PAZIENTE ACUTO E PAZIENTE CRONICO: ANTITESI O CONTINUUM?

DR. MATTEO GIORGI-PIERFRANCESCHI

U.OC. MEDICINA INTERNA

ASST-CREMONA

L'HF è un problema di salute pubblica importante e in crescita

PREVALENZA

~1 su 5 persone di età >40 anni svilupperanno HF nel corso della loro vita[3,4]

INCIDENZA[4–6]

(nuovi casi per 100.000 per anno)

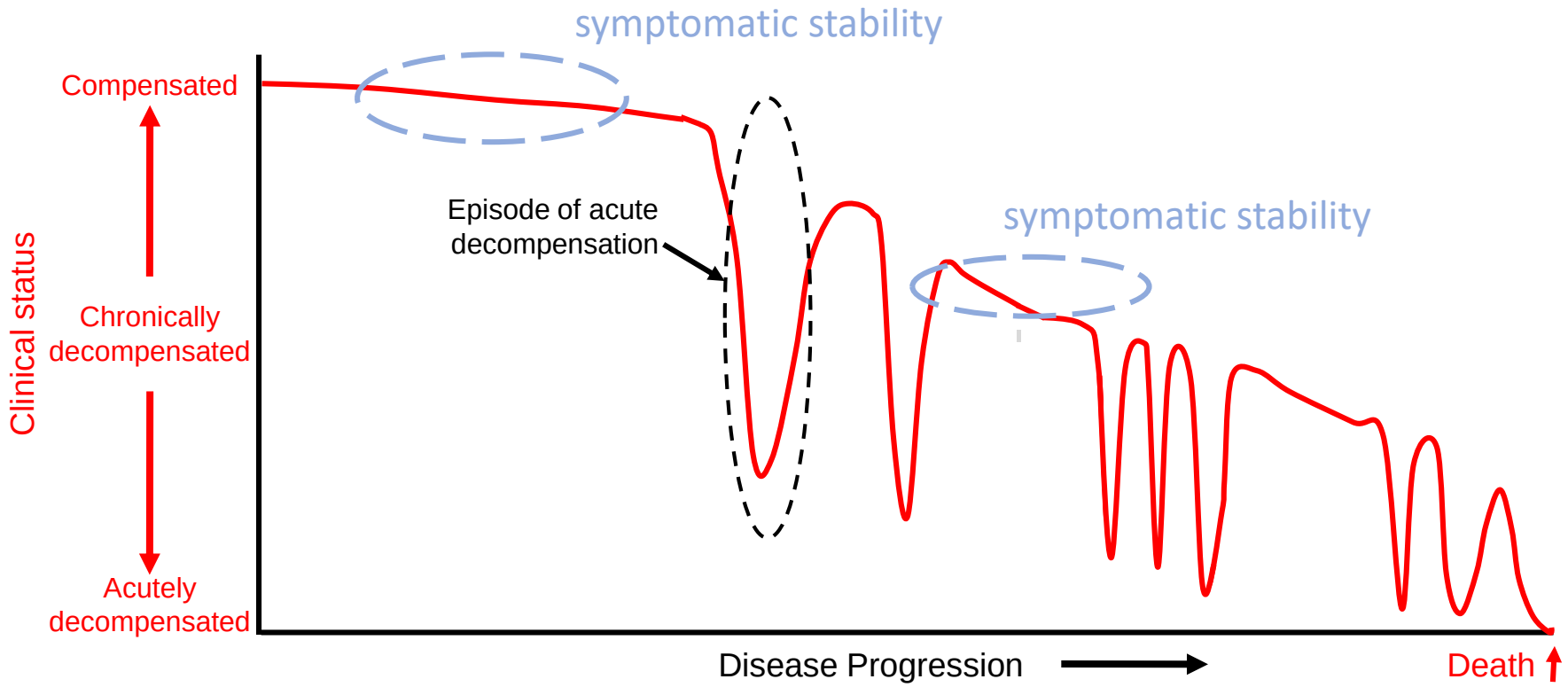
CRESCITA[8]

*Calcolata usando il tasso d'incidenza di HF nel 1997 per la popolazione di Hong Kong e applicandolo alla popolazione cinese

1. Mozaffarian et al. Circulation 2015;131(4):e29-e322; 2. Global Burden of Disease Study 2013 Collaborators. Lancet 2015;386:743-800; 3. Lloyd-Jones et al. Circulation 2002;106:3068–72; 4. Go et al. Circulation 2014;129:e28–e292; 5. Allender et al. Coronary Heart Disease Statistics 2008. Disponibile a: https://www.bhf.org.uk/~/media/files/research/heart-statistics/hs2008_coronary_heart_disease_statistics.pdf; 6. Hung et al. Hong Kong Med J 2000;6:159–62; 7. Hunt et al. J Am Coll Cardiol 2009;53:e1–90; 8. Kearney et al. Lancet 2005; 365:217–23

HF is a progressive disease whereby cardiac structure and function continue to deteriorate

- Increasing frequency of acute events with disease progression leads to high rates of hospitalization and increased risk of mortality[1–7]



Adapted from Gheorghiade et al. 2005[2]

HF, heart failure

1. Ahmed et al. Am Heart J 2006;151:444–50; 2. Gheorghiade et al. Am J Cardiol 2005;96:11G–17G; 3. Gheorghiade, Pang. J Am Coll Cardiol 2009;53:557–73; 4. Holland et al. J Card Fail 2010;16:150–6; 5. Muntwyler et al. Eur Heart J 2002;23:1861–6; 6. McCullough et al. J Am Coll Cardiol 2002;39:60–9; 7. McMurray JJ. et al. Eur Heart J. 2012;33(14):1787–1847

HF in Italia: dati epidemiologici e costi

Attualmente lo scompenso cardiaco cronico è uno dei maggiori problemi sanitari

Crescita media nei prossimi 10 anni

2.3%

~190.000

Ospedalizzazioni per HF in un anno (2)

HF è la **seconda causa di ospedalizzazione** dopo il parto naturale

Alto tasso di riospedalizzazioni

1ª causa di morte in Italia

> 11.000 €

Spesa media di gestione per paziente/anno (3)

€

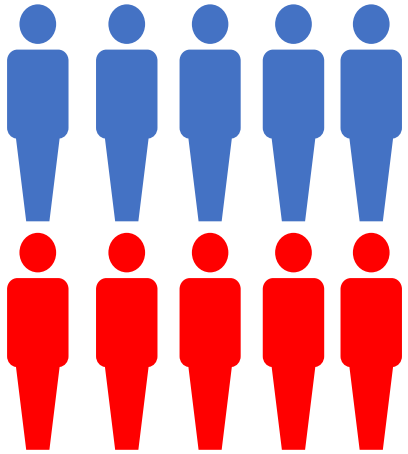
3bn €: la spesa per HF rappresenta il 2% dei costi sostenuti dal Sistema Sanitario Nazionale (una delle voci di spesa maggiore)

Lo HF riguarda 1,5%(1) della popolazione, circa 1.000.000 di pazienti in Italia

(1) Health Search Database
(2) Istituto Superiore Sanità Italian DRG
(3) Corrao et Al. Eur J Heart Fail. 2014 Jul;16(7):729-36.

L’HF cronico ha un impatto importante sulla prognosi a lungo termine

5
anni

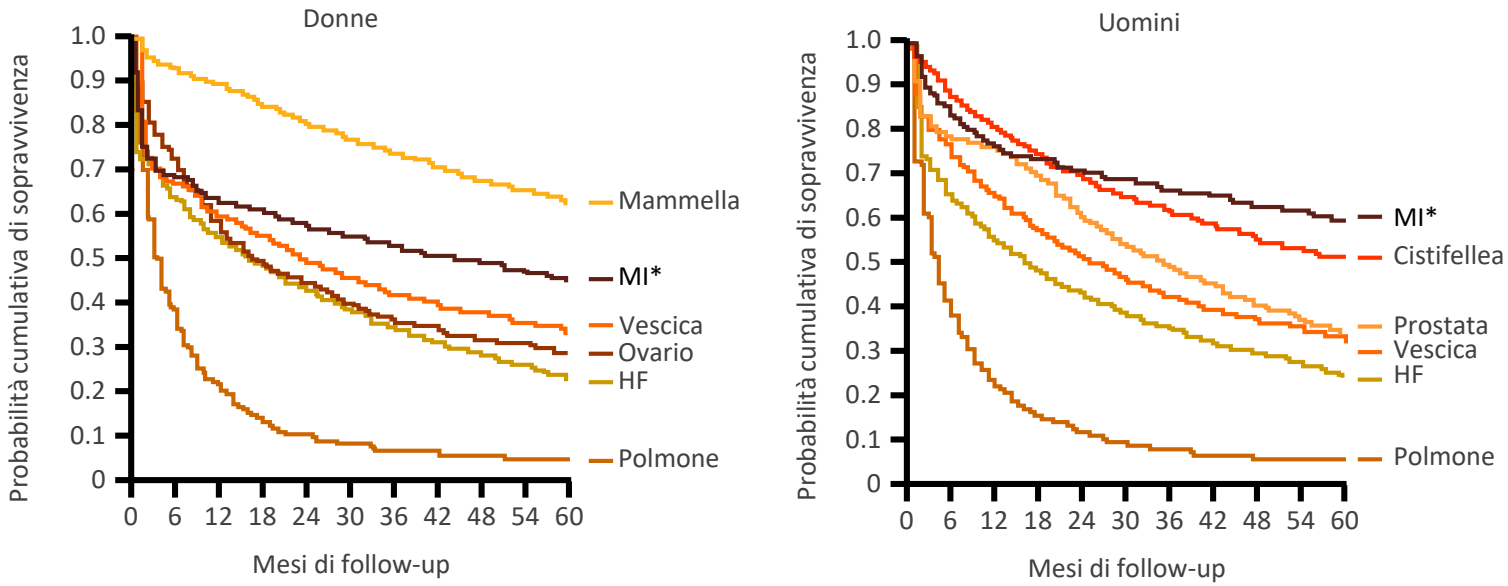


~50%
di mortalità dopo la diagnosi dell’HF[1–4]

1. Roger et al. JAMA 2004;292:344–50;
2. Levy et al. N Engl J Med 2002;347:1397–402;
3. Go et al. Circulation 2014;129:e28-e292;
4. Yancy et al. Circulation 2013;128:e240–327;

L’HF è associato a una prognosi peggiore di quella dei tumori maligni in fase avanzata, compresi cancro della vescica, della prostata e mammario

Sopravvivenza a 5 anni dopo il primo ricovero in qualsiasi ospedale scozzese nel 1991 per HF, MI* e i quattro tipi di cancro più comuni nelle donne e negli uomini



+myocardial infarction

Stewart et al. Eur J Heart Fail 2001;3:315–22

International Journal of Cardiology 152 (2011) 88–94

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Clinical profile and predictors of in-hospital outcome in patients with heart failure: The FADOI "CONFINE" Study ☆

P. Biagi [a], G. Gussoni [b,*], I. Iori [c], R. Nardi [d], G. Mathieu [e], A. Mazzone [f], D. Panuccio [g], G. Scanelli [h], C. Cicatello [i], C. Rinollo [i], M. Muriago [j], D. Galasso [k], E. Bonizzoni [l], G. Vescovo [b,j] and on behalf of the CONFINE Study Group [1]

Methods: In this observational study, we recruited patients admitted with diagnosis of HF and present in five index days, in 91 units of IM in Italy. Characteristics and management of HF, comorbidities, functional and cognitive status, and quality of life, were analyzed.

Results: We observed 1411 patients, with a mean age of 78.7 ± 9.6 years. At admission, 81.7% of the patients were in NYHA classes III–IV. Ninety percent of the patients had at least one comorbidity. Dementia or severely impaired functional status were registered in 21.5% and 22.8% of the patients. In 89 patients (6,3%) a negative outcome (death or clinical worsening) occurred during hospitalization. A number of variables were

1440 pz classe III-IV, 91 MI, età media 79 aa circa

International Journal of Cardiology 152 (2011) 88–94

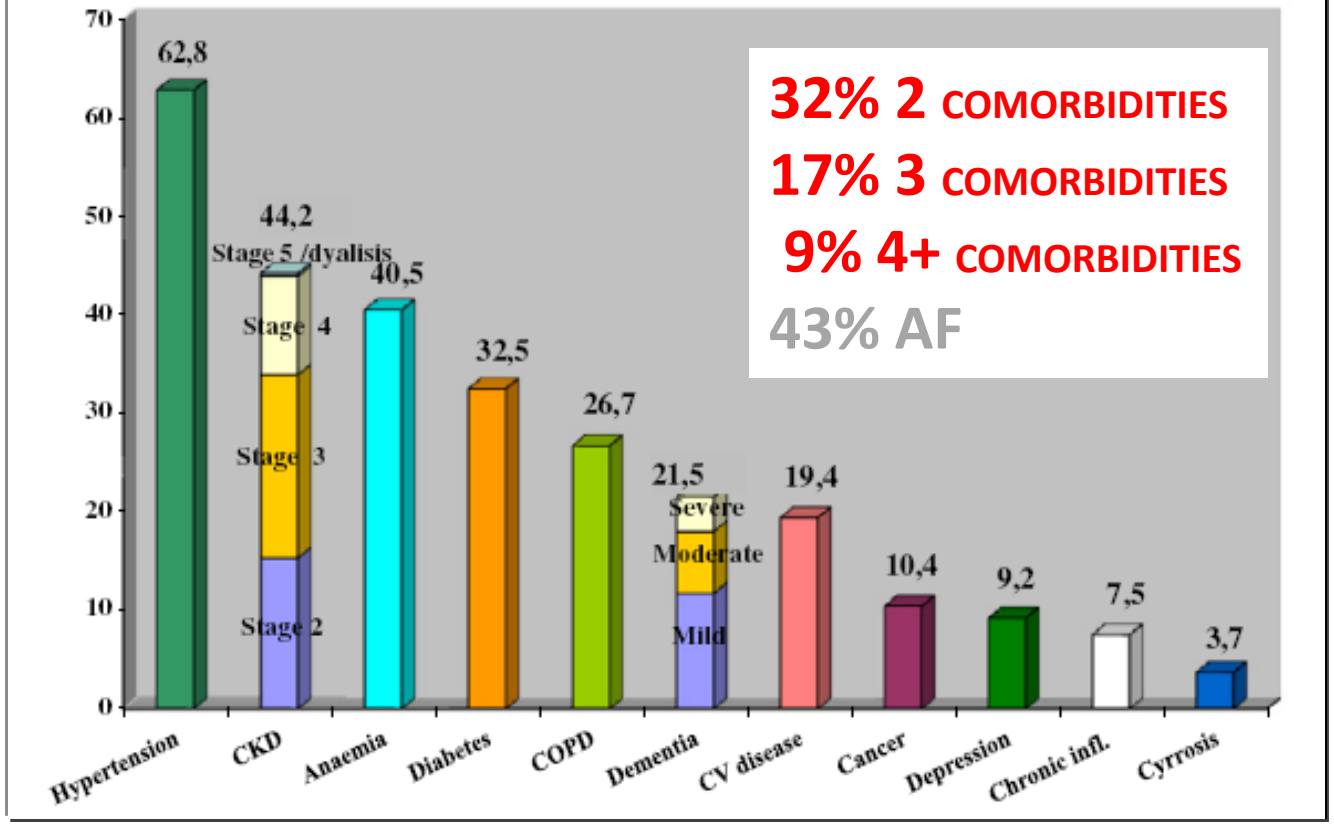
Contents lists available at ScienceDirect

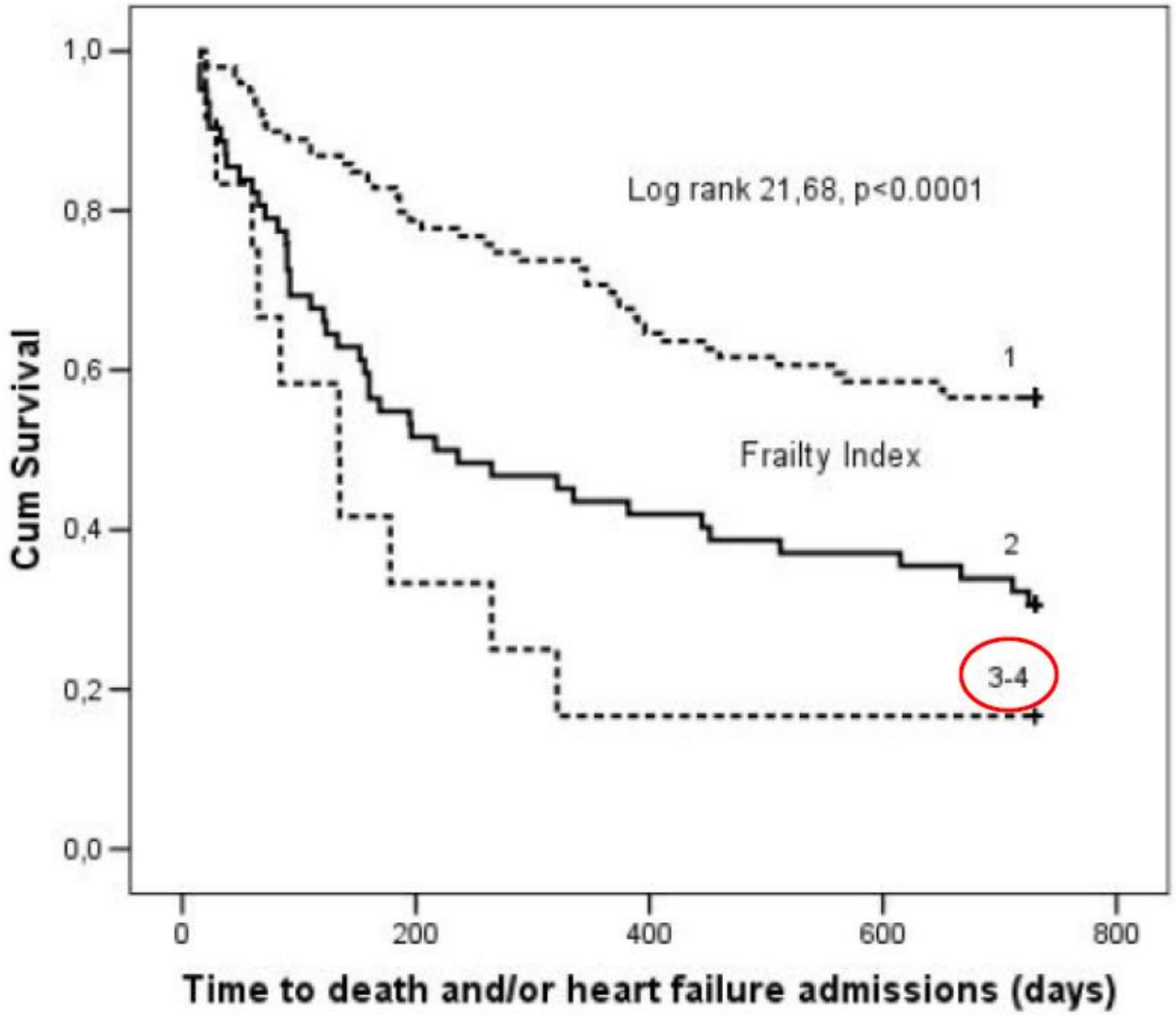
International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Clinical profile and predictors of in-hospital outcome in patients with heart failure: The FADOI "CONFINE" Study ☆

P. Biagi [a], G. Gussoni [b,*], I. Iori [c], R. Nardi [d], G. Mathieu [e], A. Mazzone [f], D. Panuccio [g], G. Scanelli [h], C. Cicatello [i], C. Rinollo [i], M. Muriago [j], D. Galasso [k], E. Bonizzoni [l], G. Vescovo [b,j] and on behalf of the CONFINE Study Group [1]





G.Pulignano, et al. Eur Heart J 2004 (abst.suppl)

Patient with symptomatic[a] HFrEF[b]

Therapy with ACE-I[c] and beta-blocker
(Up-titrate to maximum tolerated evidence-based doses)

Still symptomatic and LVEF ≤35%

No

Yes

Add MR antagonist[d,e]
(up-titrate to maximum tolerated evidence-based dose)

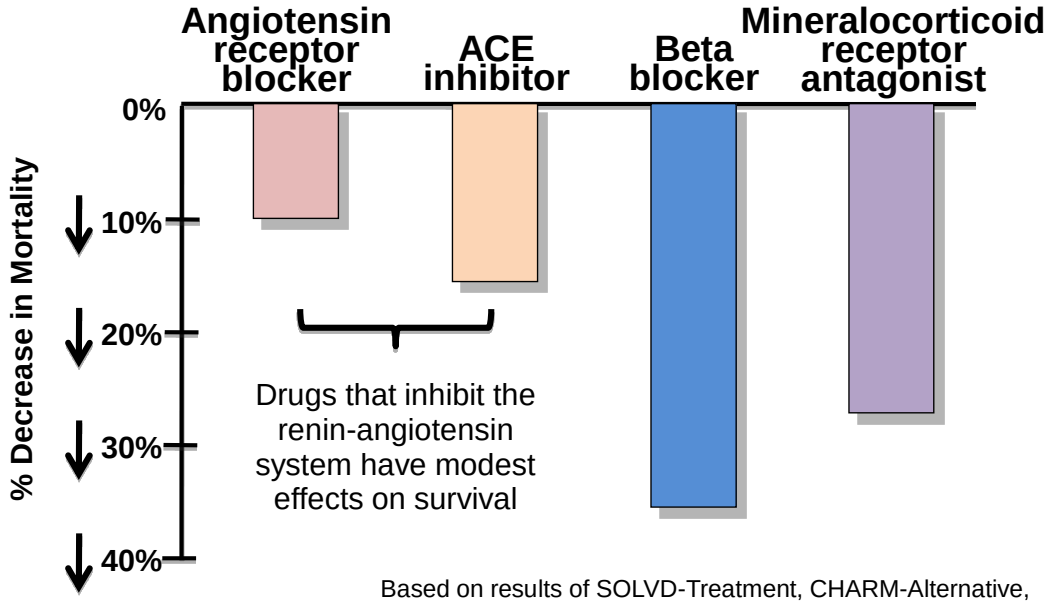
Class I

Class IIa

Diuretics to relieve symptoms and signs of congestion

If LVEF ≤35% despite OMT
or a history of symptomatic VT/VF, implant ICD

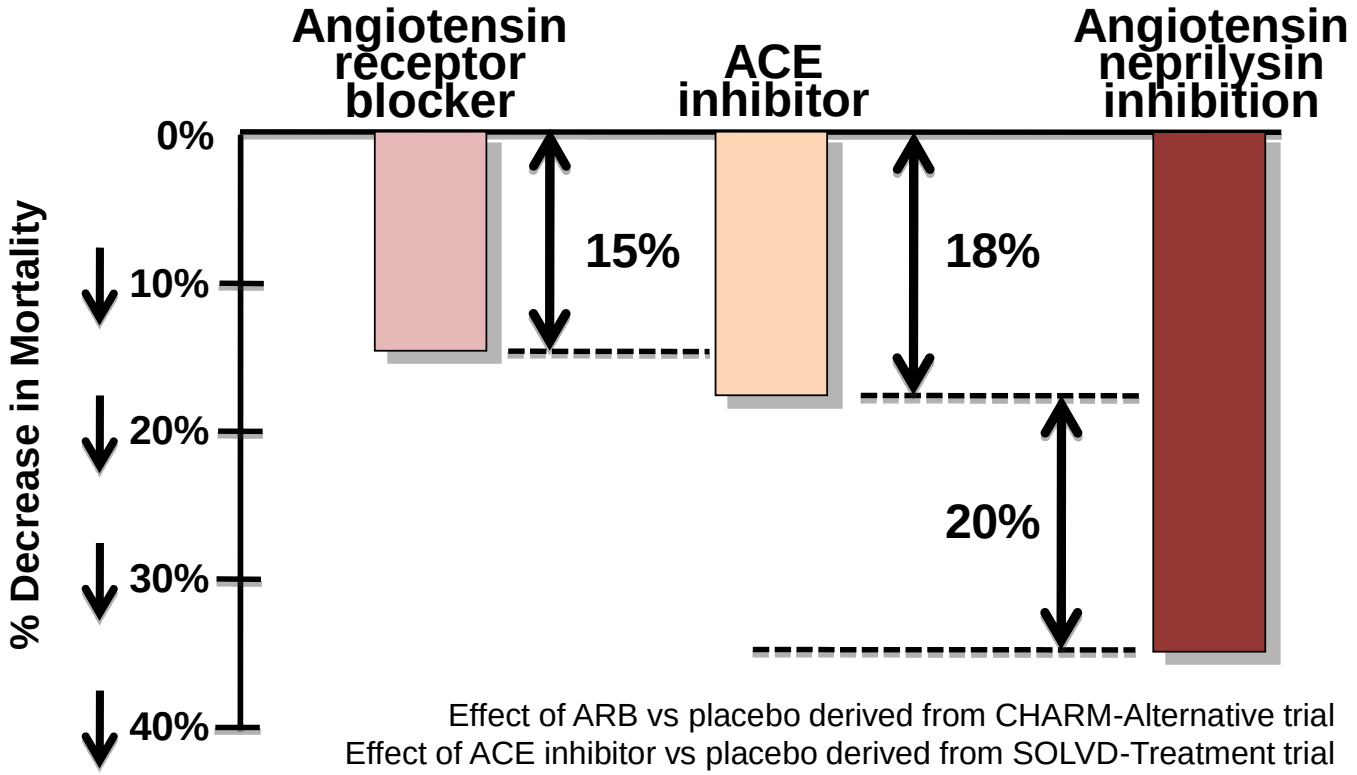
Drugs That Reduce Mortality in Heart Failure With Reduced Ejection Fraction



Based on results of SOLVD-Treatment, CHARM-Alternative, COPERNICUS, MERIT-HF, CIBIS II, RALES and EMPHASIS-HF

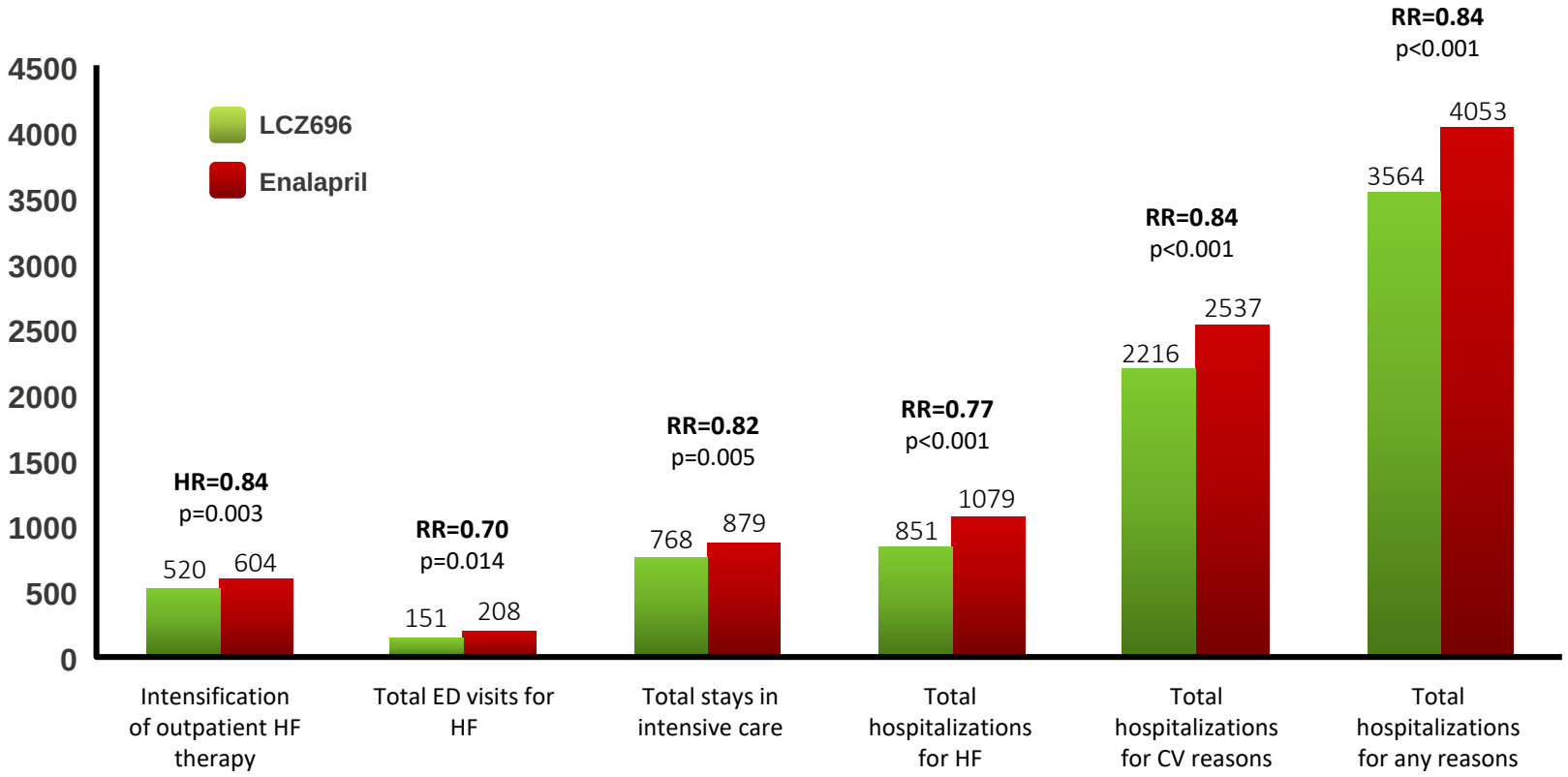
GET WITH THE GUIDELINES. HEART FAILURE

Angiotensin Neprilysin Inhibition With LCZ696 Doubles Effect on Cardiovascular Death of Current Inhibitors of the Renin-Angiotensin



Effect of ARB vs placebo derived from CHARM-Alternative trial
Effect of ACE inhibitor vs placebo derived from SOLVD-Treatment trial
Effect of LCZ696 vs ACE inhibitor derived from PARADIGM-HF trial

Sacubitril/valsartan risponde ai requisiti delle Linee Guida ESC: previene le ospedalizzazioni e riduce sia quelle per scompenso, sia quelle CV che quelle per tutte le cause



HF = heart failure; ED = emergency department; CV = cardiovascular

Packer et al. Circulation 2015;131:54–61

International Journal of Cardiology 152 (2011) 88–94

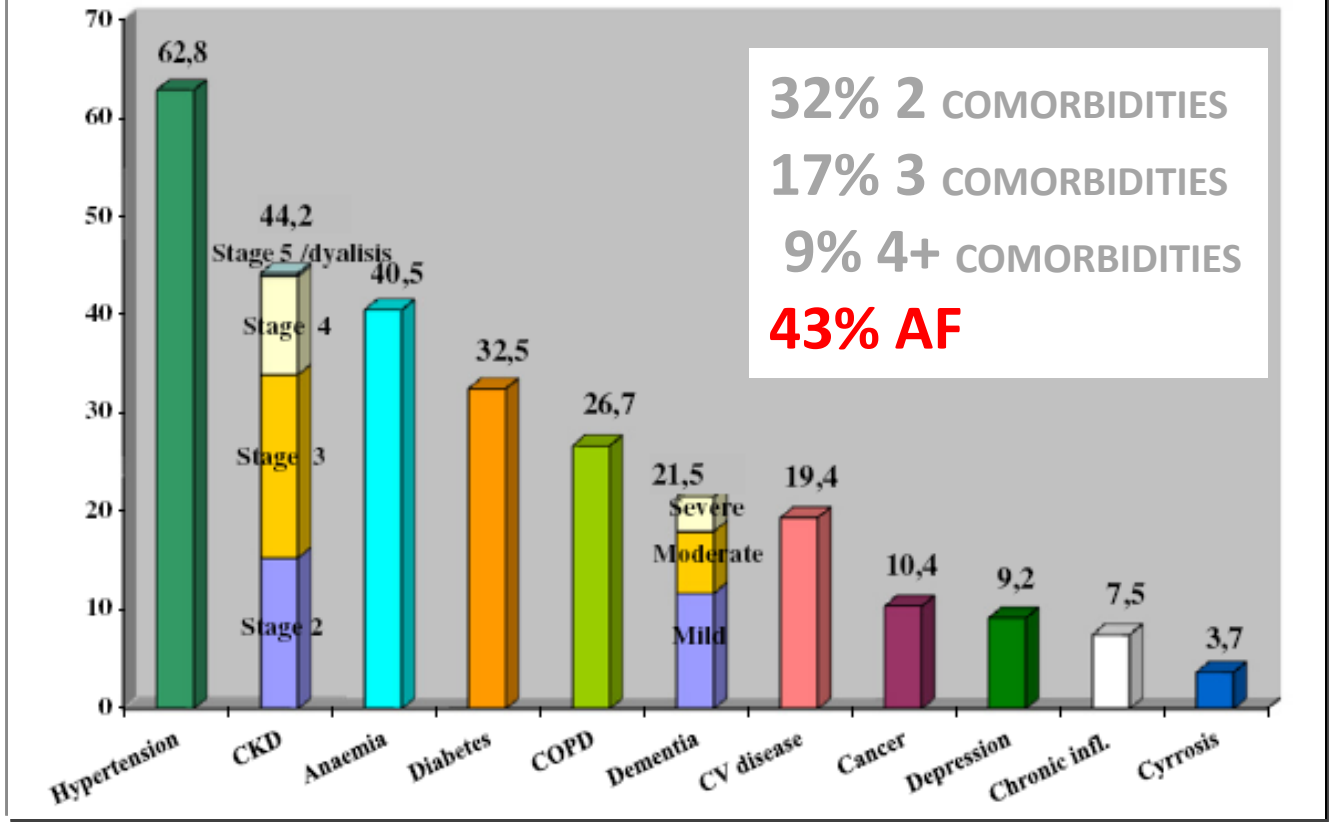
Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Clinical profile and predictors of in-hospital outcome in patients with heart failure: The FADOI "CONFINE" Study ☆

P. Biagi [a], G. Gussoni [b,*], I. Iori [c], R. Nardi [d], G. Mathieu [e], A. Mazzone [f], D. Panuccio [g], G. Scanelli [h], C. Cicatello [i], C. Rinollo [i], M. Muriago [j], D. Galasso [k], E. Bonizzoni [l], G. Vescovo [b,j] and on behalf of the CONFINE Study Group [1]



International Journal of Cardiology 167 (2013) 2895–2903

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Current presentation and management of 7148 patients with atrial fibrillation in cardiology and internal medicine hospital centers: The ATA AF study☆

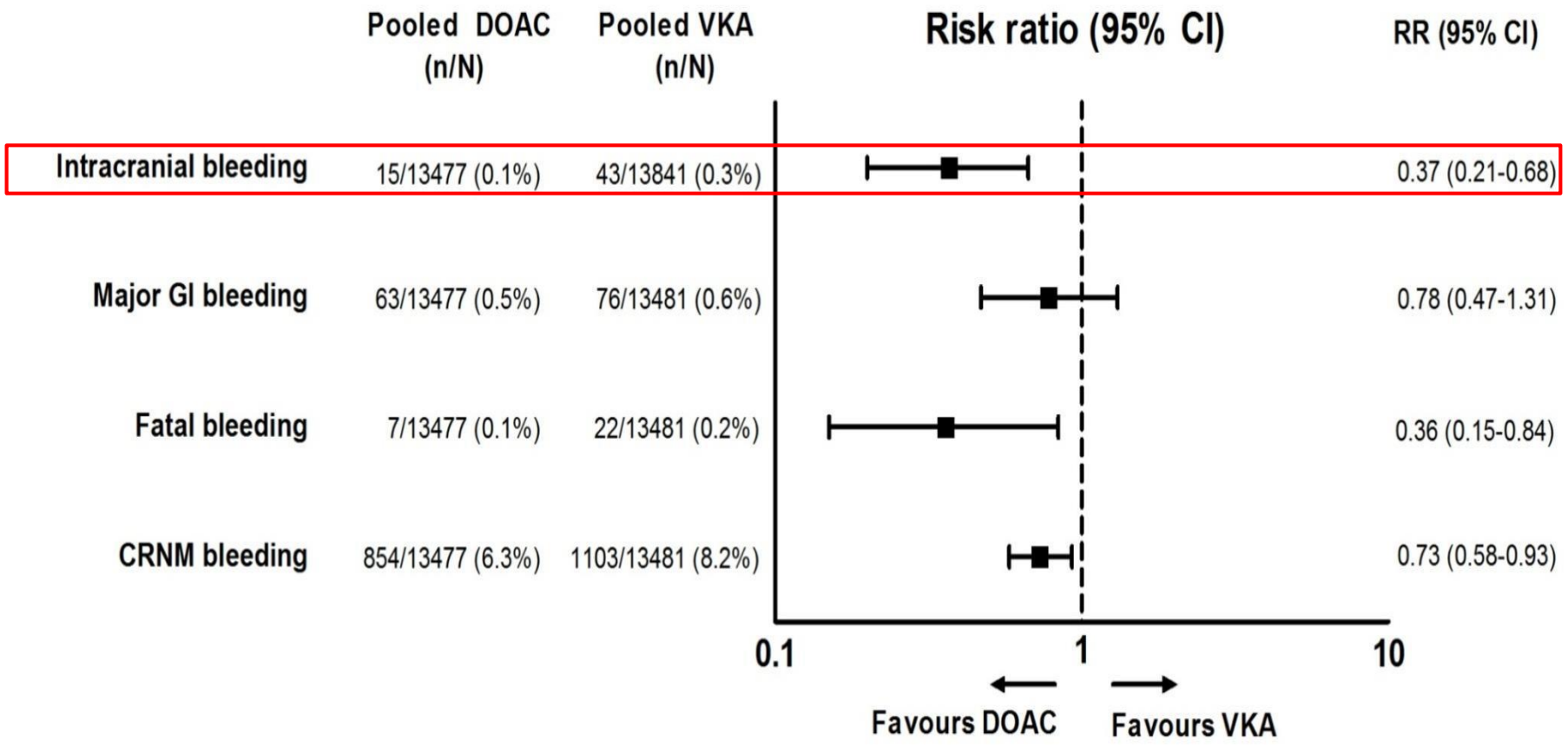
Pz ricoverati in **medicina** vs cardiologia:
80 vs 74 anni
HF 31 vs 24%
DM 28 vs 21%
stroke 20 vs 10%
PAD 15 vs 7%
CKD 23 vs 14%
COPD 26 vs 16%
Dementia 19 vs 3 %

Table 1
Baseline characteristics of the patients.

Characteristics	Total (n. 7148)	Cardiology (n. 3862)	Internal medicine (n. 3286)	p
Age (years), median [IQR]	77 [70–83]	74 [66–80]	80 [74–86]	<.0001
Females, %	47.0	43.4	51.3	<.0001
Hypertension, %	75.2	74.7	75.8	0.27
Hypercholesterolemia, %	28.9	33.9	22.9	<.0001
Heart failure, %	27.7	24.5	31.5	<.0001
Diabetes, %	24.3	21.4	27.8	<.0001
Coronary artery disease, %	19.9	19.9	20.0	0.91
Valvular heart disease, %	33.1	36.2	29.5	<.0001
Prior stroke/TIA, %	14.6	9.7	20.5	<.0001
Peripheral embolism, %	2.0	1.4	2.8	<.0001
Peripheral artery disease, %	10.9	7.3	15.1	<.0001
Renal dysfunction, %	18.5	14.0	23.7	<.0001
COPD, %	20.8	16.0	26.6	<.0001
Anemia, %	15.8	7.7	25.3	<.0001
Cognitive deficit/Dementia, %	10.4	3.2	18.8	<.0001
Need of assistance				
No assistance, %	65.9	80.0	49.3	<.0001
Partial assistance, %	24.1	16.6	32.8	
24 h-assistance, %	6.2	2.4	10.7	
In bed, %	3.9	1.0	7.2	

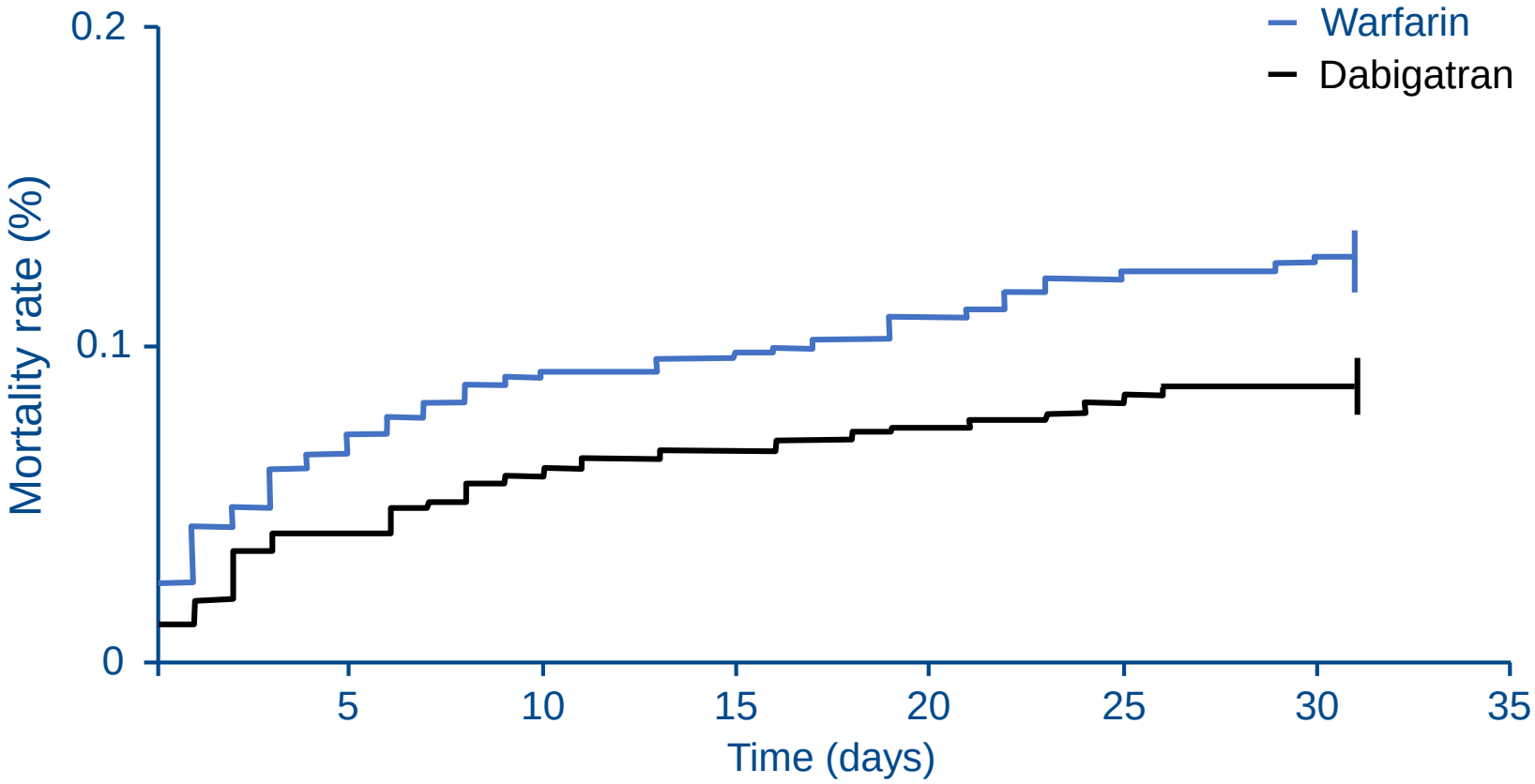
IQR = interquartile range, TIA = transient ischemic attack, COPD = chronic obstructive pulmonary disease.

DOACS vs AVK
Bleeding components



Van Es, Blood, 2014

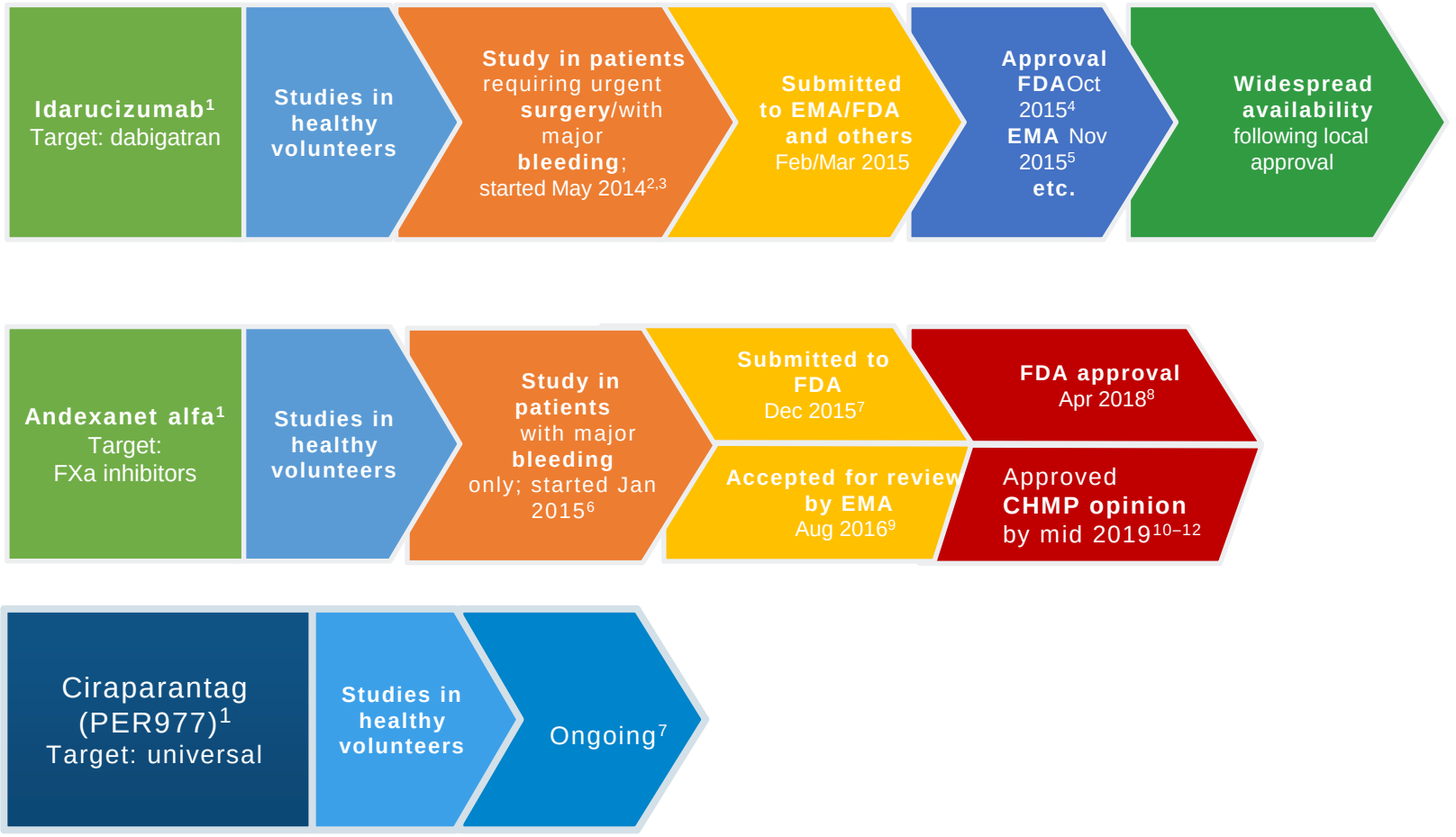
Mortality after a major bleed: Phase III trials – results



The Kaplan–Meier analysis indicated a reduced risk for death with dabigatran* vs warfarin during 30 days from the bleeding (P=0.052)

*Data combined from dabigatran 150 mg and 110 mg BID treatment groups. Only first major bleed included. Analysis not adjusted for covariates

Antidotes



- **Idarucizumab is not approved in all countries. Please check your local prescribing information for details. Andexanet alfa is not approved in all country.**
- 1. Adapted from Greinacher A et al. Thromb Haemost 2015; 2. Pollack C et al. N Engl J Med 2015; 3. Pollack C et al. Thromb Haemost 2015; 4. US FDA 2015 press release, 16 October 2015; 5. European Commission Community Register of Medicinal Products for Human Use 2015; 6. ClinicalTrials.gov Identifier: NCT02329327; 7. Portola Pharmaceuticals press release, 18 Dec 2015; 8. Portola Pharmaceuticals press release 03 May 2018; 9. Portola Pharmaceuticals press release 19 August 2016

European Journal of Internal Medicine 57 (2018) e38–e40

Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

Letter to the Editor

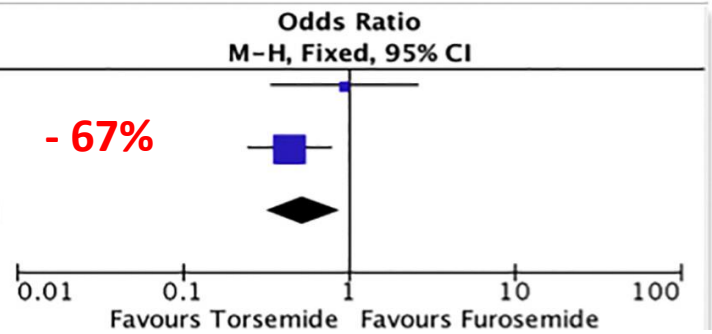
Torsemide versus furosemide in heart failure patients: A meta-analysis of randomized controlled trials

Panel B – CV Readmissions

Study or Subgroup	Torsemide Events	Torsemide Total	Furosemide Events	Furosemide Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Muller et al. (2003)	8	122	8	115	18.1%	0.94 [0.34, 2.59]
Murray et al. (2001)	78	113	130	121		Not estimable
Stroupe et al. (2000)	35	93	58	100	81.9%	0.44 [0.25, 0.78]
Total (95% CI)		**328**		**336**	**100.0%**	**0.53 [0.32, 0.87]**
Total events	121		196			

Heterogeneity: $Chi^2 = 1.65$, $df = 1$ ($P = 0.20$); $I^2 = 39\%$

Test for overall effect: $Z = 2.51$ ($P = 0.01$)



In 2012, **total cost** for heart failure (HF) was **$30.7 billion** and by 2030, it is **projected to increase to $69.7 billion**.

If all these patients were treated with torsemide, there would be 67% reduction in HF readmissions, which would translate to a reduction of ~ 0.3 million HF readmissions/year (0.67 × 0.44). The average **estimated cost of HF readmission is approximately $13,500** [11]. **Hence using torsemide instead of furosemide** would **save approximately 4 billion dollars/year** (13500 × 0.3 million).

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. ■, NO. ■, 2019

PUBLISHED BY ELSEVIER

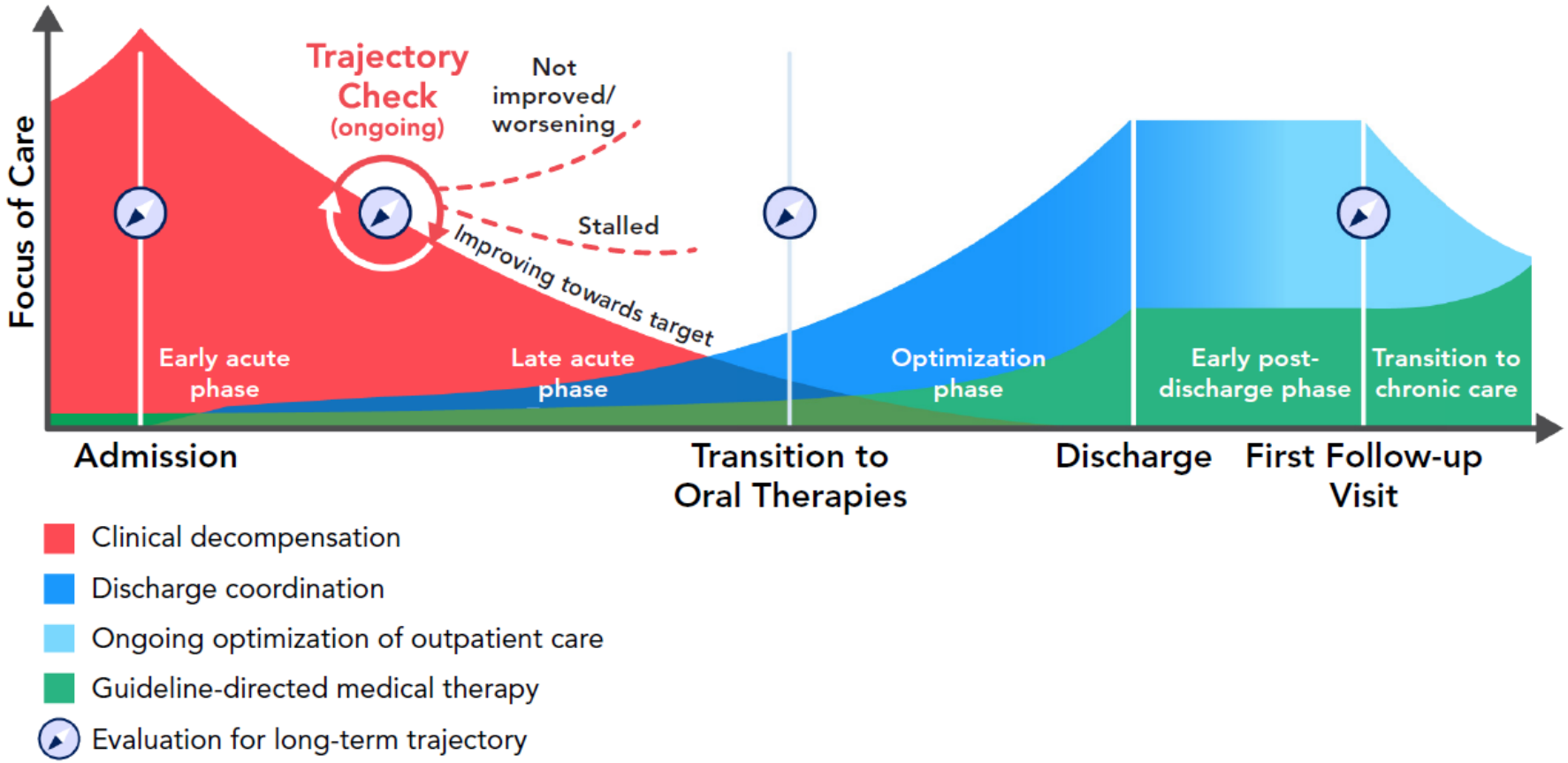
EXPERT CONSENSUS DECISION PATHWAY

2019 ACC Expert Consensus Decision Pathway on Risk Assessment, Management, and Clinical Trajectory of Patients Hospitalized With Heart Failure

A Report of the American College of Cardiology Solution Set Oversight Committee

4. PATHWAY SUMMARY GRAPHIC

FIGURE 1 Clinical Course of Heart Failure



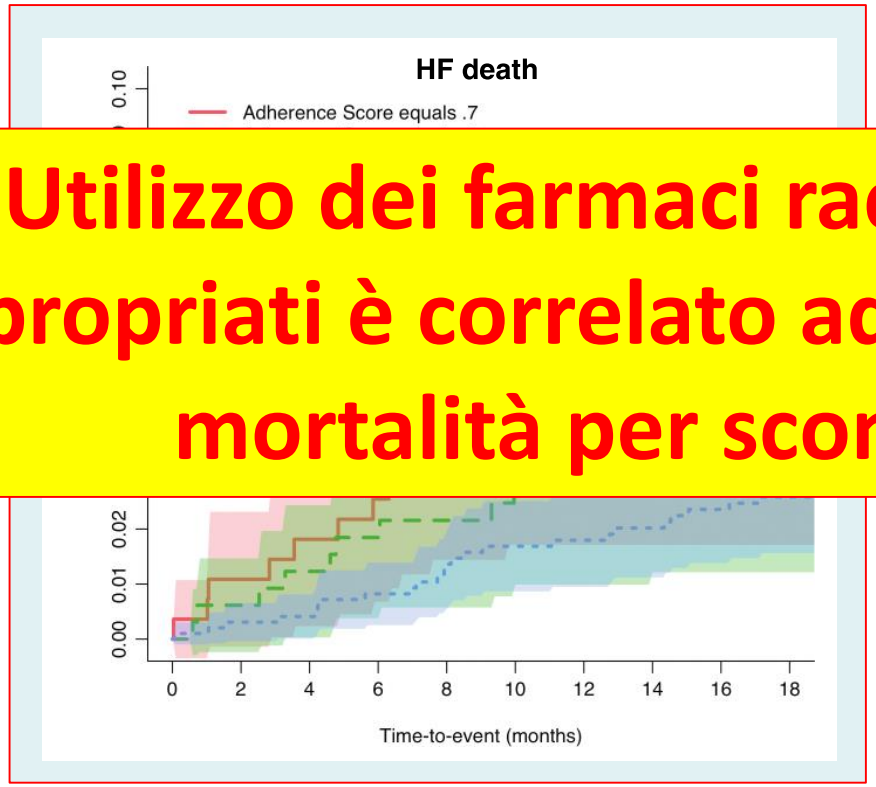
Graphic depiction of course of heart failure admission, showing the degree of focus on clinical decompensation (red), discharge coordination (blue), ongoing coordination of outpatient care (light blue), and optimization of guideline-directed medical therapy (green), with ongoing assessment of the clinical course (circle with arrows), and key time points for review and revision of the long-term disease trajectory for the HF journey (compass signs).

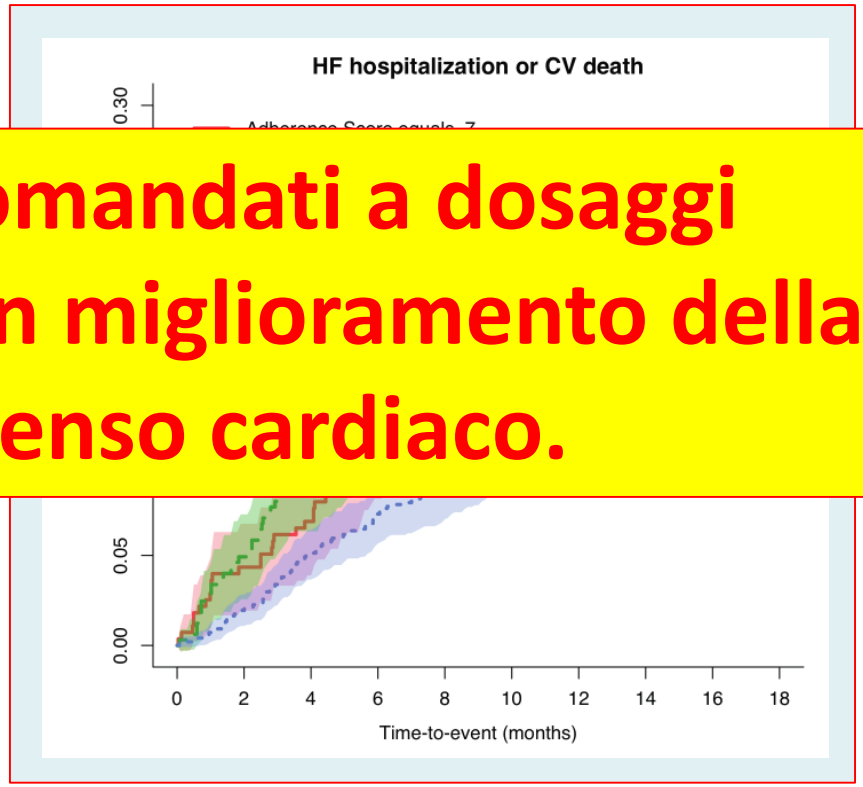
ESC European Society of Cardiology
European Journal of Heart Failure (2019) 21, 921–929
doi:10.1002/ejhf.1459
RESEARCH ARTICLE

Physicians' guideline adherence is associated with long-term heart failure mortality in outpatients with heart failure with reduced ejection fraction: the QUALIFY international registry

Table 2 Relationship between physicians' guideline adherence score at baseline* and outcomes at 18 months

	Univariable analysis		Multivariable analysis	
	HR/SHR [95% CI]	*P*-value	HR/SHR [95% CI]	*P*-value
All-cause death[a] ($n = 394$)				
Adherence score*	0.96 [0.92;1.00]	0.073	0.97 [0.92;1.01]	0.172
CV death, including HF[b] ($n = 228$)				
Adherence score*	0.93 [0.88;0.99]	0.022	0.95 [0.89;1.01]	0.074
HF death[c] ($n = 191$)				
Adherence score*	0.91[0.86;0.97]	0.006	0.93 [0.87;0.99]	0.034
All cause unplanned hospitalization[d] ($n = 1541$)				
Adherence score*	1.00 [0.98;1.03]	0.808	0.99 [0.97;1.02]	0.520
Unplanned CV hospitalization[e] ($n = 1175$)				
Adherence score*	0.99 [0.97;1.02]	0.625	0.98 [0.96;1.01]	0.200
Unplanned HF hospitalization[f] ($n = 861$)				
Adherence score*	1.00 [0.97;1.03]	0.851	0.99 [0.96;1.02]	0.400
Hospitalization attributable to HF or death attributable to CV death[g] ($n = 1089$)				
Adherence score*	0.98 [0.96;1.01]	0.189	0.97 [0.94;0.99]	0.043





Utilizzo dei farmaci raccomandati a dosaggi appropriati è correlato ad un miglioramento della mortalità per scompenso cardiaco.

European Journal of Heart Failure (2013) 1
doi:10.1093/eurjhf/hft134

Are hospitalize ts with heart failure treate an Society of Ca from 12 440 patie Failure Long-Term Re

ha un dosaggio appropriato di ACEi, ARB, BB,MRA

< 30% dei pazienti

21 Paesi europei 2011-2013
12.440 pazienti da 211 Cardiologie

Table 5 Number of patients at target dosages of recommended pharmacologic

	At target, *n* (%)	Not at target, *n* (%)
ACE-I (4710 pts)	1380 (29.3)	3330 (70.7)
ARBs (1500 pts)	362 (24.1)	1138 (75.9)
pts)	1130 (17.5)	5338 (82.5)
MRAs (		2936 (69.5)

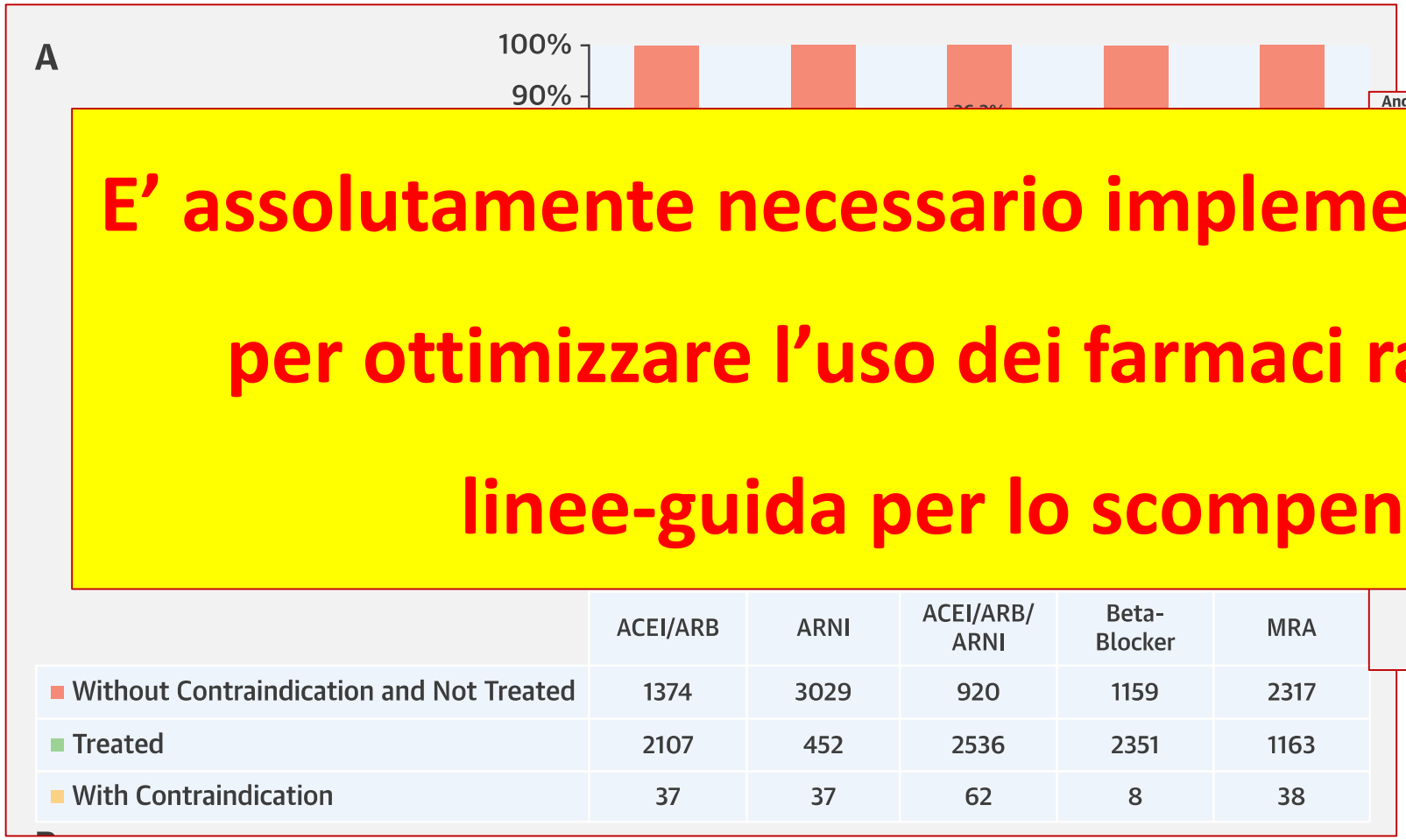
ACE-I, ACE inhibitor; HF, heart failure; MRAs, mineralo or blockers; PAD, peripheral artery disease.

Medical Therapy for Heart Failure With Reduced Ejection Fraction

The CHAMP-HF Registry

Stephen J. Greene, MD,[a,b] Javed Butler, MD, MPH, MBA,[c] Nancy M. Albert, PhD,[d] Adam D. DeVore, MD, MHS,[a,b] Puza P. Sharma, MBBS, MPH, PhD,[e] Carol I. Duffy, DO,[e] C. Larry Hill, PhD,[a] Kevin McCague, MA,[e] Xiaojuan Mi, PhD,[a] J. Herbert Patterson, PharmD,[f] John A. Spertus, MD, MPH,[g] Laine Thomas, PhD,[a] Fredonia B. Williams, EdD,[h] Adrian F. Hernandez, MD, MHS,[a,b] Gregg C. Fonarow, MD[i]

E' assolutamente necessario implementare nuove strategie per ottimizzare l'uso dei farmaci raccomandati dalle linee-guida per lo scompenso cardiaco



	ACEI/ARB	ARNI	ACEI/ARB/ ARNI	Beta-Blocker	MRA
Without Contraindication and Not Treated	1374	3029	920	1159	2317
Treated	2107	452	2536	2351	1163
With Contraindication	37	37	62	8	38

J Am Coll Cardiol 2018;72:351–66

MAGGIC SCORE

come calcolare la complessità del pzt?

MAGGIC Risk Calculator for Heart Failure

Estimates 1- and 3- year mortality in heart failure.

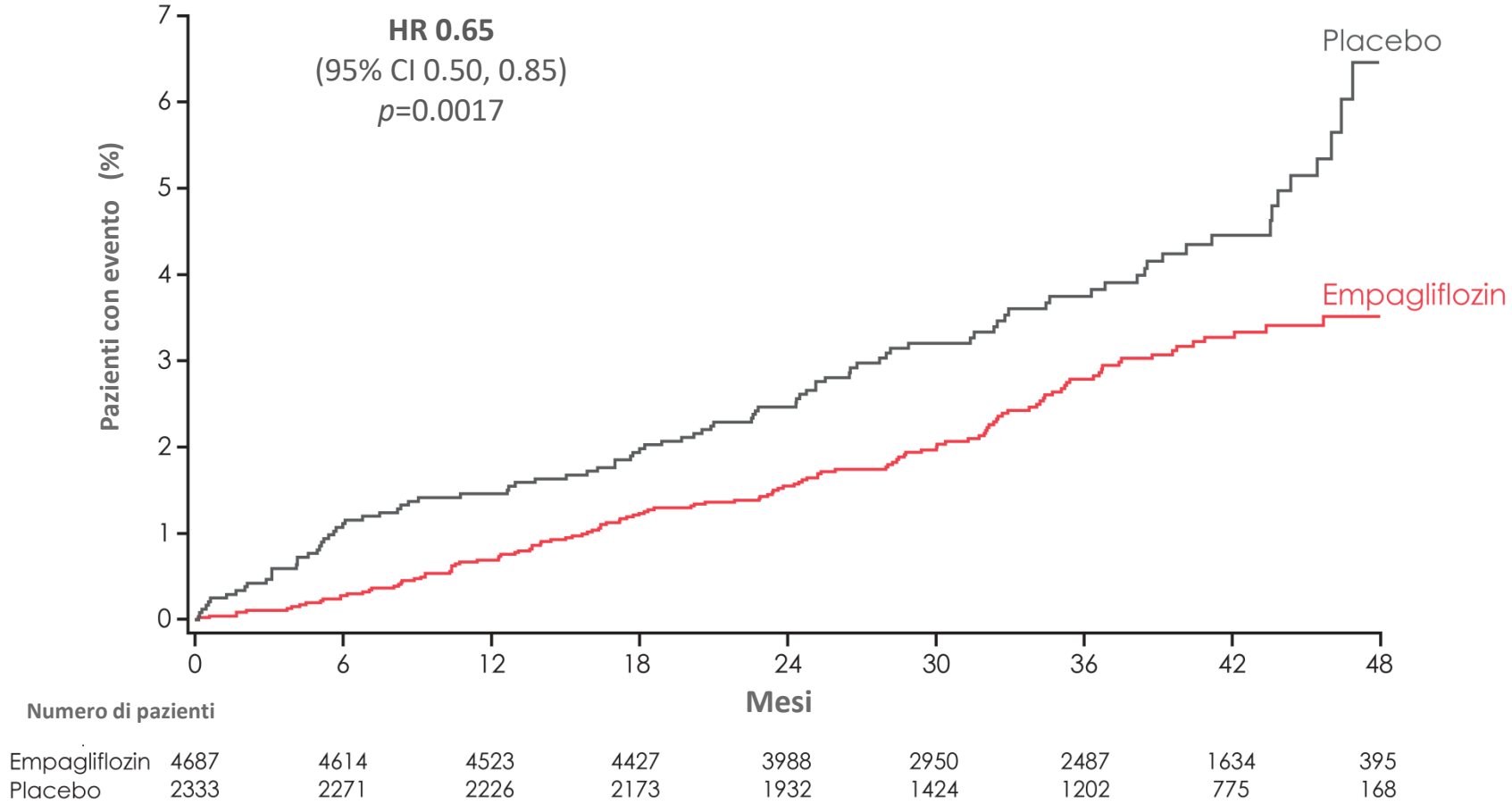
INSTRUCTIONS
Use in adult patients (≥18 years). Use with caution in patients with reduced ejection fraction (not yet externally validated in this population).

When to Use | Pearls/Pitfalls | Why Use

Age		years
Ejection Fraction		%
sBP	Norm: 100 - 120	mm Hg
BMI	Norm: 20 - 25	kg/m²
Creatinine Note: while this score uses creatinine as a proxy for renal function, eGFR is generally	Norm: 62 - 115	µmol/L

NYHA Class	Class I	0
	Class II	+2
	Class III	+6
	Class IV	+8
Gender	Female 0	Male +1
Current smoker	**No 0**	Yes +1
Diabetes	**No 0**	Yes +3
COPD	**No 0**	Yes +2
Heart failure first diagnosed ≥18 months ago	**No 0**	Yes +2
Beta blocker	No +3	**Yes 0**

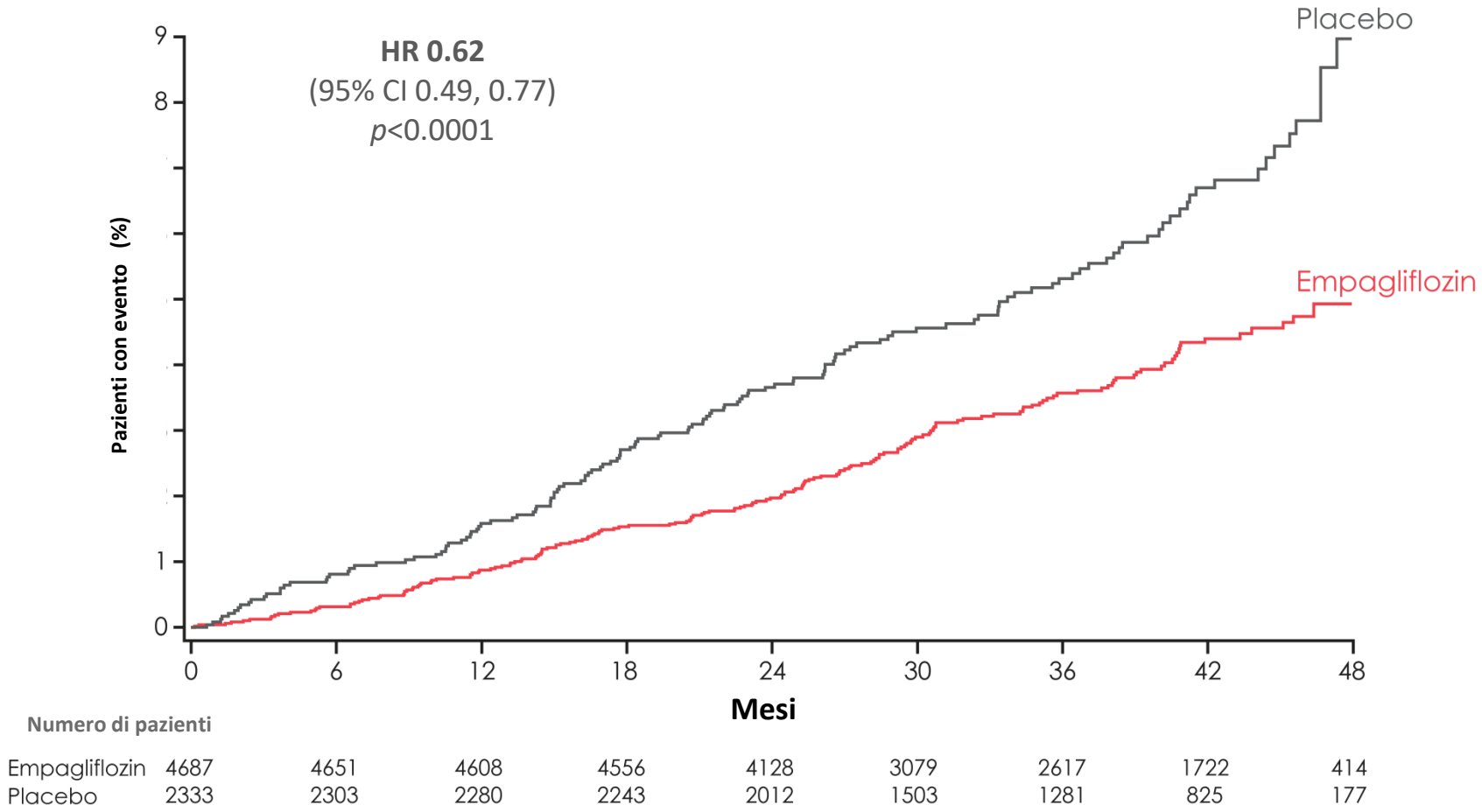
Ospedalizzazione per scompenso cardiaco



Funzione di incidenza cumulativa. HR, hazard ratio

Zinman B *et al. N Engl J Med* 2015;373:2117

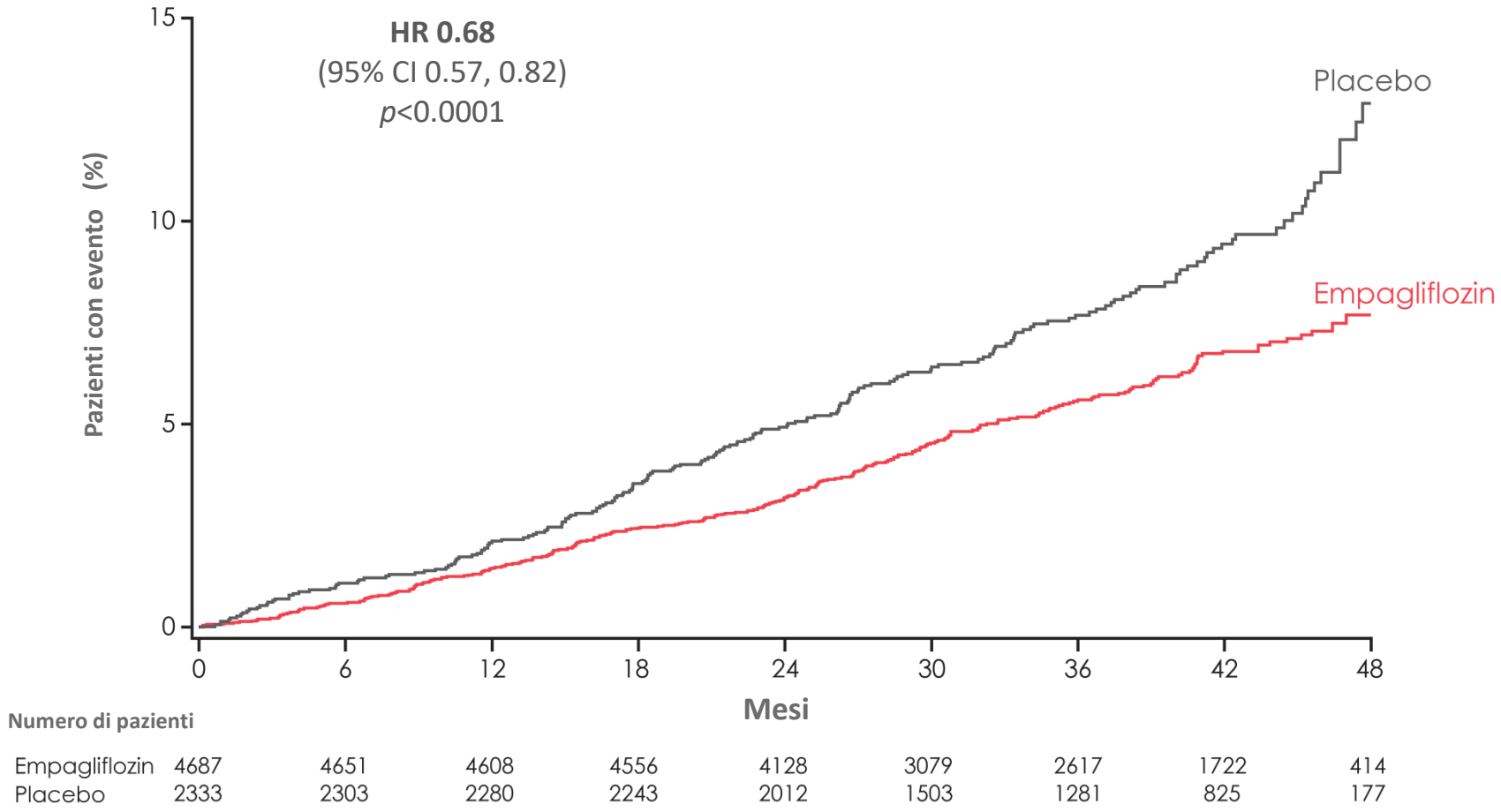
Morte cardiovascolare



Funzione di incidenza cumulativa. HR, hazard ratio

Zinman B *et al. N Engl J Med* 2015;373:2117

Mortalità per tutte le cause



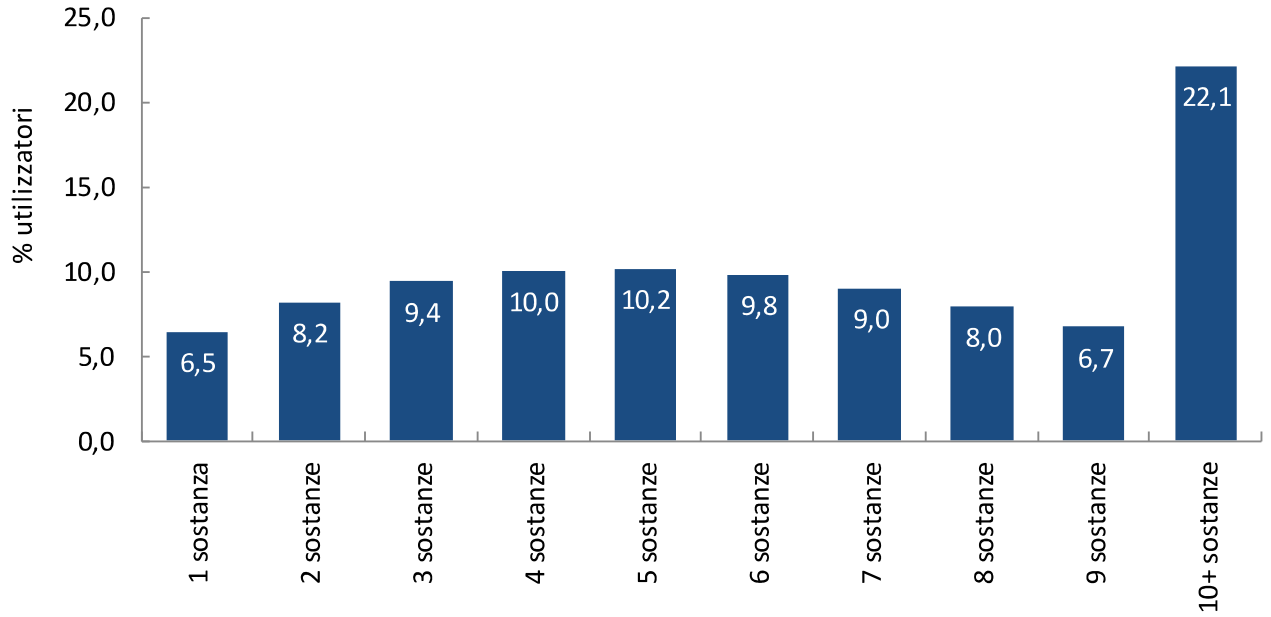
Stima di Kaplan-Meier. HR, hazard ratio

Zinman B *et al. N Engl J Med* 2015;373:2117

Sono state erogate **in media 6,7 diverse sostanze per utilizzatore**, con un valore medio più basso pari a 5,4 registrato nella fascia di età 65-69 anni e un valore medio più elevato di **7,7 sostanze per utilizzatore registrato nei soggetti con età pari o superiore agli 85 anni.** In particolare in entrambi i generi si è assistito a un progressivo incremento del numero di principi attivi diversi assunti all'aumentare delle decadi di età.

Figura 2.3.2. Distribuzione degli utilizzatori nella popolazione di età ≥65 anni per numero di sostanze diverse (2018)

14M

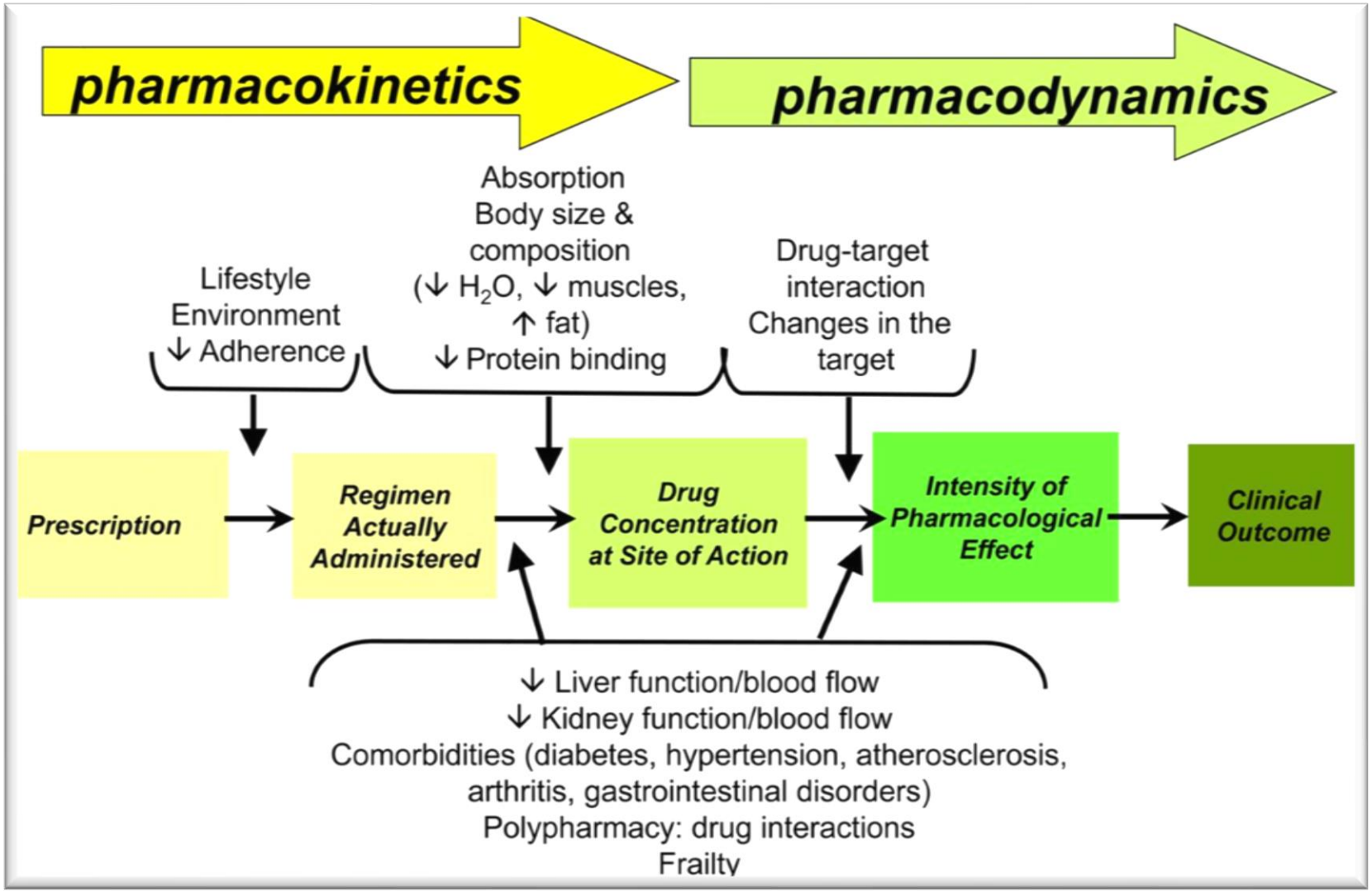


L'uso dei Farmaci in Italia
Rapporto Nazionale
Anno 2018
OSSERVATORIO NAZIONALE SULL'IMPIEGO DEI MEDICINALI

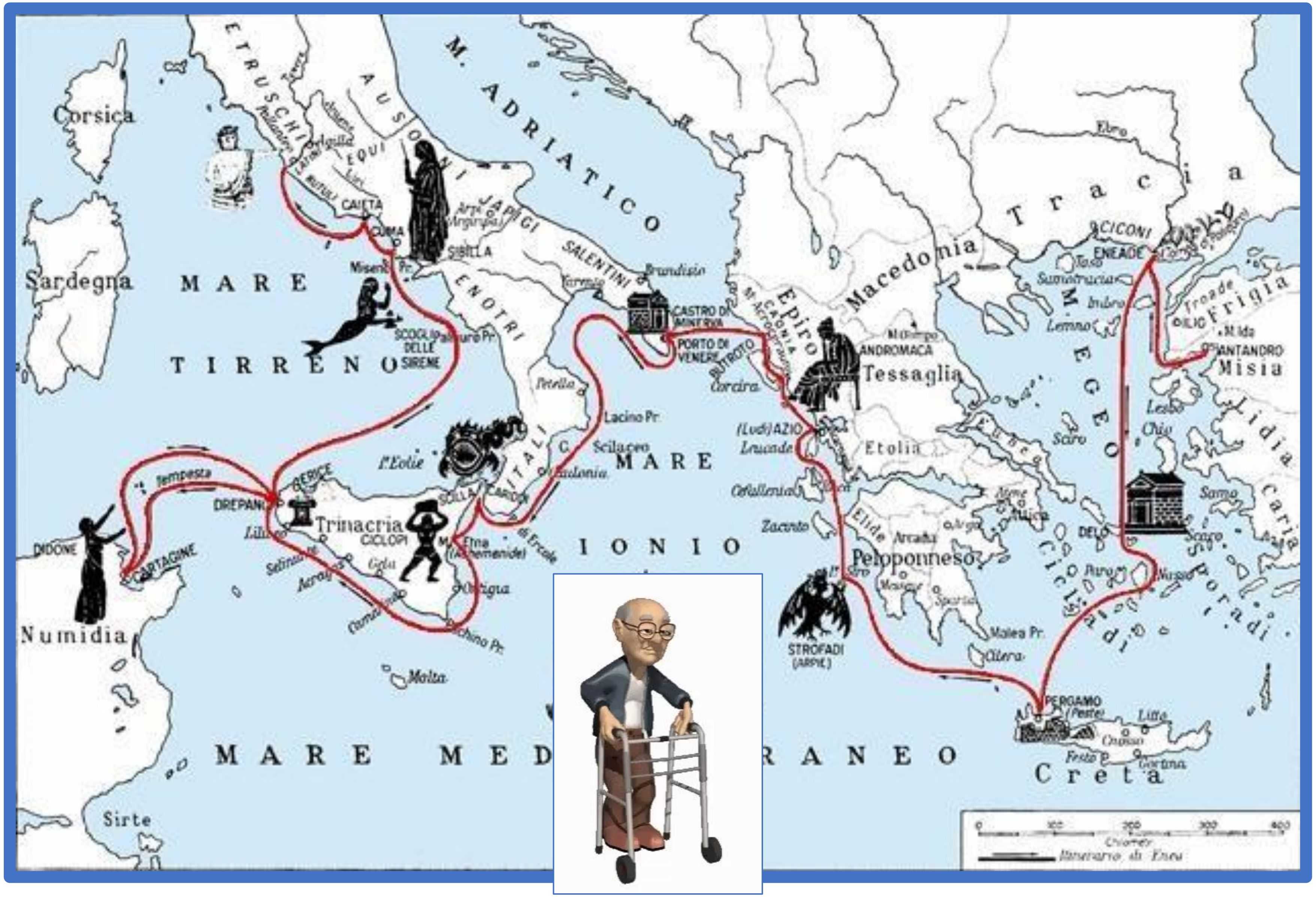
Le categorie terapeutiche maggiormente prescritte nella popolazione geriatrica sono risultate quella dei farmaci per **l'apparato cardiovascolare**, dei medicinali **antimicrobici** per uso sistemico e dei medicinali per l'apparato **gastrointestinale e metabolismo** (Rapporto OSMED 2018)

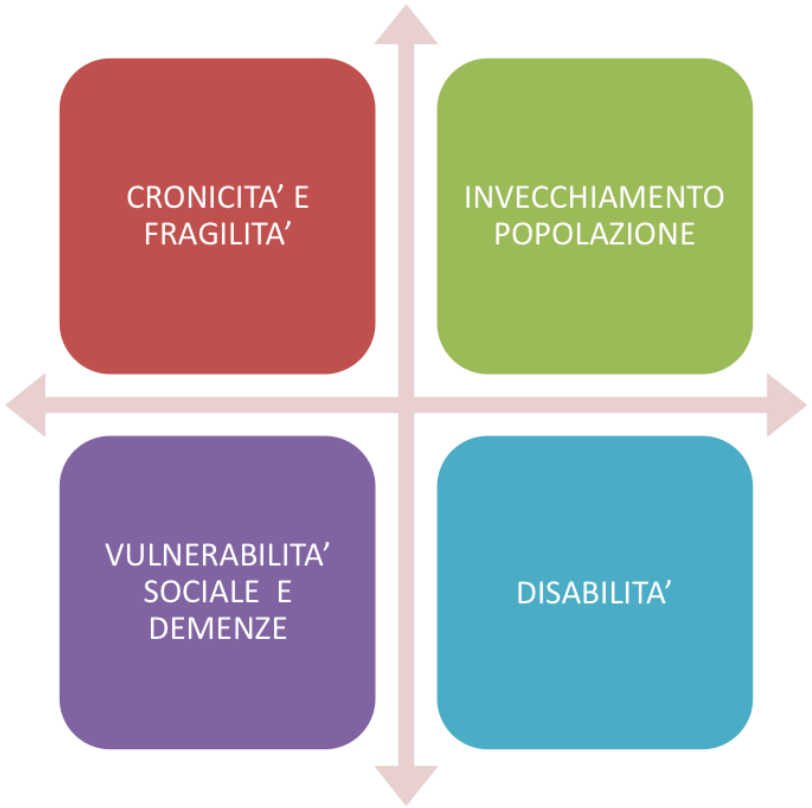
Antithrombotic therapy in the elderly: expert position paper of the European Society of Cardiology Working Group on Thrombosis

Pharmacokinetic and pharmacodynamic variables influencing the efficacy and safety of drugs in elderly



Andreotti F Eur Heart J 2015; 36: 3238-3249


Corsica
Sardegna
MARE
TIRRENO
MARE MED
RANEO
Numidia
Sirte
DIDONE
CARTAGINE
Tempesta
DREPANO
ERICE
Trinacria
CICLOPI
Etna
Ortigia
Malta
SCILLA
CARIDDI
SCOGLIO DELLE SIRENE
SIBILLA
CUMA
CAIETA
Miseno Pr.
ETRUSCHI
AUSONI
EQUI
JAPIGI
ENOTRI
SALENTINI
ITALIA
M. ADRIATICO
Brundisio
CASTRO DI MINERVA
PORTO DI VENERE
BUTROTO
Corcira
Lacino Pr.
Scilaceo
Caulonia
MARE
IONIO
(Ludi) AZIO
Leucade
Cefallenia
Zacinto
Epiro
Macedonia
Tessaglia
ANDROMACA
Etolia
Elide
Arcadia
Peloponneso
STROFADI (ARPIE)
Malea Pr.
Citera
PERGAMO (Peste)
Creta
Tracia
CICONI
ENEADE
Taso
Samotracia
Imbro
Lemno
EGEO
Troade
ILIO
Frigia
M. Ida
ANTANDRO
Misia
Lesbo
Chio
Lidia
Samo
Caria
DELO
Paro
Nasso
Cicladi
Sporadi
Itinerario di Enea



- ASSICURARE CONTINUITA' E COERENZA TRA I DIVERSI *SETTING* DI CURA E DI ASSISTENZA

- RIPENSARE LA GOVERNANCE DELLA FILIERA DEI SERVIZI

- SVILUPPO DI MODELLI ORGANIZZATIVI
- INNOVATIVI

Sistema Socio Sanitario
Regione Lombardia
ASST Cremona

CONCLUSIONI

CAMBIA L'EQUAZIONE DI CURA

Non si deve più considerare l'introduzione di un farmaco innovativo come un costo aggiuntivo, ma come una *risorsa* finalizzata a ridurre le ospedalizzazioni, la mortalità, e a mantenere la produttività dei soggetti affetti da patologie croniche.

Questo *investimento* porterà ad un vantaggio nel lungo periodo anche in termini di *cost saving*.

matteo.giorgipierfranceschi@asst-cremona.it