

Heart Failure 2005

The octogenarian failing heart

Lisbon, 14 June 2005

**Pharmacological Treatment: is There
Any Evidence-based Medicine for
the Very Old?**

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**No, not even for the
slightly old !**

Mean Age of the Patients with Heart Failure in Epidemiological Studies

Author (year)	No. of patients	Age (years), M \pm SD
Chae (1999)	221	77.9 \pm 5
EPICA, Portugal (2000)	551	70 \pm 11
Ghali (1997)	1133	77.6 \pm 7.9
Lowe (1998)	579	77
MacIntyre (2000)	66 547	♀: 78; ♂: 72
McCulloch (2002)	29 686	♀: 73.7; ♂: 69.2
Mosterd, Netherlands (2000)	24 868	♀: 77.7; ♂: 72.9
Senni, Minnesota (1998)	216	77.3 \pm 12.1
SEOSI (1997)	3 921	67 \pm 12
EuroHeart Failure (2003)	46 788	71

Mean Age and Proportions of Elderly Patients in Multicenter Trials

Trial	No. of patients	Mean Age	% > 70 years
CONSENSUS I	253	71	50%
SOLVD-T	6 797	61	15%
DIG	7 788	63	27%
MERIT-HF	3 991	64	32%
CIBIS-II	2 647	61	...
COPERNICUS	2 289	63	...
RALES	1 633	61	...
EPHESUS	6 642	64	
ELITE-II	3 152	71	58%
Val-HeFT	5 010	62	...
CHARM	7 601	66	23% (>75)

Factors Distinguishing HF in the Elderly from HF at Middle Age

	Middle age	Elderly
Prevalence	<1%	~ 10%
Sex	Men > women	Women > men
Etiology	CAD	Hypertension
Clinical features	Typical	Atypical
LVEF	Reduced	Normal
Comorbidities	Few	Multiple
Physician	Cardiologist	Primary care
RCTs	Many	Few
Therapy	Evidence-based	Empiric

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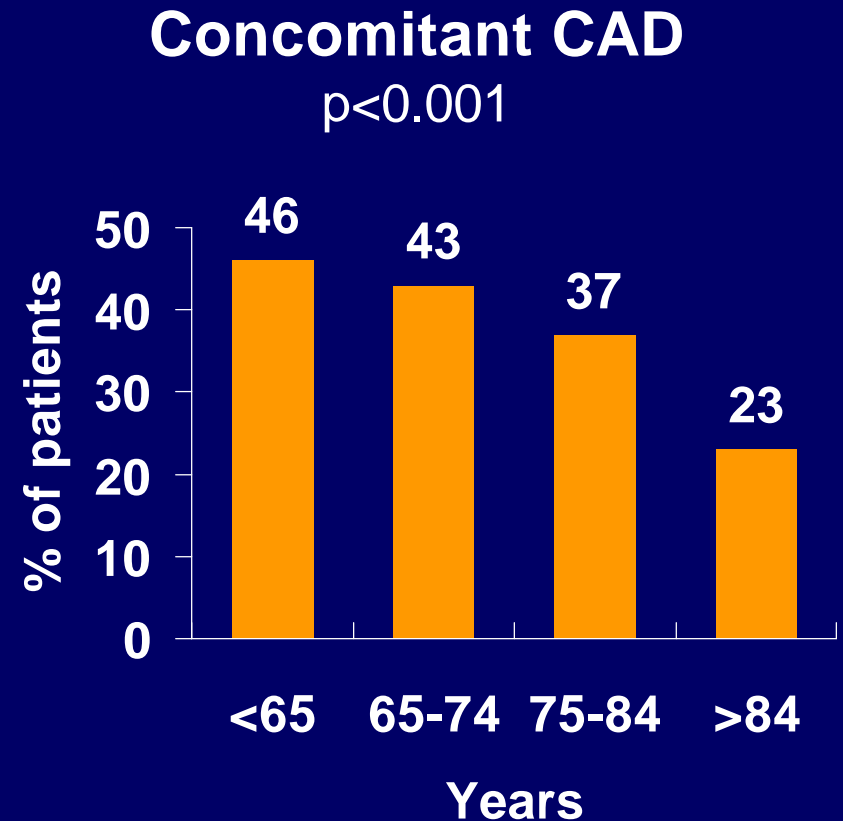
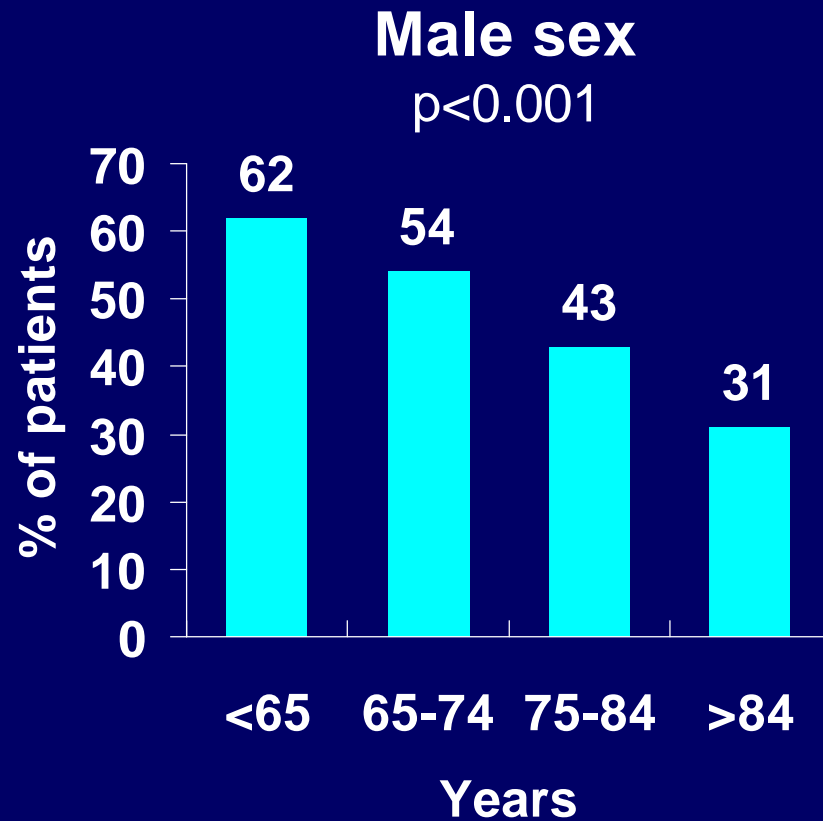
Baseline Characteristics of Patients Recruited in COMET Subdivided According to Age (mean, 62 ys.; range, 18-90)

	< 60 years (n = 1171)	60-70 years (n = 1119)	> 70 years (n = 739)
Female, %	17%	19%	26%
BMI, m \pm sd	28 \pm 5	27 \pm 4	25 \pm 4
Dyspnoea score \geq 4, %	13%	18%	27%
Fatigue score \geq 4, %	13%	16%	26%
NT-ProBNP, median	804	1314	1826
Creatinine, median	92	102	114
Diabetes, %	20%	29%	25%
Atrial fibrillation, %	15%	20%	27%
Paced rhythm, %	2%	7%	12%

All these variables were significantly different between the different age subgroups

Clinical Characteristics of the Patients with HF According to Age: IMPROVEMENT Study

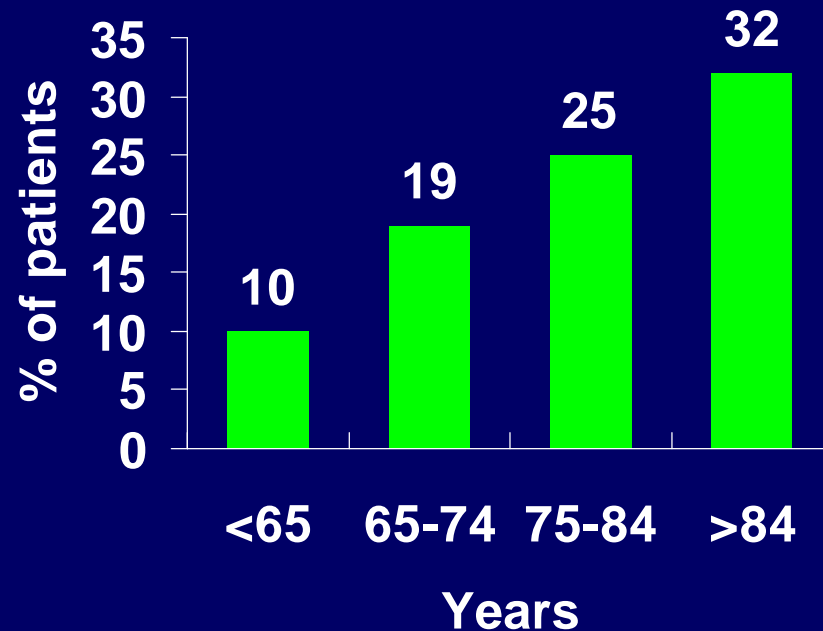
8256 patients in 15 countries, 1999-2000



Concomitant Diseases of the Patients with HF According to Age: IMPROVEMENT Study 8256 patients in 15 countries, 1999-2000

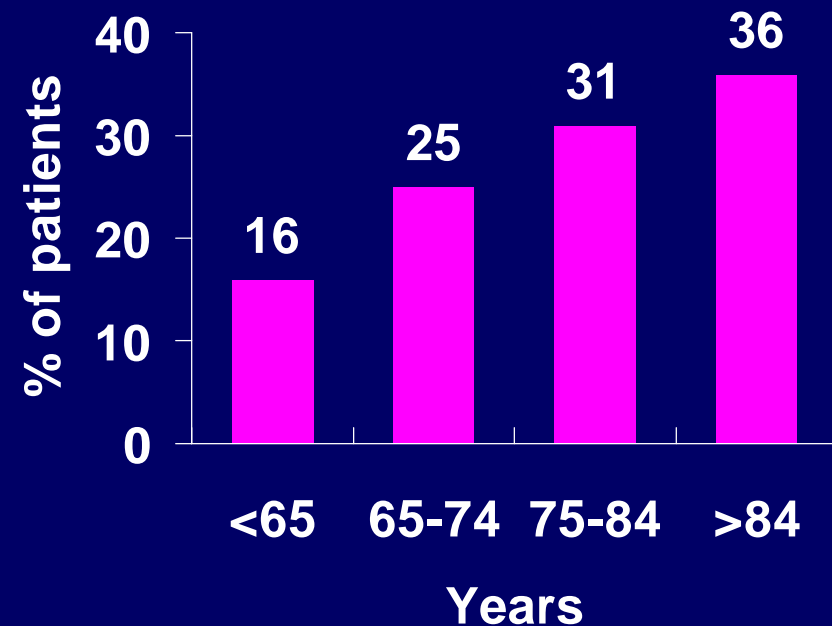
Renal dysfunction

$p < 0.001$



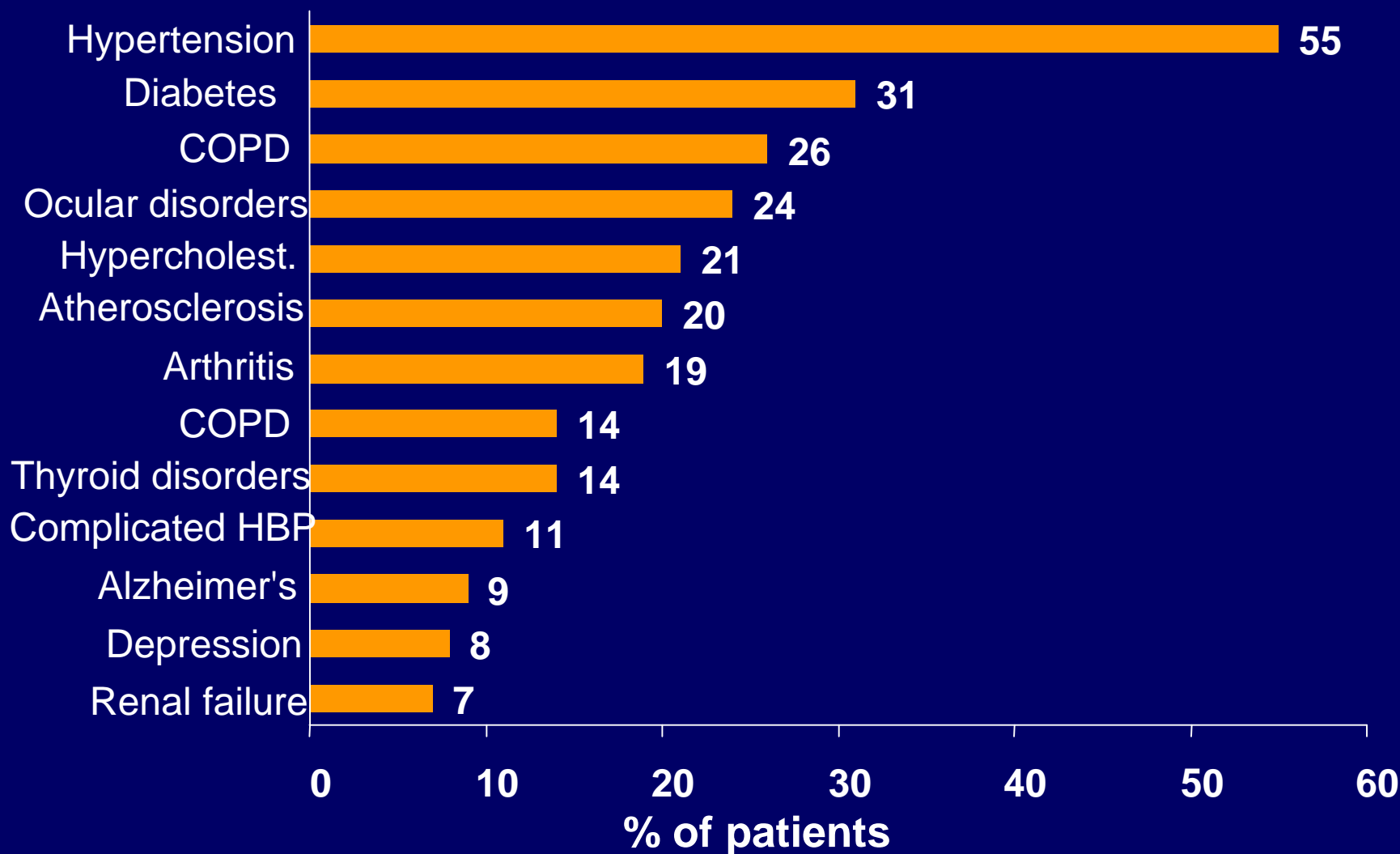
Atrial Fibrillation

$p < 0.001$



~ prevalence of hypertension and pulmonary disease
↓ prevalence of diabetes and ↑ prevalence of stroke with ↑ age

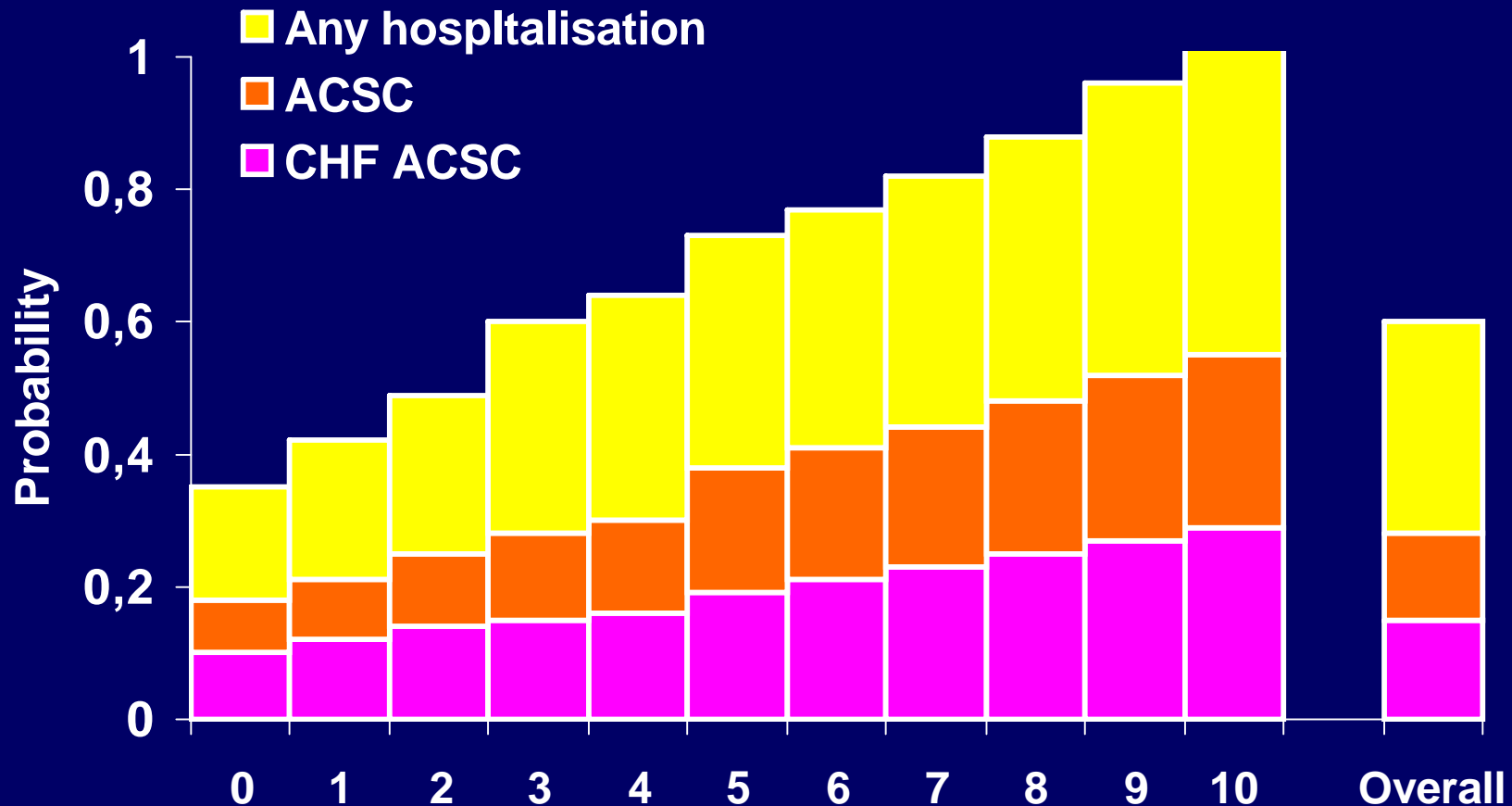
Most Common Non-cardiac Diseases for Patients \geq 65 years with CHF: An analysis of 122 630 subjects



Braunstein et al., J Am Coll Cardiol 2003;42:1226

Non-cardiac Comorbidity Increases Preventable Hospitalizations among Medicare Beneficiaries with CHF

A survey of 122 630 Subjects Aged ≥ 65 years

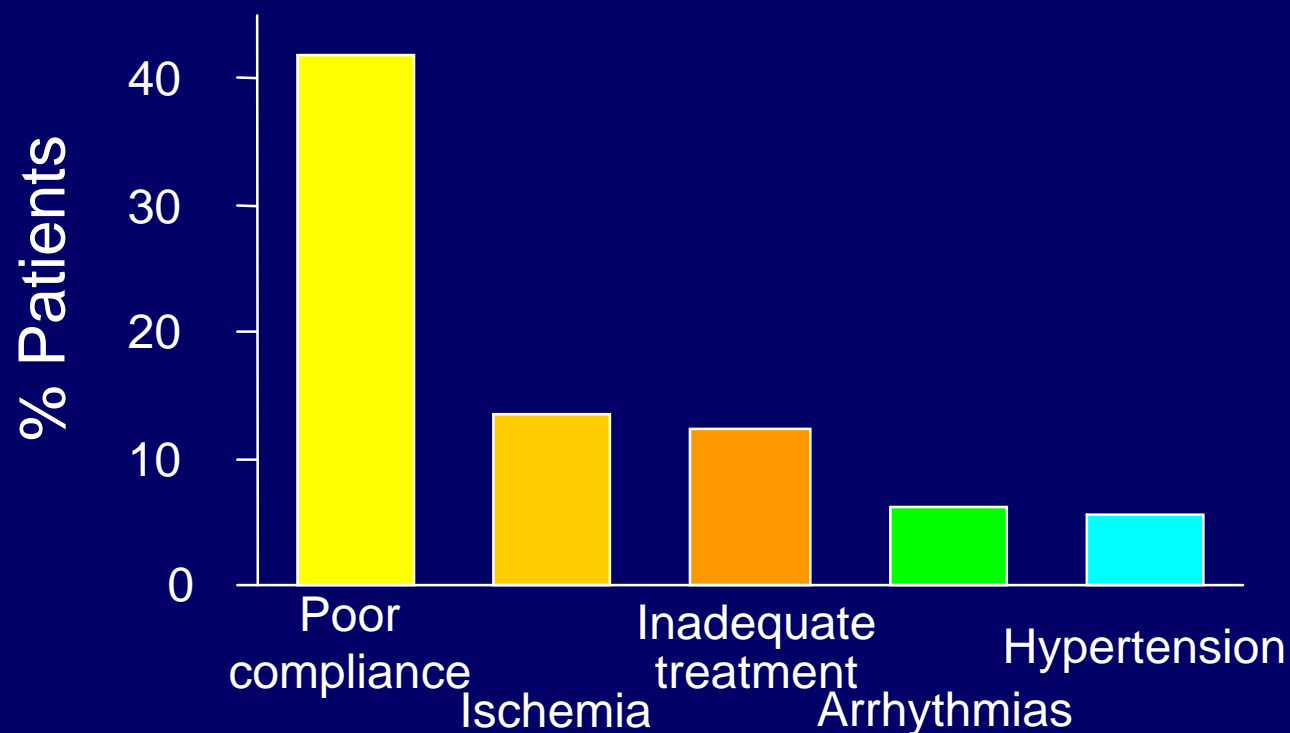


ACSC = Ambulatory Care Sensitive
(e.g. preventable) Condition

Braunstein et al., JACC 2003;42:1226

Incidence of Precipitating Factors as Causes of Hospital Admissions in Patients with Heart Failure

Causes of hospitalizations
(179 pts.; age, 75±10 years)



Michaelsen et al., Heart 1998;80:437

Management of HF in the Elderly: General Measures

- Educate the patients and their family → ↑ compliance!
- Limit sodium intake (< 1.5 Gm/day)
- Monitor body weight daily
- Avoid smoking
- Only moderate alcohol consumption (e.g. < 1-2 drinks/day)
- Low-intensity aerobic exercise (3-5 times/week)
- Treat concomitant diseases
 - Hypertension, and/or diabetes, CAD...
 - anemia, thyroid disease, sleep disorders, depression...
- Minimize use of NSAIDs

Effect of Antihypertensive Therapy in the Primary Prevention of HF in Older Adults

Trial (year)	No.	Age, ys	Risk reduction for HF
EWPHE (1985)	840	>60	↓22%
Coope (1986)	884	60-79	↓ 32%
STOP-HTN (1991)	1627	70-84	↓ 51%
SHEP (1991)	4736	≥60	↓ 55%
STONE (1996)	1632	60-79	↓ 68%
Syst-Eur (1997)	4695	≥60	↓ 36%
Syst-China (1998)	2934	≥60	↓ 38%

Pharmacological therapy of heart failure due to Left Ventricular Systolic Dysfunction

For Survival/Morbidity
mandatory therapy

For Symptoms

NYHA I

Cont. ACE inhibitor/ARB if ACE inhibitor intolerant, continue aldosterone antagonist if post-MI
add beta-blocker if post-MI

reduce / stop diuretic

NYHA II

ACE inhibitor as first-line treatment/ARB if ACE inhibitor intolerant
add beta-blocker
and aldosterone antagonist if post MI

+/- diuretic
depending on fluid retention

NYHA III

ACE inhibitor plus ARB or ARB alone if ACE intolerant
beta-blocker
add aldosterone antagonist

+ diuretics + digitalis
If still symptomatic

NYHA IV

Continue ACE inhibitor/ARB
beta-blocker
Aldosterone antagonist

+diuretics + digitalis
+ consider temporary inotropic support

Treatment of HF in the Elderly: What Do the Guidelines Say

Drug		Efficacy	Side effects	Tolerance
ACEi	(+)	+	↑	↓
Loop diuretics		+	↑	↓
Beta-blockers	+	+	↑	↓
Aldosterone antagonists		+	↑↑	↓
ARBs	+	+	↑	↓
Digoxin		+	↑	↓

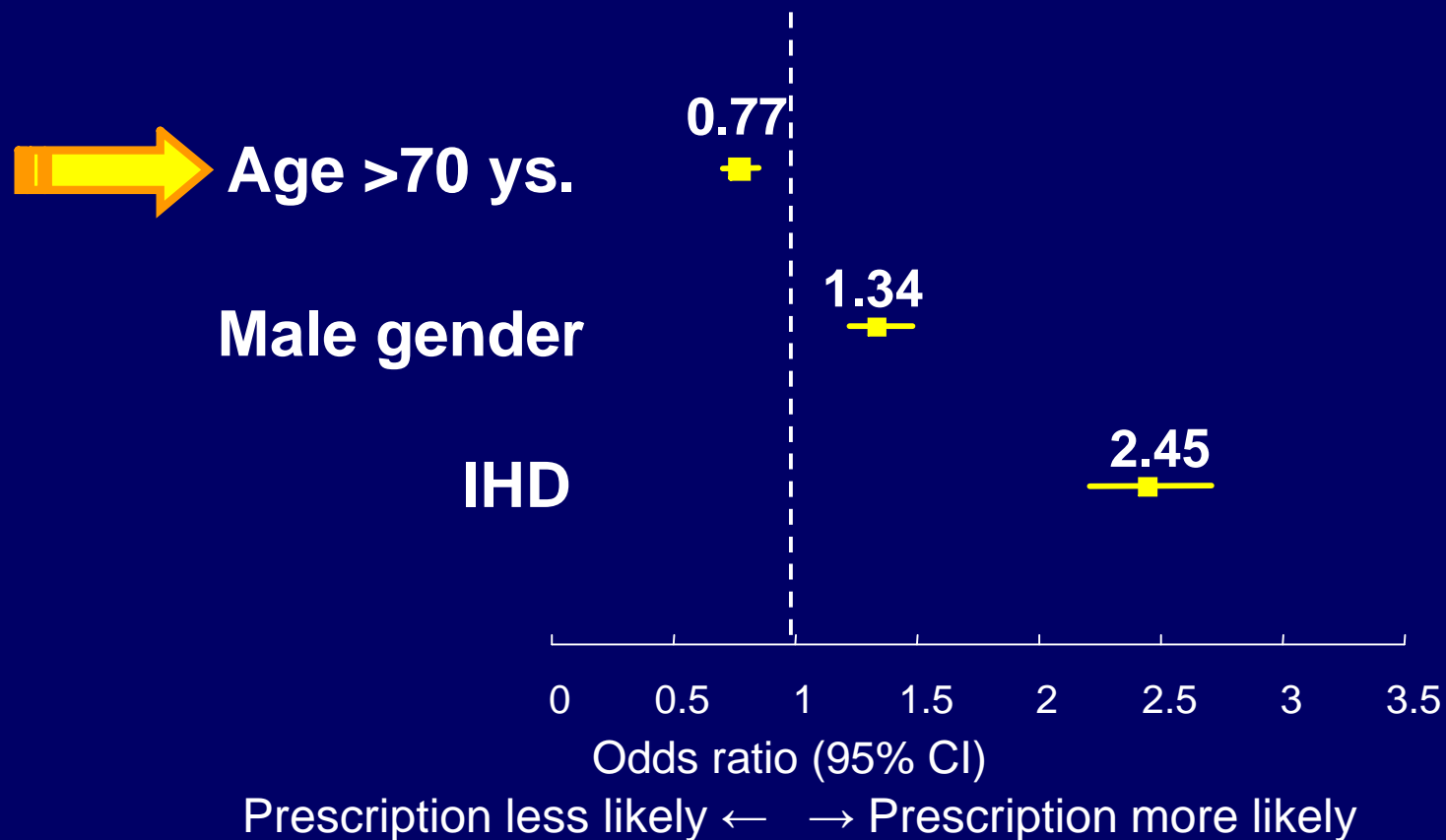
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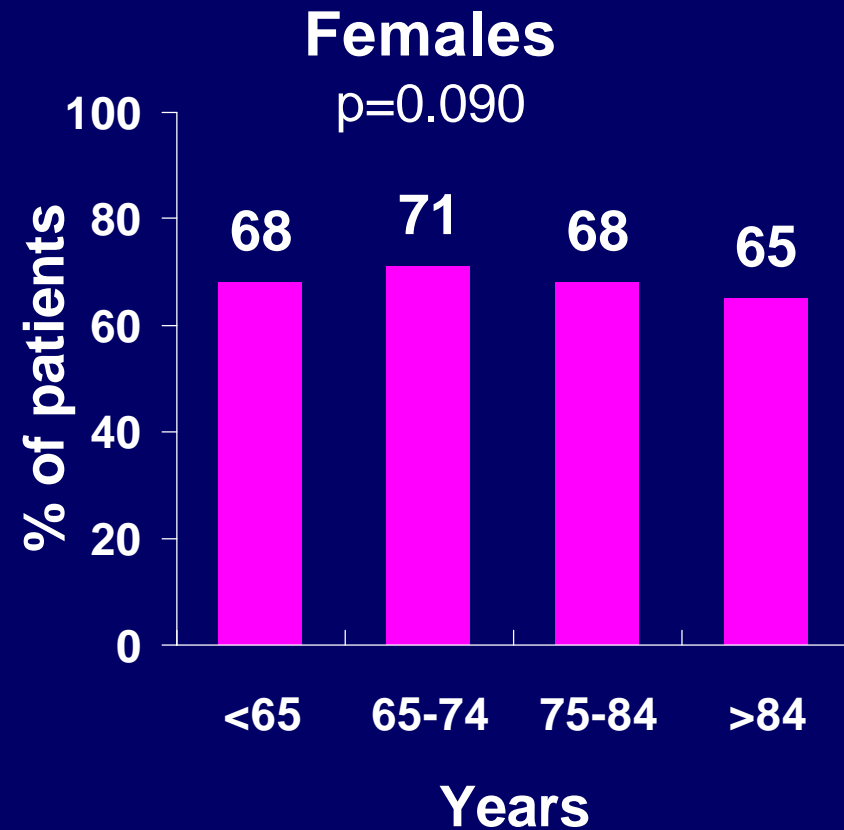
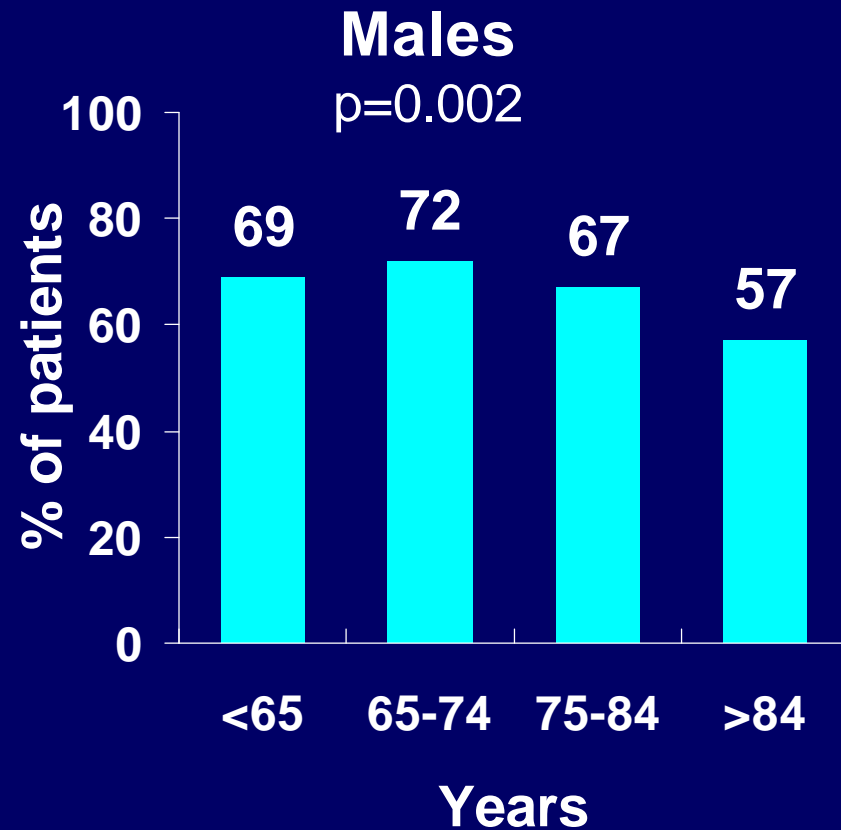
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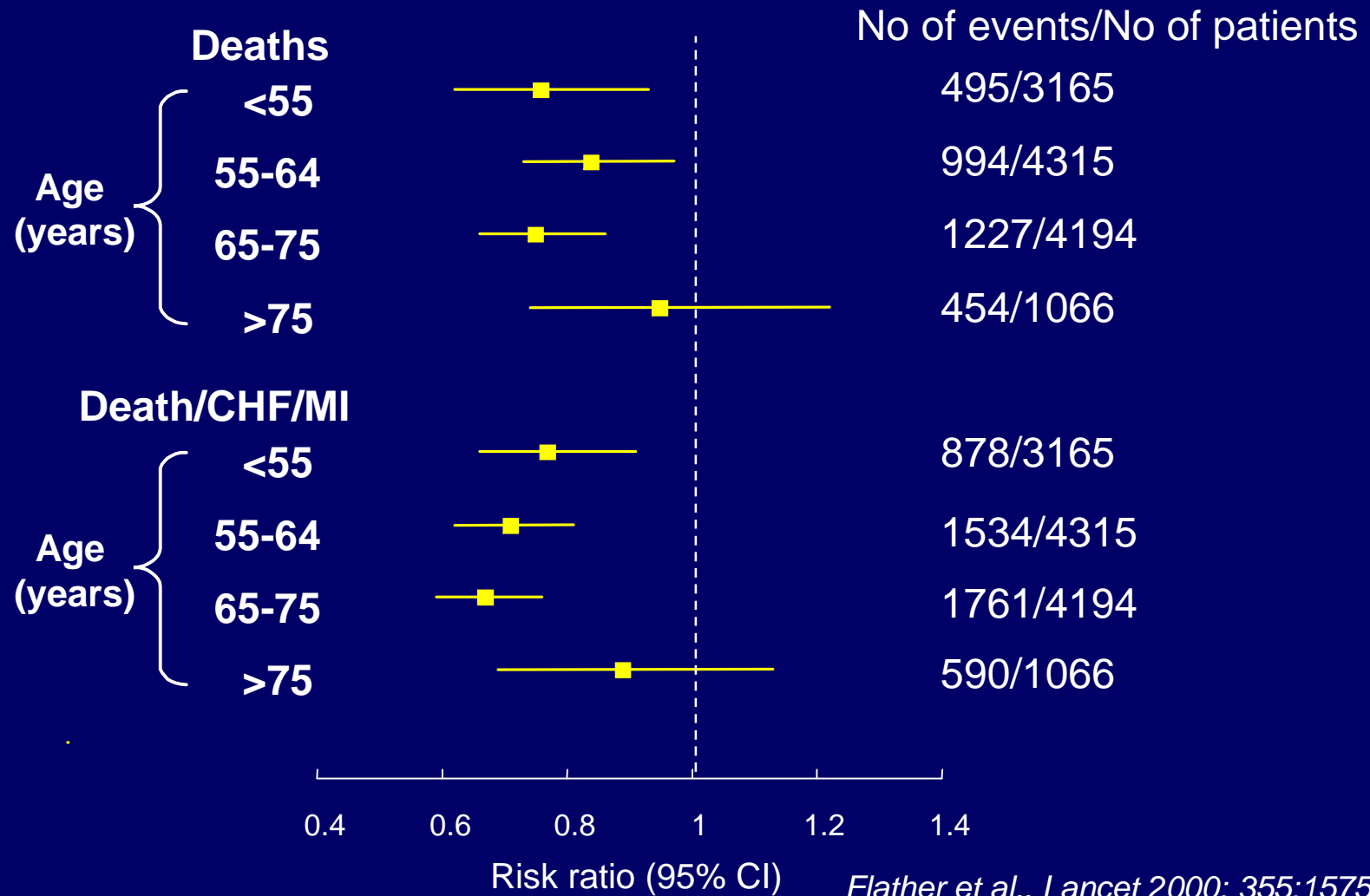
Elderly Age is an Independent Predictor of Lack of Prescription of ACE Inhibitors: Results from the EuroHeart Failure Survey



ACEi/ARBs Prescriptions in the Patients with HF According to Age: IMPROVEMENT Study 8256 patients in 15 countries, 1999-2000



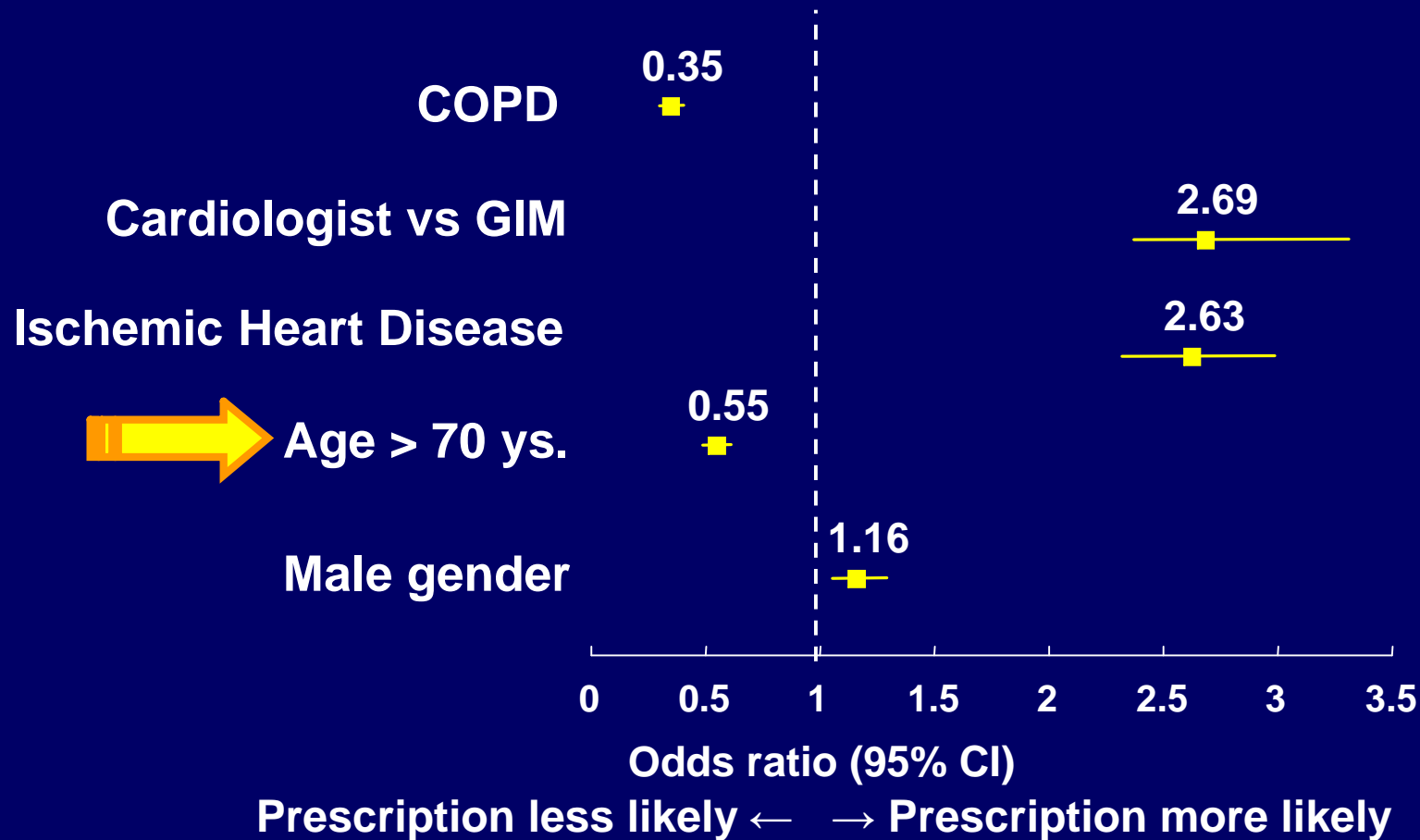
Effects of ACE inhibitors on outcome in patients subdivided on the basis of their age: Meta-analysis of the SOLVD, SAVE, AIRE and TRACE trials



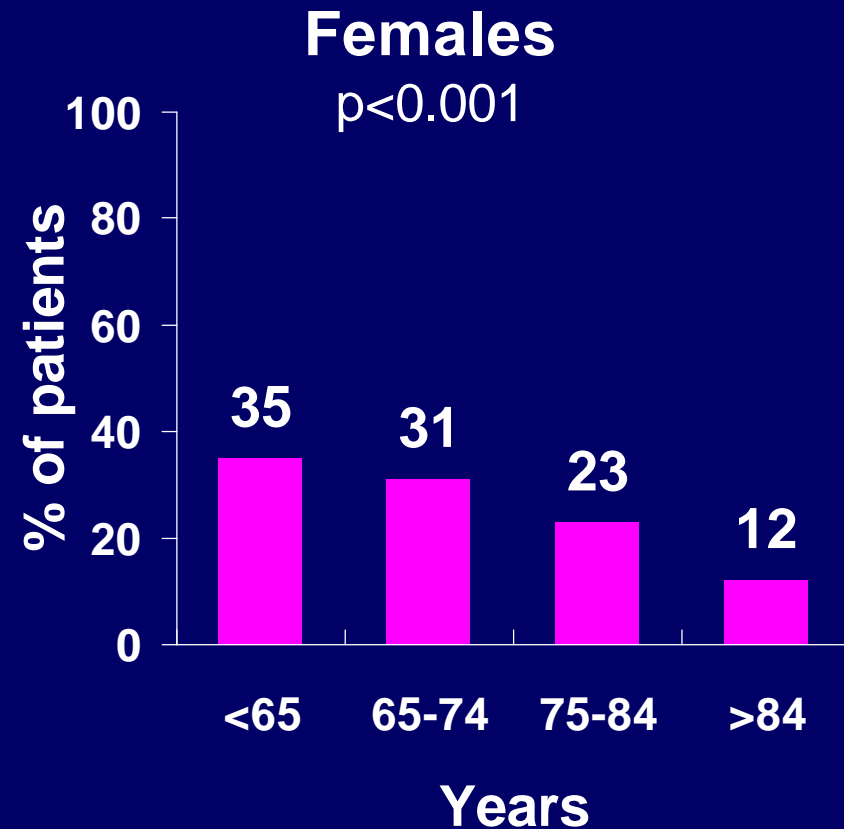
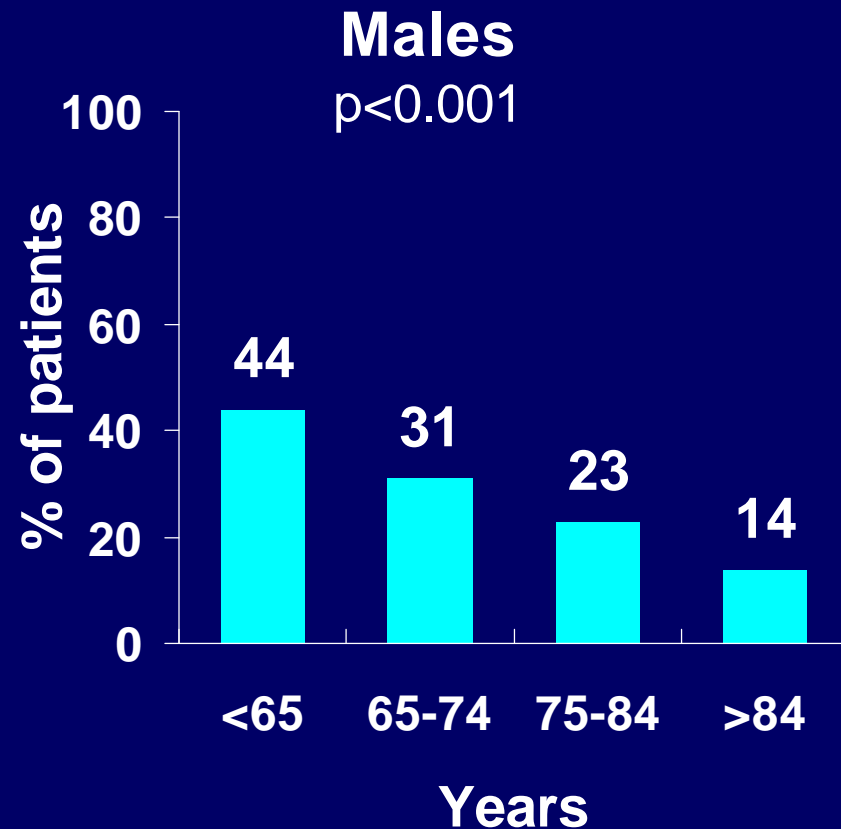
Treatment of HF in the Elderly: What Do the Guidelines Say

Drug	Evidence	Efficacy	Side effects	Tolerance
ACEi	(+)	+	↑	↓
Loop diuretics	0	+	↑	↓
Beta-blockers	+	+	↑	↓

Elderly Age is an Independent Predictor of Lack of Prescription of Beta-blockers: Results from the EuroHeart Failure Survey



Beta-blockers Prescriptions in the Patients with HF According to Age: IMPROVEMENT Study 8256 patients in 15 countries, 1999-2000



BRING UP

Reasons for Not Commencing β -Blockade

	On β blockers (n = 771)	β blockers started (n = 865)	No β blockers (n = 1455)	P value
Age \geq 70 years	24%	25%	43%	0.001
NYHA III-IV	26%	29%	42%	0.001
Pulmonary rales	10%	20%	26%	0.001
Periph. oedema	12%	13%	21%	0.001
Atrial fibrillation	14%	17%	21%	0.001
EF not available	5%	3%	6%	0.008
EF $<$ 30%	30%	30%	35%	0.017

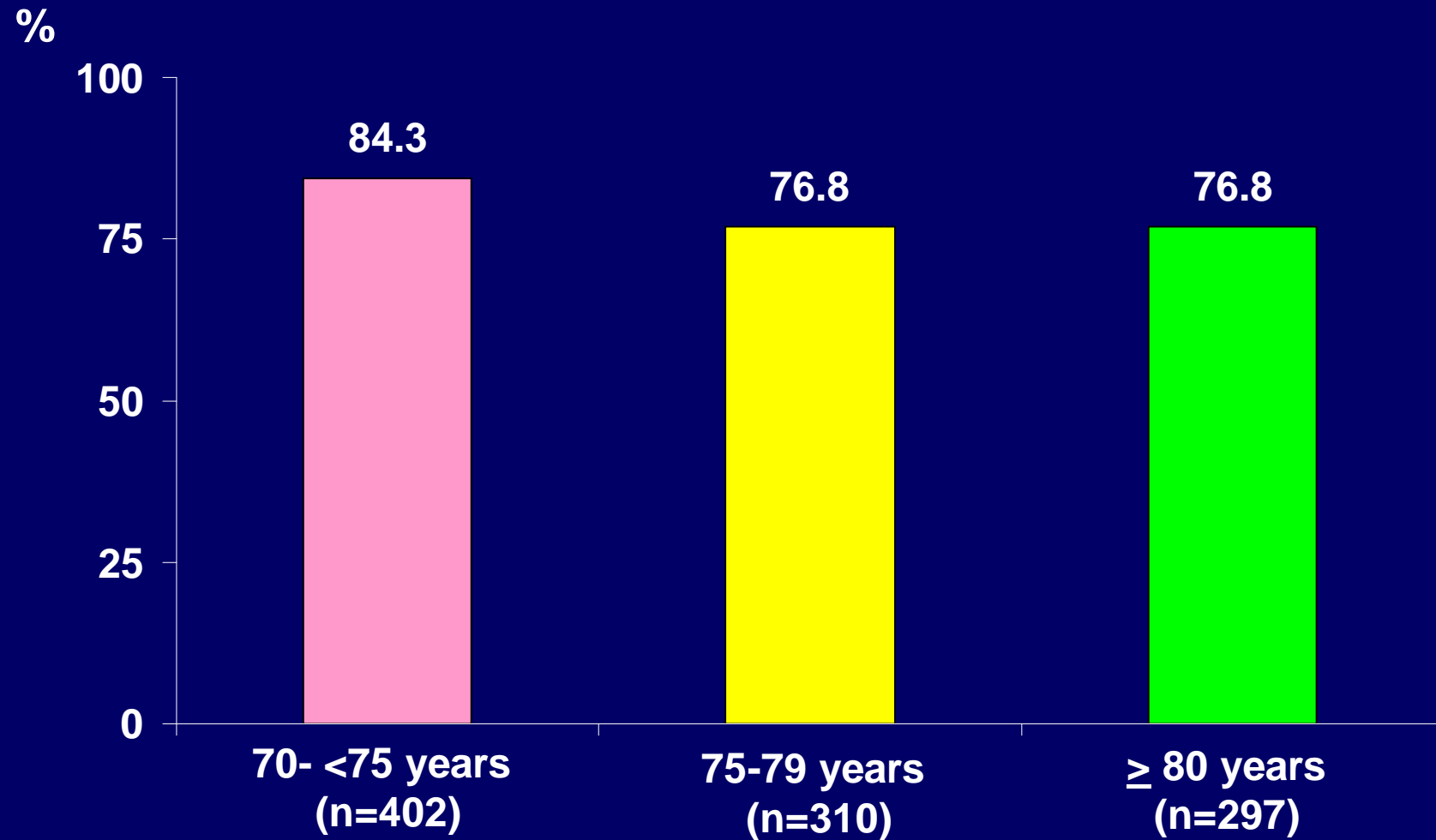
BRING UP

Independent Predictors of β Blocker Tolerability

	OR	95% CI	P value
Age (as a continuous variable)	0.97	0.96 - 0.97	0.0001
NYHA class (III-IV v I-II)	0.62	0.51 - 0.75	0.0001
Systolic blood pressure (as a continuous variable)	1.02	1.01 - 1.02	0.0001
Heart rate (as a continuous variable)	1.01	1.01 - 1.02	0.0001
Ejection fraction (not available v available)	0.46	0.28 - 0.76	0.0022

COLA II

Tolerability according to Age

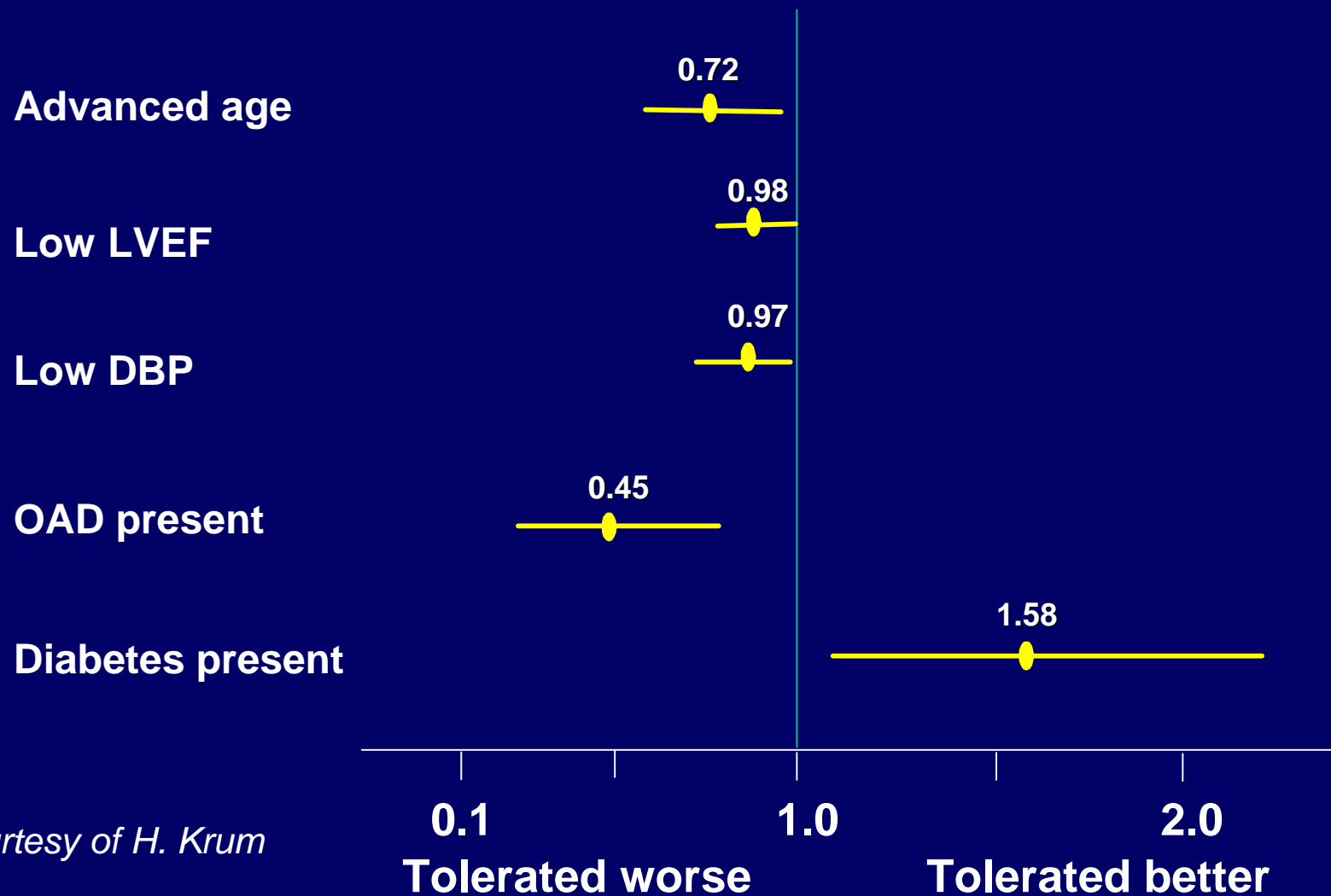


Courtesy of Henry Krum

P<0.05 by ANOVA

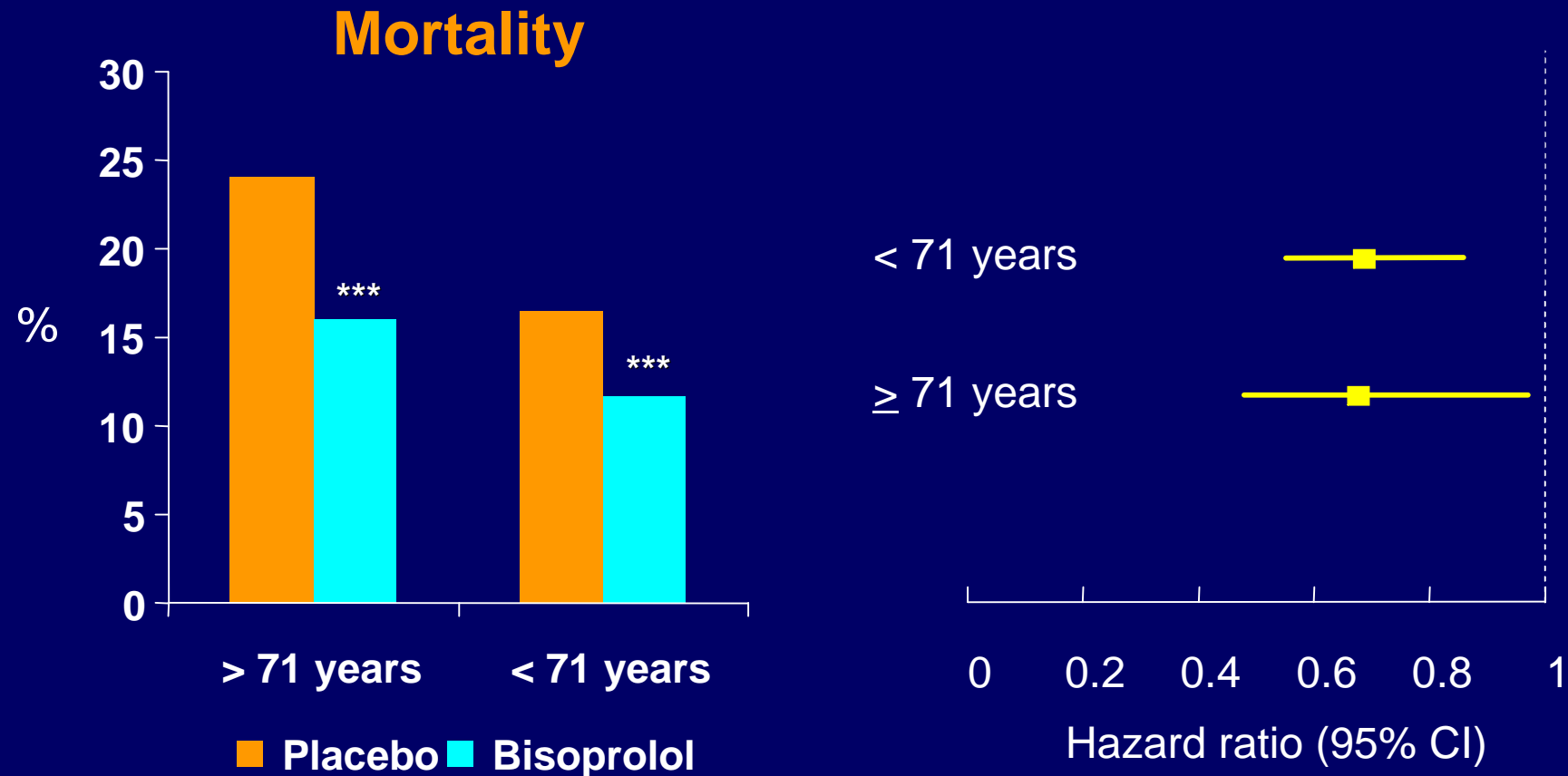
COLA II

Multivariate predictors of tolerability

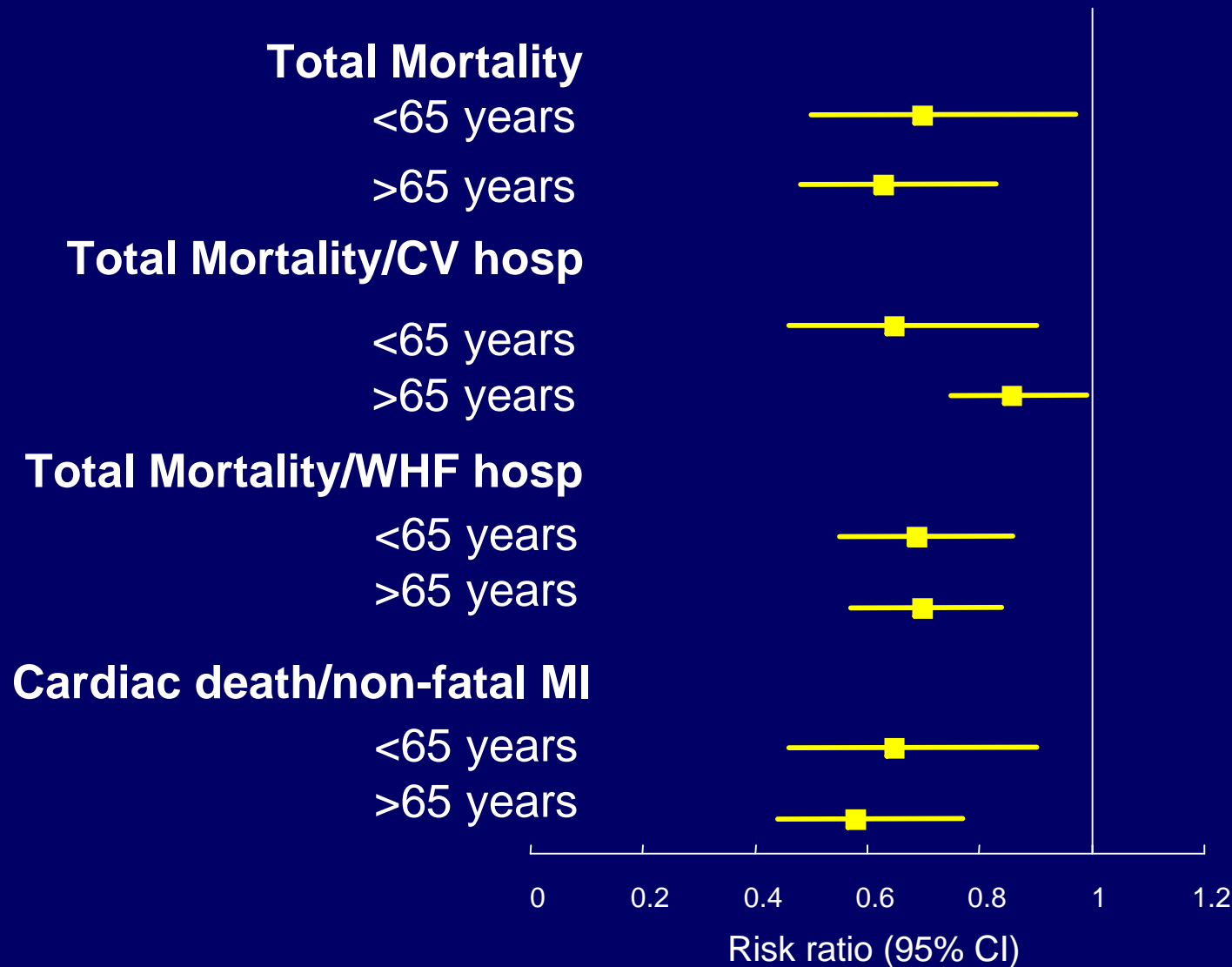


Courtesy of H. Krum

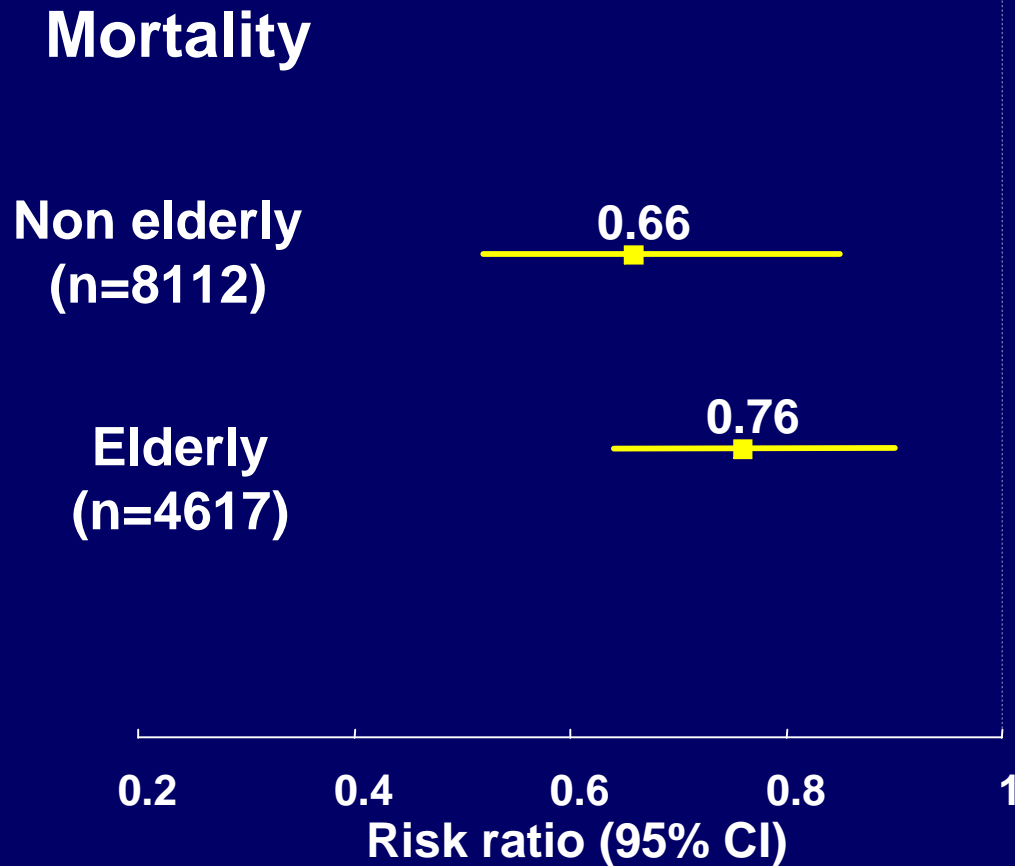
Effect of Bisoprolol on Mortality in Different Age Subgroups



Efficacy of Metoprolol CR/XL in Elderly Patients with Heart Failure: the MERIT-HF Study



Beta-blockers Reduce Mortality also in Elderly Patients: Meta-analysis of >12,000 Patients in Large-scale Trials (BEST, Carvedilol US, CIBIS-II, COPERNICUS, MERIT-HF)



SENIORS Trial: Inclusion Criteria

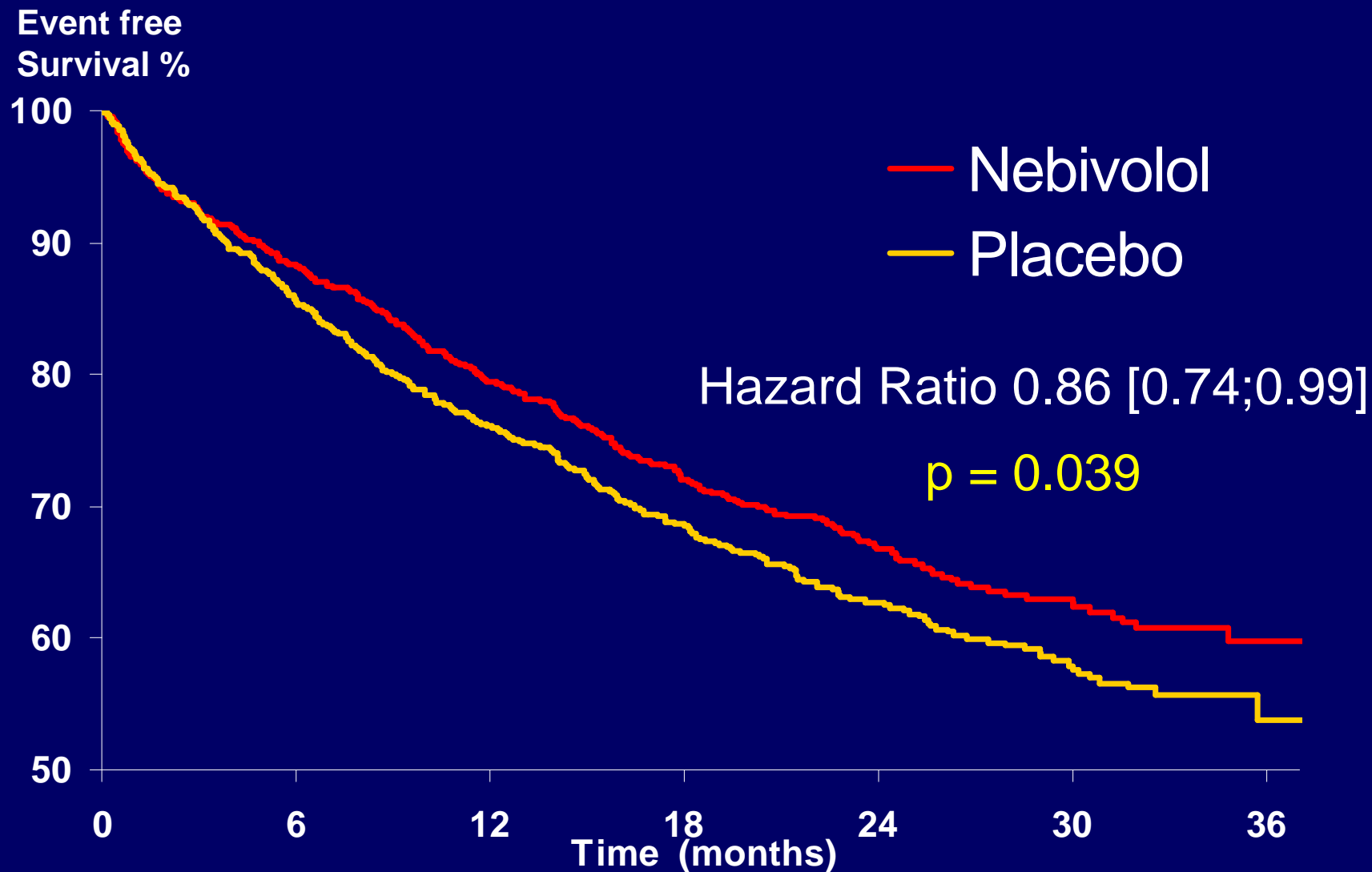
- **Age \geq 70 years**
- A clinical diagnosis of chronic heart failure (HF) and either of:
 - a) documented LVEF \leq 35% within previous 6 months
 - or
 - b) hospital admission within previous 1 year for congestive HF
- Written consent prior to enrolment into the study

SENIORS: Baseline Characteristics

	Nebivolol	Placebo
Age (mean, yrs)	76.1	76.1
Male (n, %)	657 (61.6)	686 (64.7)
LVEF \leq 35 % (n, %) *	683 (64.3)	686 (64.8)
LVEF (mean, %)	36.0	36.0
NYHA Class (n, %)		
I	32 (3.0)	29 (2.7)
II	603 (56.5)	597 (56.3)
III	413 (38.7)	411 (38.7)
IV	19 (1.8)	24 (2.3)

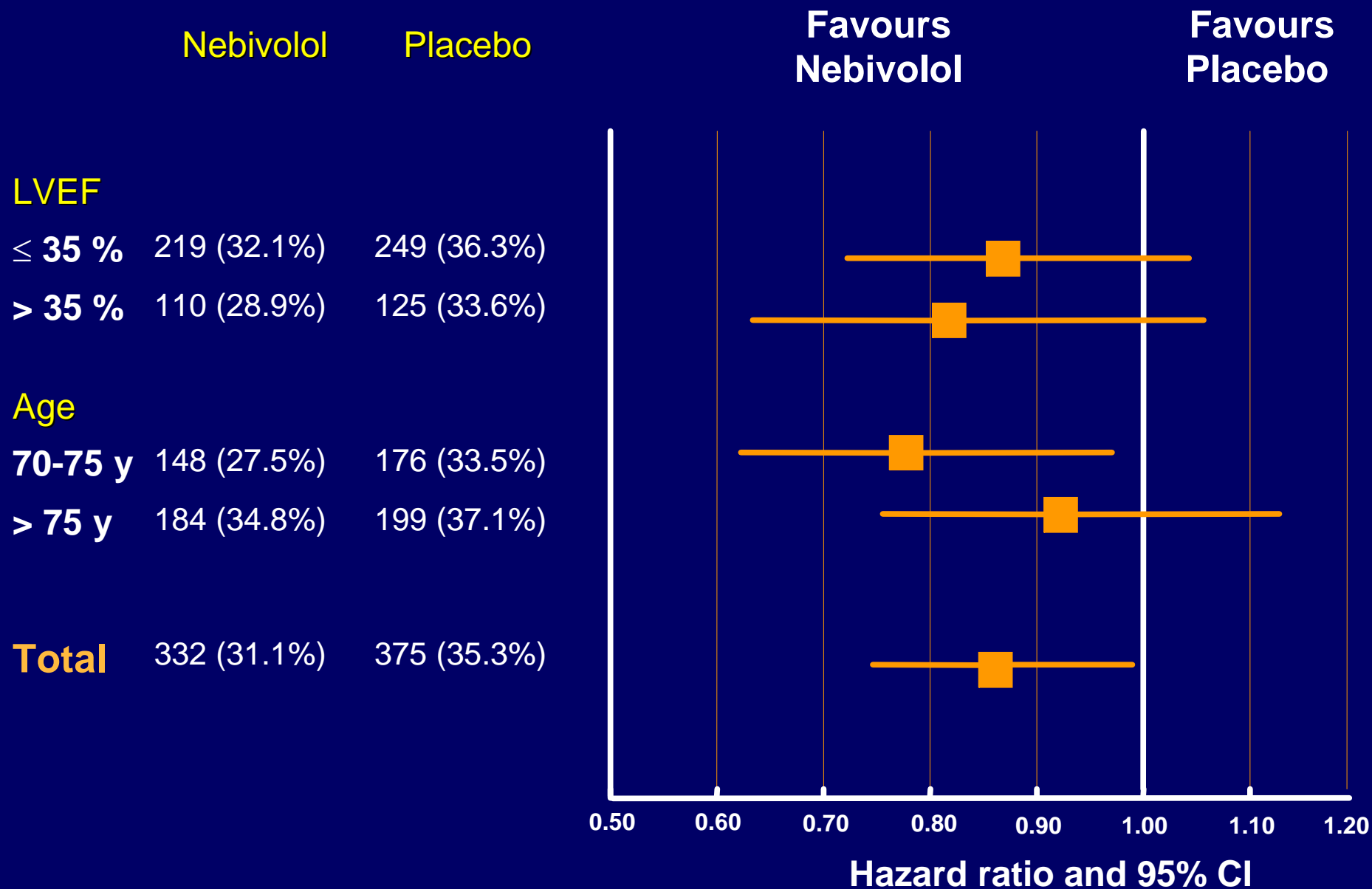
* 7 patients with missing LVEF at baseline

SENIORS Trial: All Cause Mortality or CV Hospital Admission (Primary Outcome)



No. of events: Nebivolol 332 (31.1%); Placebo 375 (35.3%)

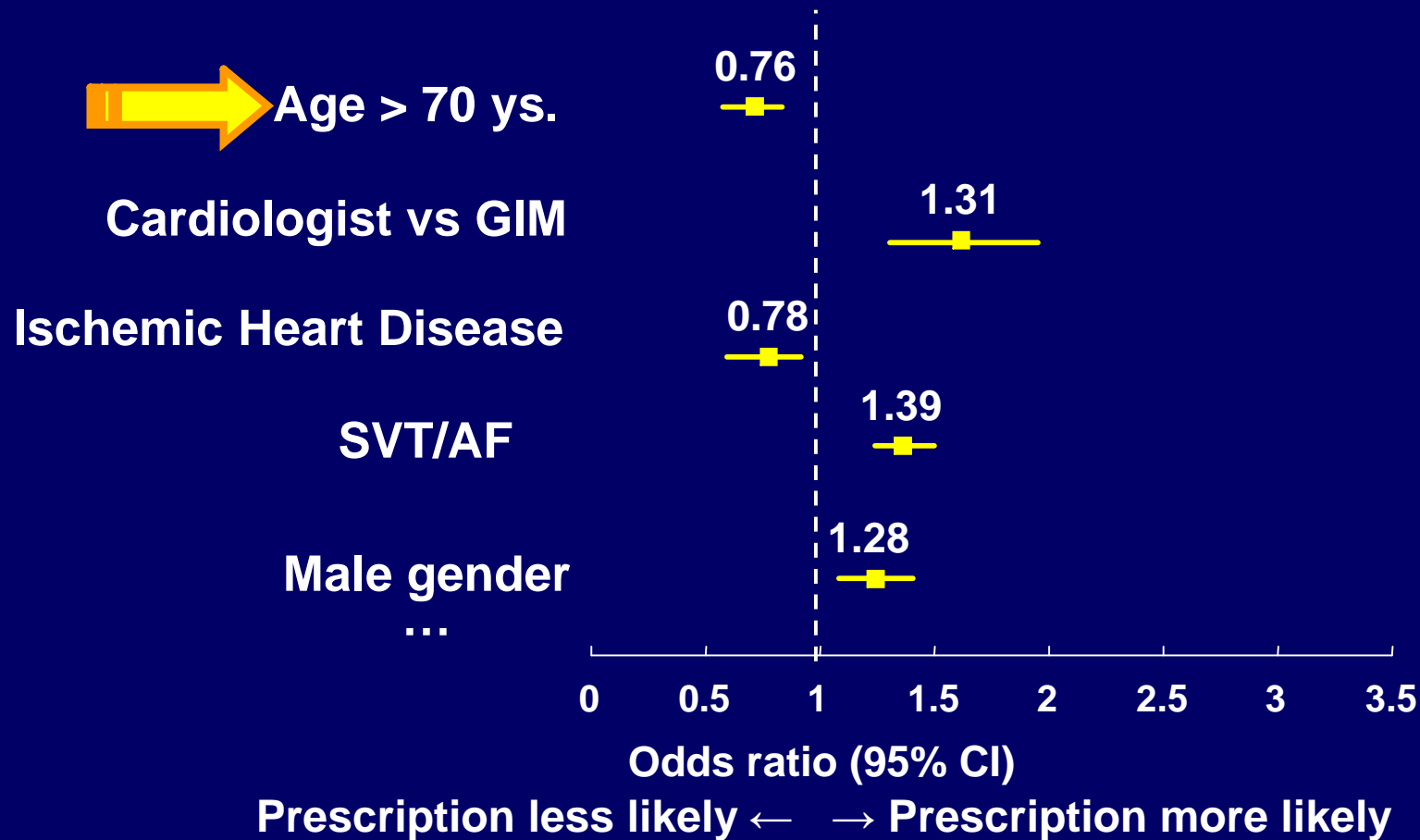
Death or CV Hospitalisation by Subgroup



Treatment of HF in the Elderly: What Do the Guidelines Say

Drug	Evidence	Efficacy	Side effects	Tolerance
ACEi	(+)	+	↑	↓
Loop diuretics	0	+	↑	↓
Beta-blockers	+	+	↑	↓
Aldosterone antagonists	(+)	+	↑↑	↓
ARBs	+	+	↑	↓
Digoxin	(+)	+	↑	↓

Elderly Age is an Independent Predictor of Lack of Prescription of Spironolactone: Results from the EuroHeart Failure Survey



Spironolactone-induced hyperkalemia and renal insufficiency in patients with heart failure

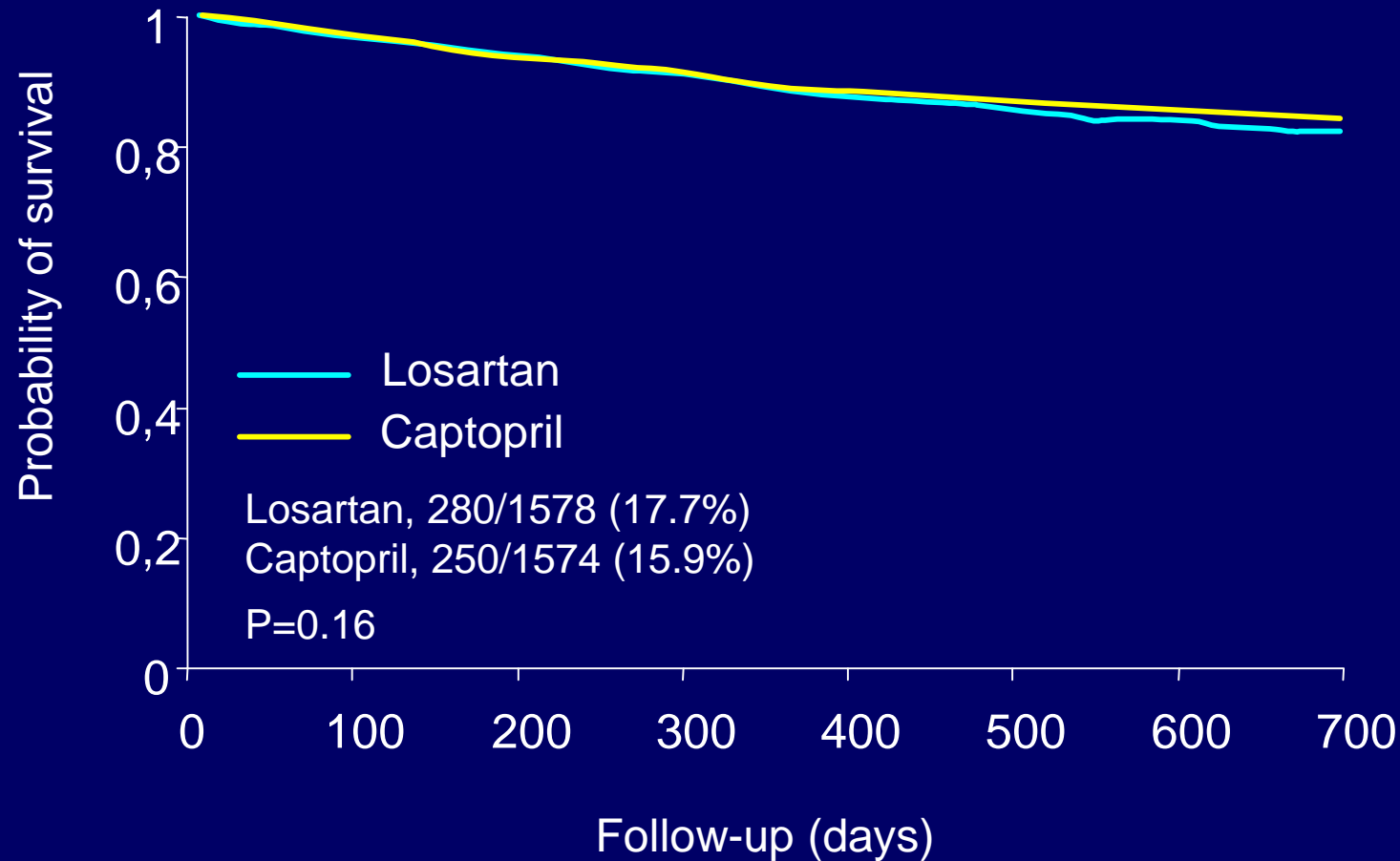
Variable	<i>P</i> value
Predictors of changes in serum potassium	
Serum potassium (baseline)	<.001
Age	.017
Beta-blocker use	.019
Predictors of change in serum creatinine	
Thiazide diuretic	.007

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ARBs	+	+	↑	↓
Digoxin	(+)	+	↑	↓

Effects of Losartan Compared with Captopril on Mortality in Patients with Symptomatic Heart Failure: ELITE II Results

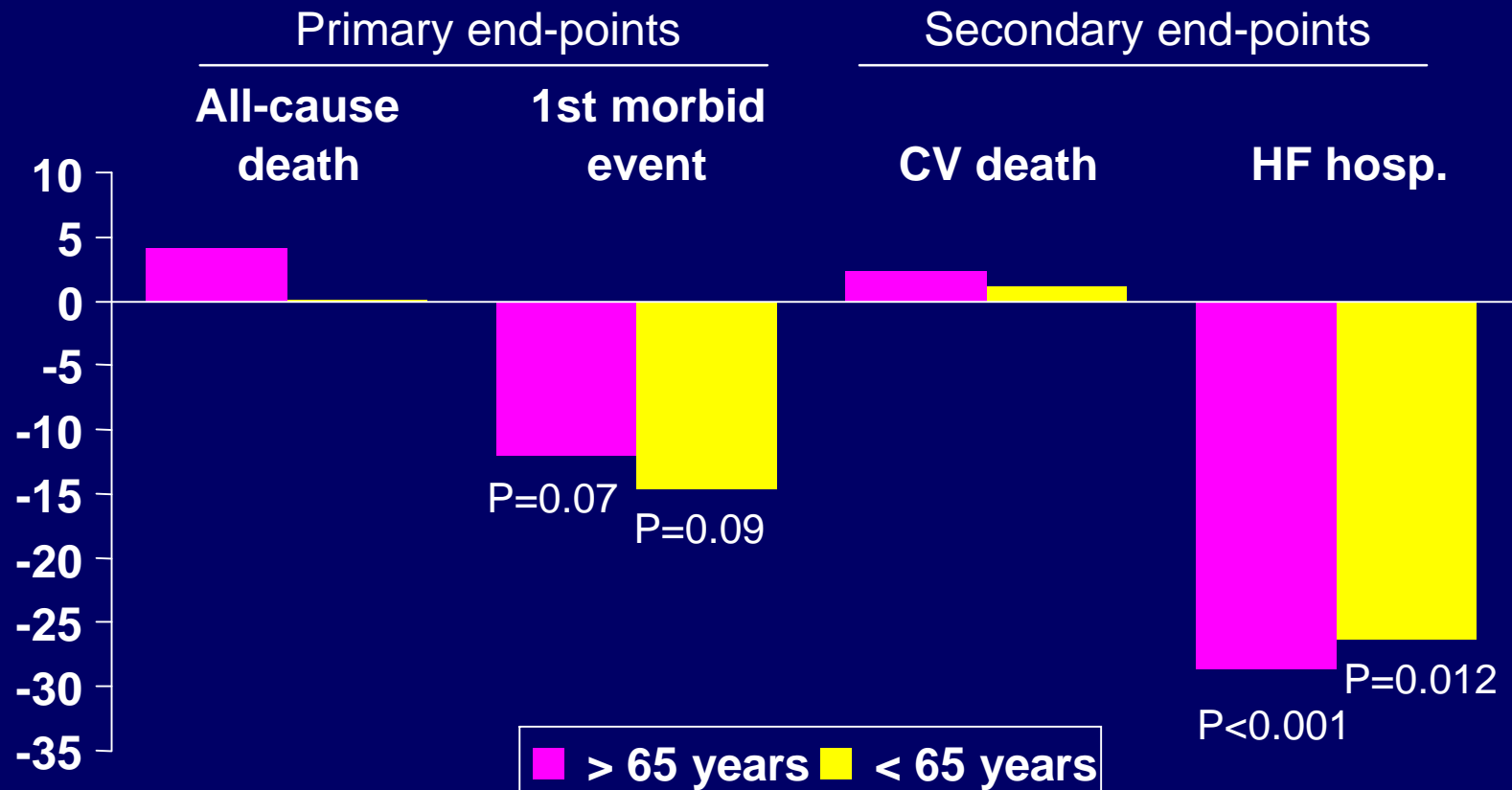
Total mortality



(Pitt et al., Lancet 2000; 355:1582)

Lack of Influence of Age on the Effects of Valsartan in Val-HeFT Trial

Risk Ratio Valsartan vs. Placebo



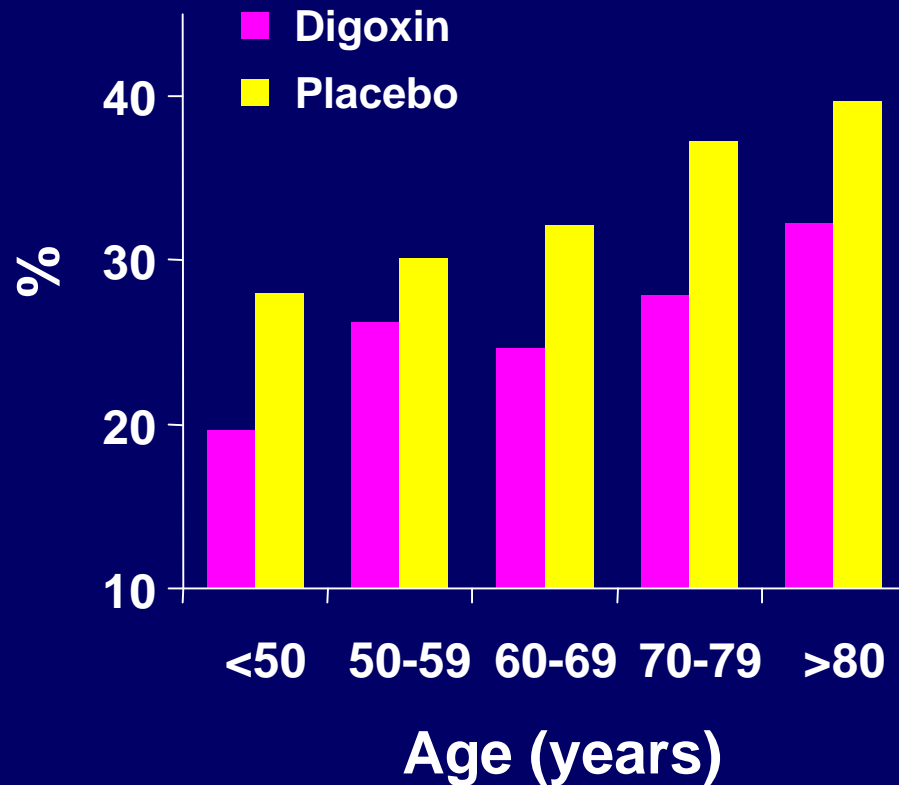
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ARBs	+	+	↑	↓
Digoxin	(+)	+	↑	↓

Lack of effect of age on the effects on digoxin on outcome: Results from the DIG study

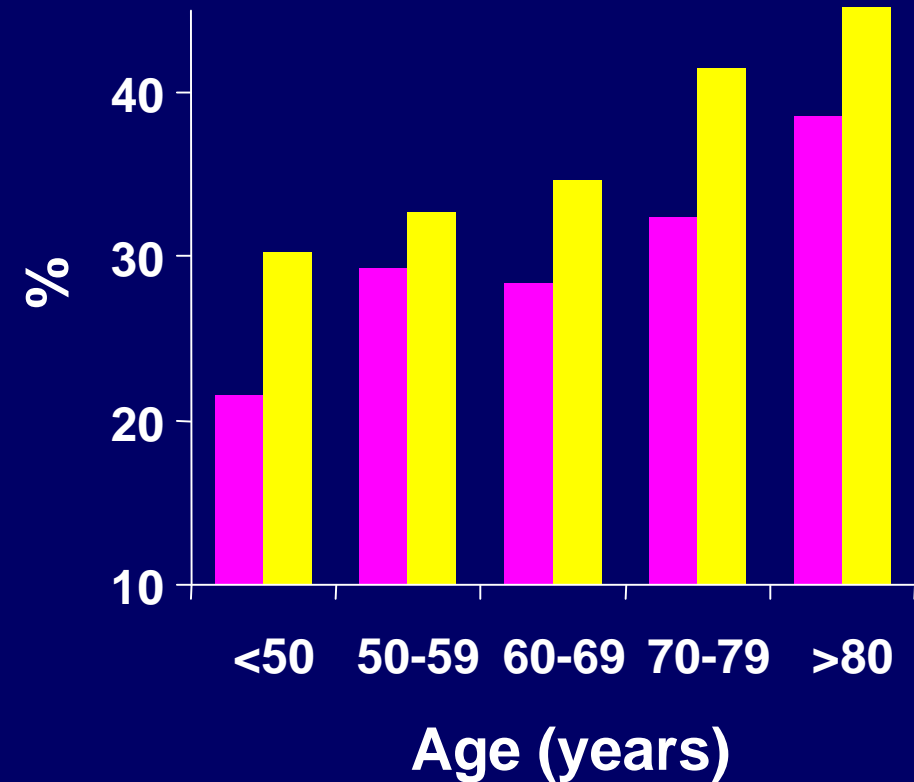
HF hospitalizations

P=0.0001



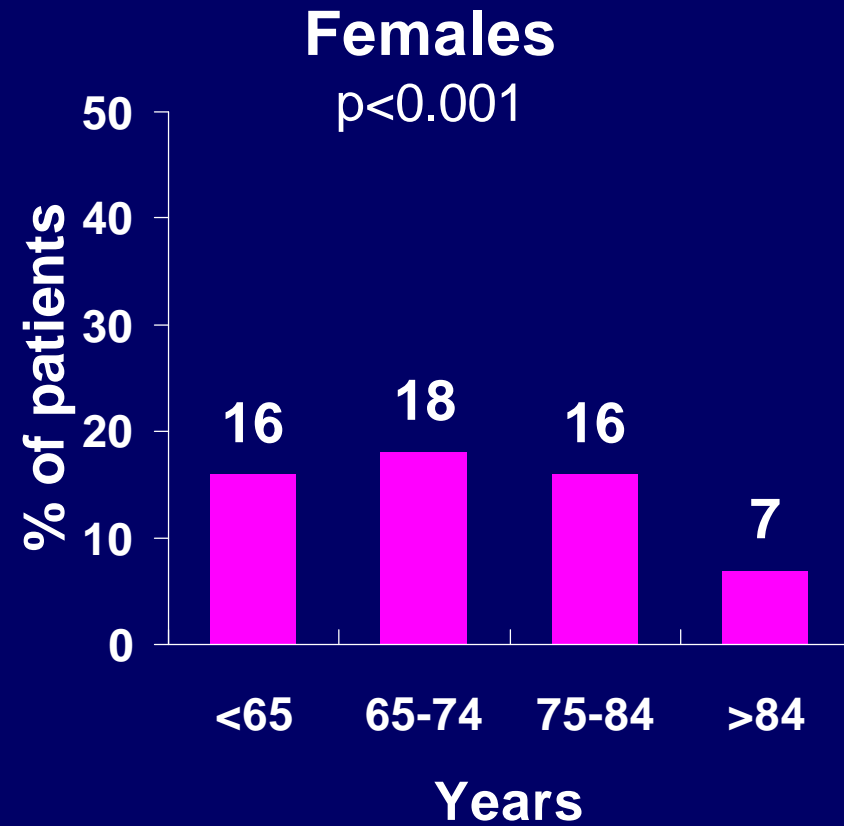
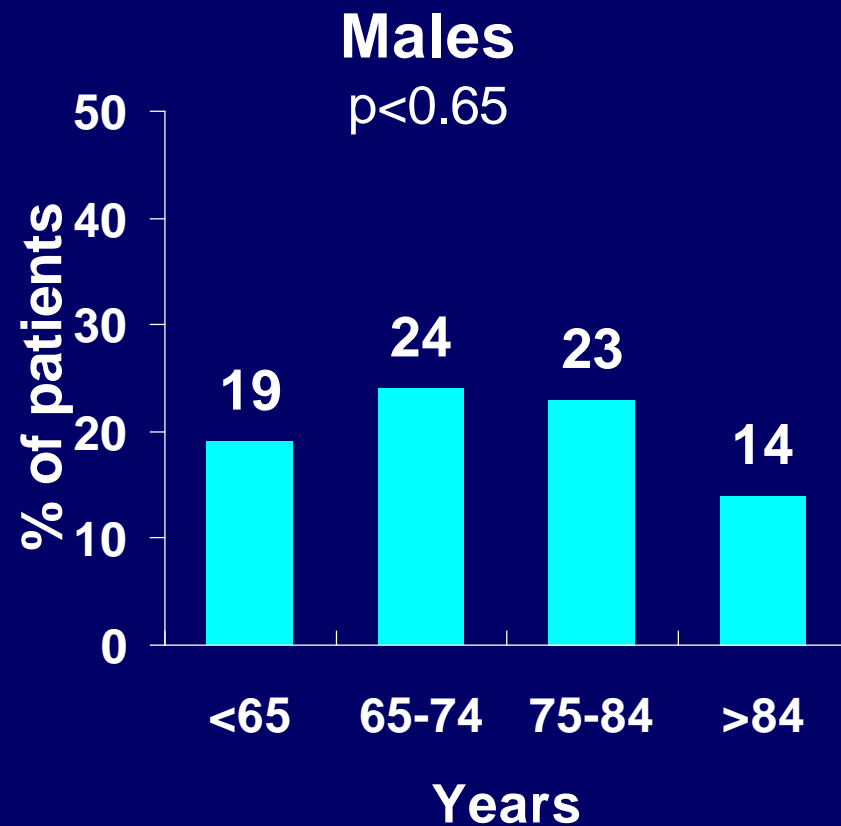
HF mortality or HF hospitalizations

P=0.0001



Rich et al. J Am Coll Cardiol 2001; 38:806

Oral Anticoagulant Prescriptions in the Patients with HF According to Age: IMPROVEMENT Study 8256 patients in 15 countries, 1999-2000



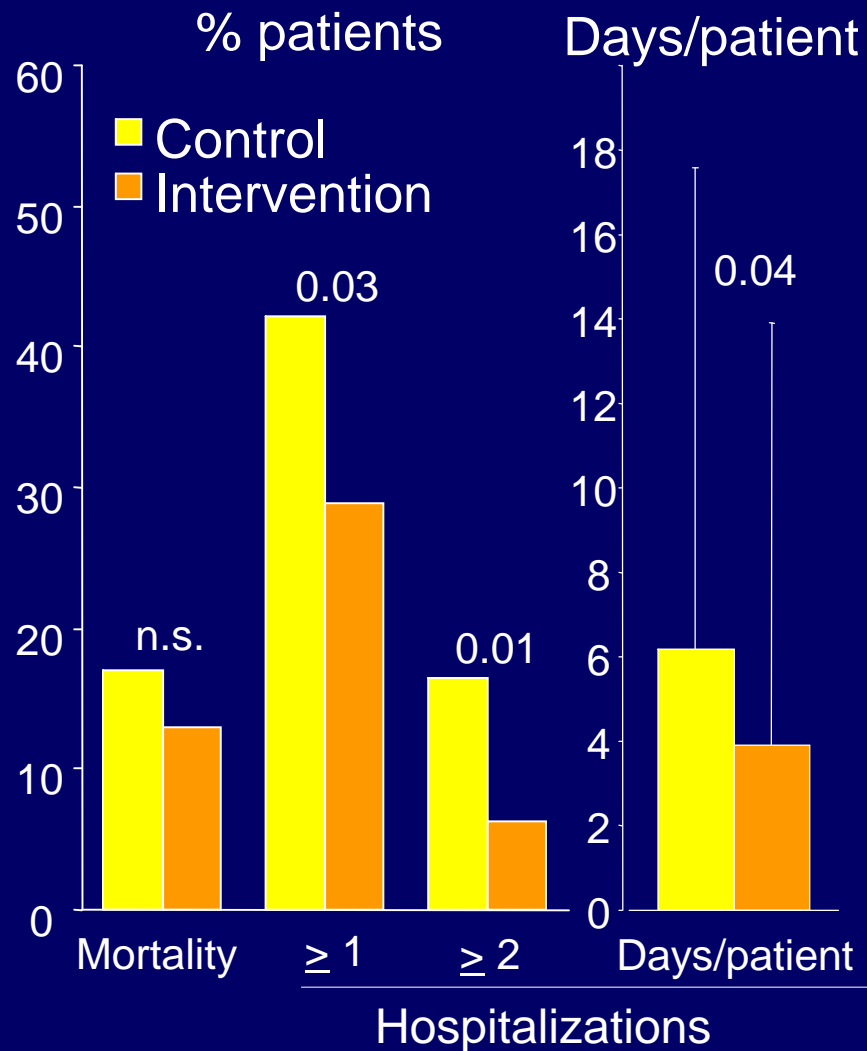
Randomised Controlled Trial of Cardiac Rehabilitation in Elderly Patients with HF

	Control		Rehabilitation	
	Baseline	24 weeks	Baseline	24 weeks
Age, m \pm SD	72 \pm 7		72 \pm 6	
6-min walk distance, mts	259	252	275	320***
MLHF score	44	37	41	23**
NYHA class	2.53	2.48	2.21	2.01***
Total hospital admissions		33		11
Days in hospital		187		41
Deaths		4		5

Effects of a Multidisciplinary Intervention to Prevent the Readmission of Patients with Heart Failure

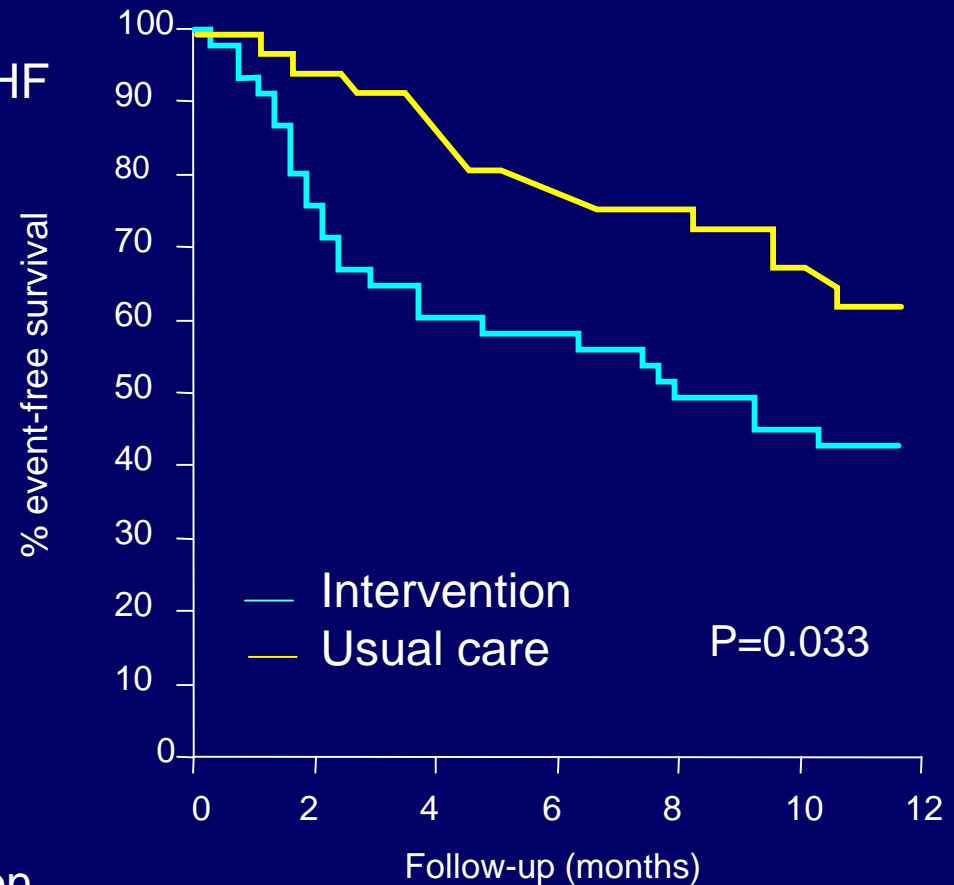
(Washington University HF disease management trial)

- Study group
 - 282 patients, selected among 1306
 - **Mean age 79 ys;** female, 65%
 - NYHA: 2.4 ±1.1; EF: 41±13%
- Randomization
 - Intervention vs control groups
- Personnel
 - Nurse, dietician, social assistant, geriatrician, cardiologist
- Follow-up
 - 90 days
- Results
 - n.s. mortality
 - ↓ hospitalizations
 - ↓ costs (↓ \$153/month/pt.)
 - ↑ compliance and quality of life



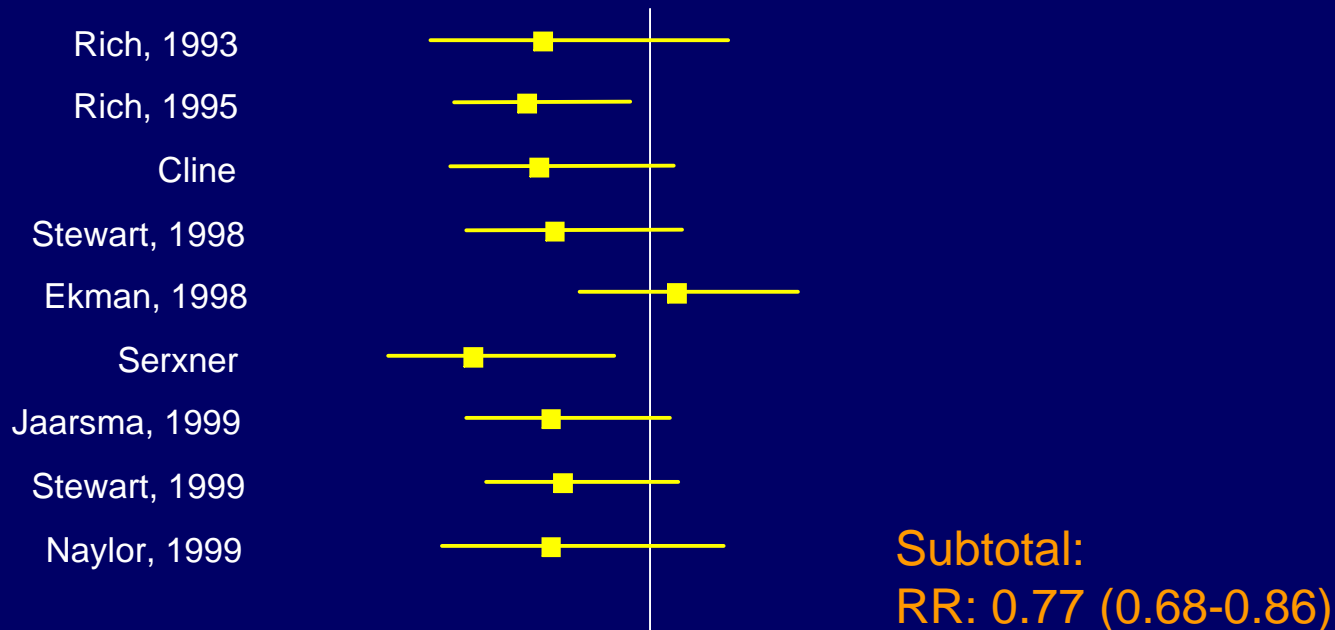
Randomized Controlled Trial of Specialist Nurse Intervention in Heart Failure

- Study group
 - 165 / 801 pts with an
 - **mean age: 75 ys,** female, 49%
 - Emergency admission for acute HF
 - Echo LV systolic dysfunction
 - NHYAII/III/IV, 43/76/81
- Randomization
 - Intervention vs control groups
- Personnel
 - Home visit by a nurse
 - Telephone contacts as needed
- Methods
 - Patient's education
 - Treatment optimization
 - Laboratory monitoring
- Results
 - Similar deaths (31% vs 30%)
 - ↓39% death or HF hospitalization
 - ↓ 28% death or all cause hospitalizations

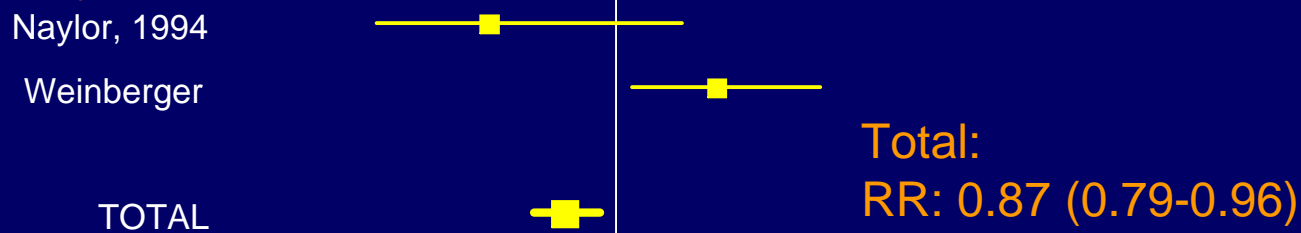


Effects of Disease Management Programs on Hospitalization Rates in Heart Failure

Multidisciplinary specialized team



Primary care



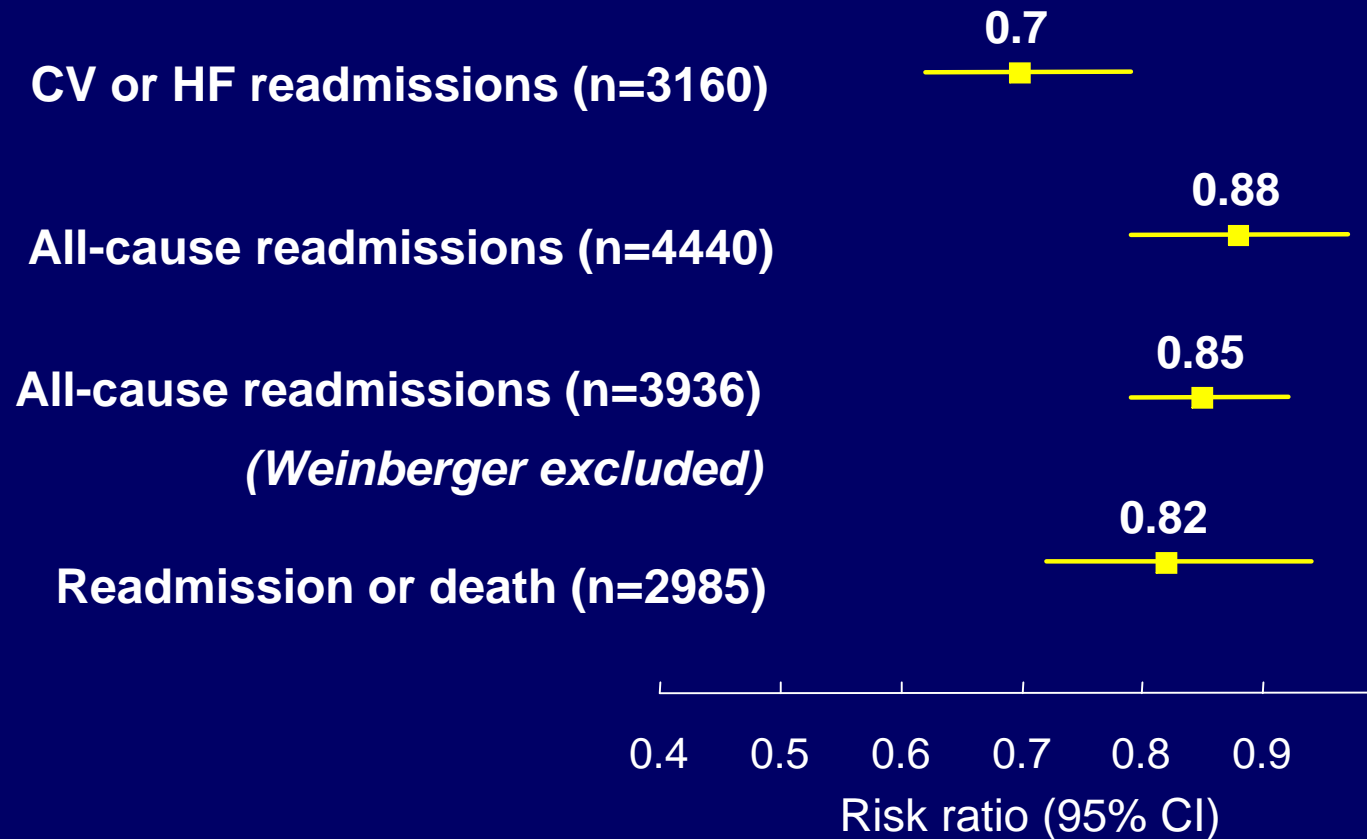
TOTAL

0 0,5 1 1,5 2

Risk ratio (95% CI)

Efficacy of Disease Management Programmes in Reducing Hospital readmissions in Older (>70 ys) Patients with HF

Randomised trials



Gonseth et al., *Eur Heart J* 2004; 25:1570