potential benefits of treatment strategies: pharmacological and non-pharmacological

Acknowledgments

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- Menarini International