The contribution of RWE to scientific knowledge in cardiovascular diseases: The Trieste Observatory of CV Diseases

Andrea Di Lenarda

Cardiovascular Center, Trieste, ASUGI

Open Access Research

BMJ Open

Developing and validating a novel multisource comorbidity score from administrative data: a large population-based cohort study from Italy

Giovanni Corrao,[1,2] Federico Rea,[1,2] Mirko Di Martino,[3] Rossana De Palma,[4] Salvatore Scondotto,[1,5] Danilo Fusco,[3] Adele Lallo,[3] Laura Maria Beatrice Belotti,[4] Mauro Ferrante,[6] Sebastiano Pollina Addario,[1,5] Luca Merlino,[1,7] Giuseppe Mancia,[8] Flavia Carle[1,9]

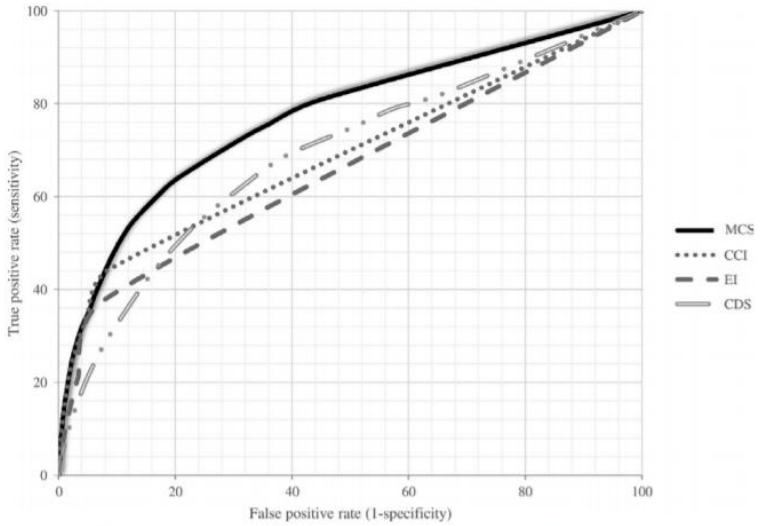


Figure 2 Receiver operating characteristic (ROC) curves comparing discriminant power of multisource comorbidity score (MCS), Charlson Comorbidity Index (CCI), Elixhauser Index (EI) and Chronic Disease Score (CDS) in predicting 1-year survival among National Health System (NHS) beneficiaries (internal validation set).

Elderly?
Multimorbidity?
Heart Failure patients?
…

Table 1 Assignment of weights in building the multisource comorbidity score (MCS) through a time-to-death multivariate Weibull model

Disease/condition	Regression coefficient (SE)	Weight
Metastatic cancer	1.63 (0.04)	18
Alcohol abuse	0.99 (0.16)	11
Cancer, without metastasis	0.91 (0.03)	10
Tuberculosis	0.88 (0.28)	10
Psychoses	0.77 (0.05)	8
Liver disease	0.72 (0.05)	8
Anxiety medication	0.52 (0.23)	6
Weight loss	0.51 (0.12)	6
Dementia	0.51 (0.06)	6
Malignancy medication	0.49 (0.05)	5
Parkinson's disease	0.49 (0.09)	5
Lymphoma	0.46 (0.08)	5
Hemiplegia and hemiparesis	0.46 (0.09)	5
Coagulation defects	0.43 (0.10)	5
Disorders of fluid, electrolyte and acid-base balance	0.40 (0.06)	4
Kidney diseases	0.39 (0.04)	4
Kidney dialysis	0.36 (0.17)	4
Heart failure	0.35 (0.02)	4
Other neurological diseases	0.32 (0.07)	3
Rheumatoid arthritis	0.27 (0.11)	3
Anaemias	0.26 (0.04)	3
Cerebrovascular diseases	0.25 (0.03)	3
Diabetes	0.20 (0.02)	2
Vascular diseases	0.20 (0.05)	2
Gout	0.18 (0.03)	2
Epilepsy	0.18 (0.03)	2
Chronic pulmonary diseases	0.16 (0.02)	2
Peptic ulcer	0.16 (0.02)	2
Acute myocardial infarction	0.11 (0.04)	1
Coronary and peripheral vascular disease	0.11 (0.02)	1
Valvular diseases	0.10 (0.06)	1
Arrhythmia	0.09 (0.02)	1
Obesity	0.08 (0.10)	1
Hypothyroidism	0.07 (0.09)	1

Contents lists available at ScienceDirect

International Journal of Cardiology

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

Editorial

Administrative database, observational research and the Tower of Babel

Annamaria Iorio [a,b], Gianfranco Sinagra [a], Andrea Di Lenarda [a,*]

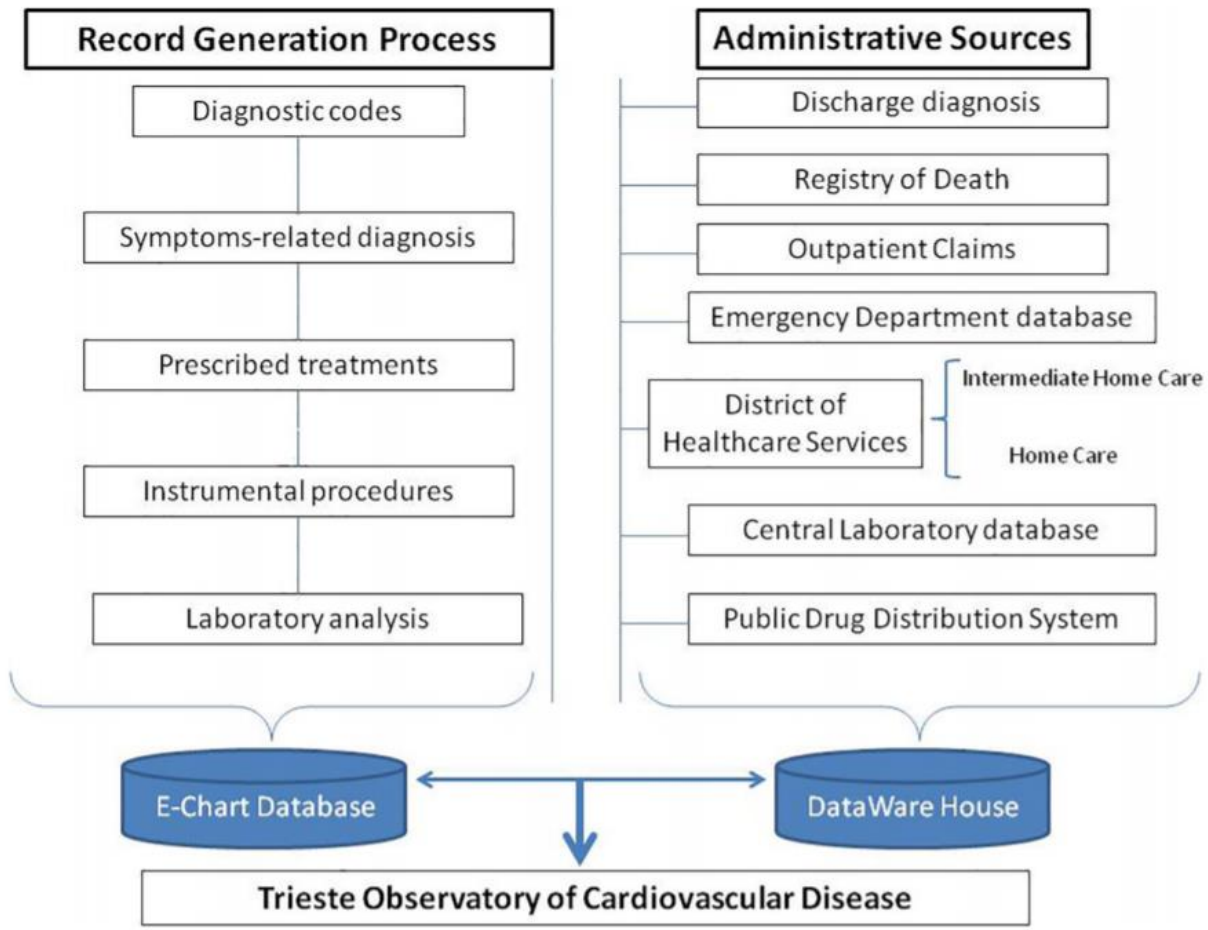


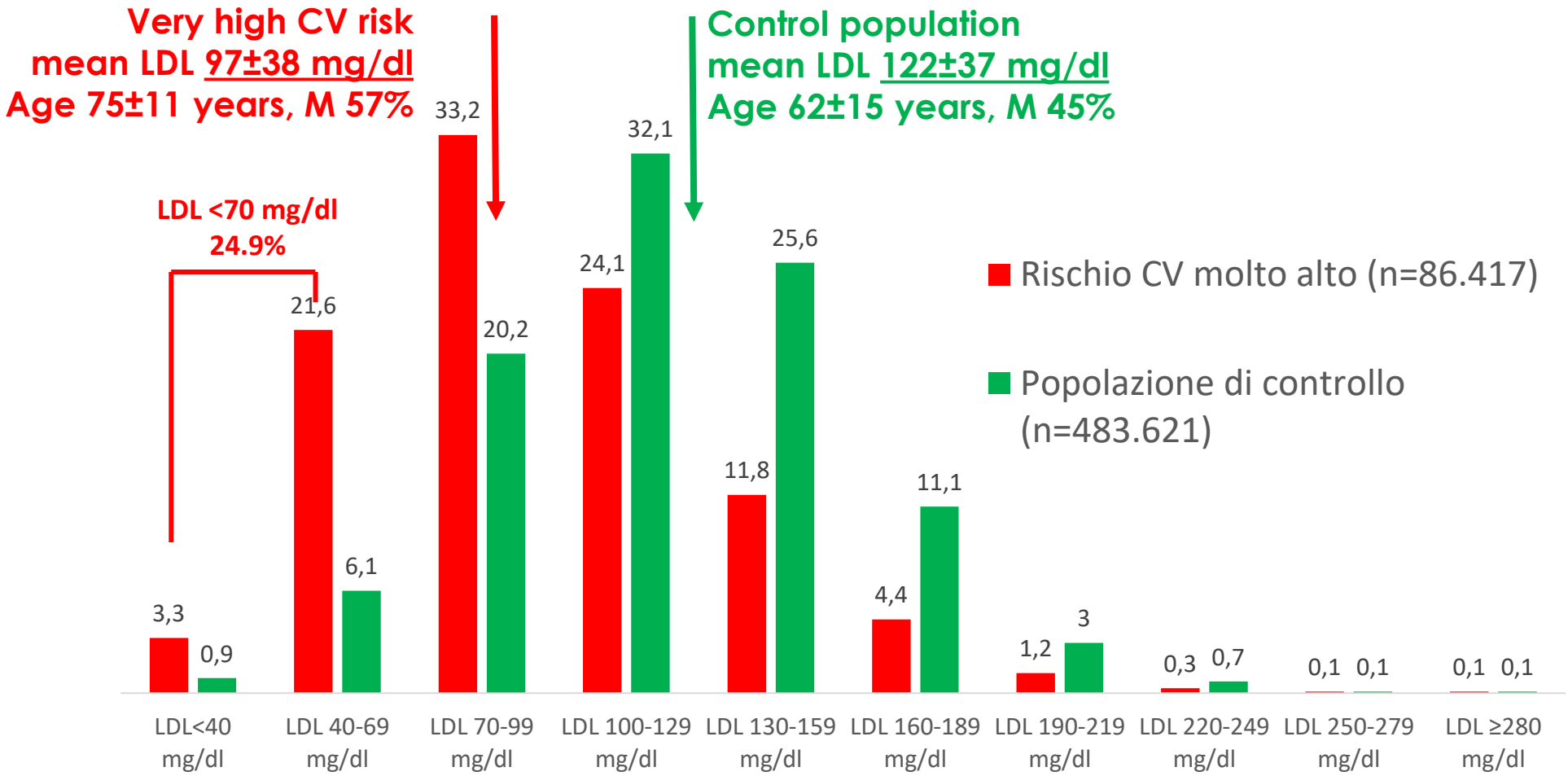
Fig. 1. Trieste Observatory of Cardiovascular Diseases is an example of population-based databases in which administrative data and clinical information are integrated within observational networks.

Agenda
(3 examples)

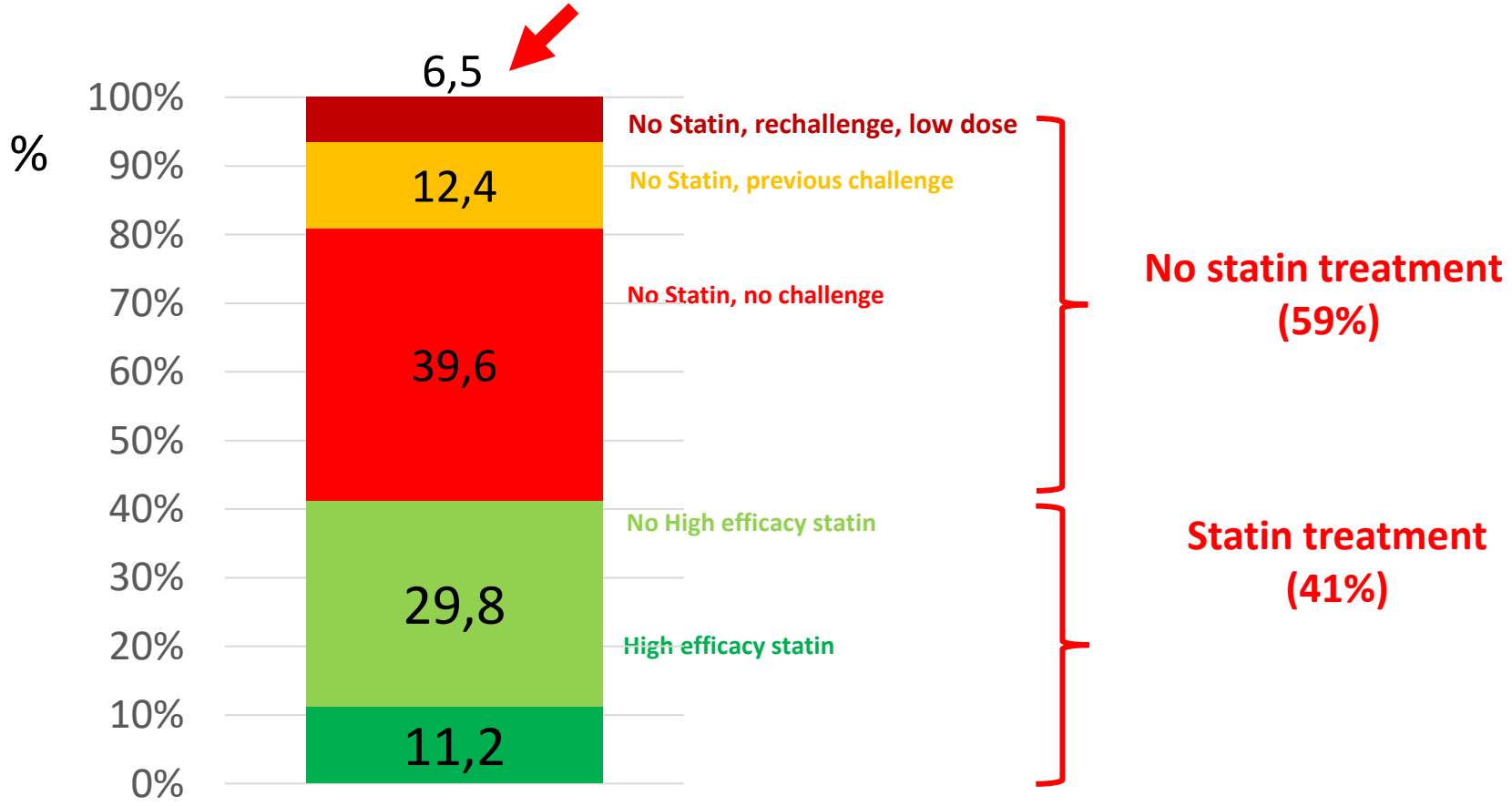
- Lipid profile, treatment and CV risk
- Atrial fibrillation and NOAC treatment
- Heart failure patients, multimorbidity, treatment and outcome

LDL distribution based on CV risk

(last available LDL disponibile - 2009-2018 in 570.038/845.669 cases:
67.4% of ≥35 yo FVG population)



Statin prescription and (possible) intolerance in Friuli Venezia Giulia region (n=98618)



Agenda
(3 examples)

- Lipid profile, treatment and CV risk
- Atrial fibrillation and NOAC treatment
- Heart failure patients, multimorbidity, treatment and outcome

IJC Heart & Vasculature 26 (2020) 100465

Contents lists available at ScienceDirect

IJC Heart & Vasculature

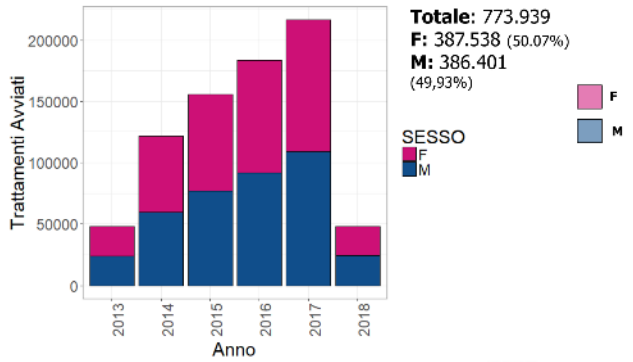
journal homepage: www.journals.elsevier.com/ijc-heart-and-vasculature

Non-vitamin K antagonist oral anticoagulation agents in patients with atrial fibrillation: Insights from Italian monitoring registries

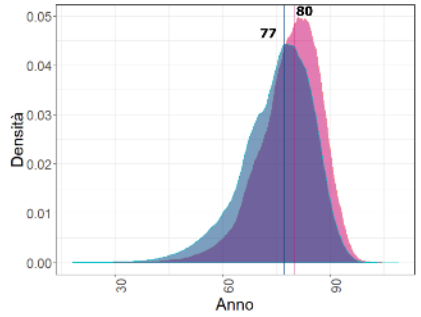
P.P. Olimpieri [a], A. Di Lenarda [b,*], F. Mammarella [a,*], L. Gozzo [a], A. Cirilli [a], M. Cuomo [a], M.M. Gulizia [c], F. Colivicchi [d], G. Murri [d], D. Gabrielli [e,1], F. Trotta [a,1]

BLITZ AF (n=4126) M 59.4%

Trattamenti avviati (FANV) Anno e Genere – nuovi trattamenti



Trattamenti avviati (FANV) Distribuzione età

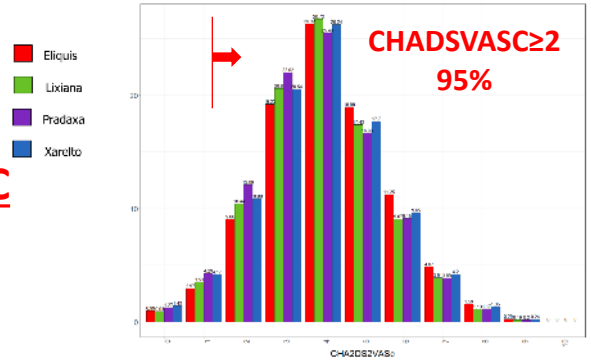


SESSO	MINIMO	1° QUARTILE	MEDIANA	3° QUARTILE	MASSIMO	MEDIA	DEV. STD
F	19	74	80	85	109	79	9
M	18	69	77	82	103	75	10

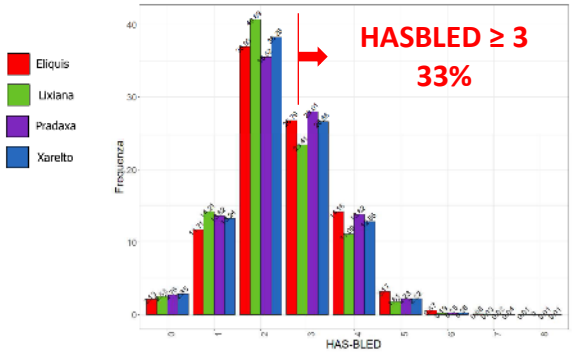
BLITZ AF (n=4126) Age 74±11 years

BLITZ AF (n=4126) CHADSVASC ≥2 83%

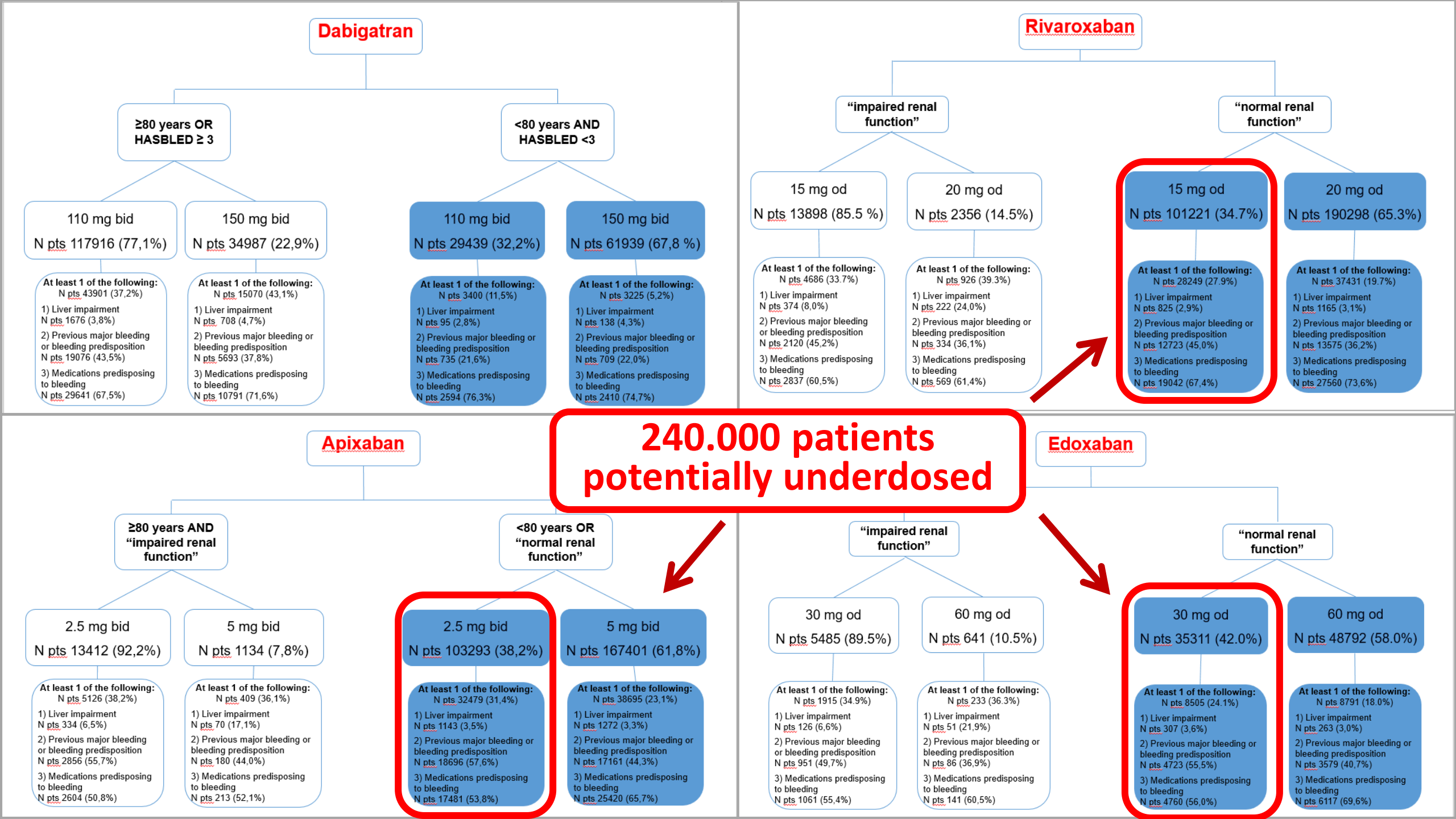
Distribuzione punteggio CHA2DS2VASc



Distribuzione punteggio HAS-BLED



BLITZ AF (n=4126) HASBLED ≥3 13%


Dabigatran
≥80 years OR HASBLED ≥ 3
<80 years AND HASBLED <3
110 mg bid
N pts 117916 (77,1%)
150 mg bid
N pts 34987 (22,9%)
110 mg bid
N pts 29439 (32,2%)
150 mg bid
N pts 61939 (67,8 %)
At least 1 of the following:
N pts 43901 (37,2%)
1) Liver impairment
N pts 1676 (3,8%)
2) Previous major bleeding or bleeding predisposition
N pts 19076 (43,5%)
3) Medications predisposing to bleeding
N pts 29641 (67,5%)
At least 1 of the following:
N pts 15070 (43,1%)
1) Liver impairment
N pts 708 (4,7%)
2) Previous major bleeding or bleeding predisposition
N pts 5693 (37,8%)
3) Medications predisposing to bleeding
N pts 10791 (71,6%)
At least 1 of the following:
N pts 3400 (11,5%)
1) Liver impairment
N pts 95 (2,8%)
2) Previous major bleeding or bleeding predisposition
N pts 735 (21,6%)
3) Medications predisposing to bleeding
N pts 2594 (76,3%)
At least 1 of the following:
N pts 3225 (5,2%)
1) Liver impairment
N pts 138 (4,3%)
2) Previous major bleeding or bleeding predisposition
N pts 709 (22,0%)
3) Medications predisposing to bleeding
N pts 2410 (74,7%)
Rivaroxaban
"impaired renal function"
"normal renal function"
15 mg od
N pts 13898 (85.5 %)
20 mg od
N pts 2356 (14.5%)
15 mg od
N pts 101221 (34.7%)
20 mg od
N pts 190298 (65.3%)
At least 1 of the following:
N pts 4686 (33.7%)
1) Liver impairment
N pts 374 (8,0%)
2) Previous major bleeding or bleeding predisposition
N pts 2120 (45,2%)
3) Medications predisposing to bleeding
N pts 2837 (60,5%)
At least 1 of the following:
N pts 926 (39.3%)
1) Liver impairment
N pts 222 (24,0%)
2) Previous major bleeding or bleeding predisposition
N pts 334 (36,1%)
3) Medications predisposing to bleeding
N pts 569 (61,4%)
At least 1 of the following:
N pts 28249 (27.9%)
1) Liver impairment
N pts 825 (2,9%)
2) Previous major bleeding or bleeding predisposition
N pts 12723 (45,0%)
3) Medications predisposing to bleeding
N pts 19042 (67,4%)
At least 1 of the following:
N pts 37431 (19.7%)
1) Liver impairment
N pts 1165 (3,1%)
2) Previous major bleeding or bleeding predisposition
N pts 13575 (36,2%)
3) Medications predisposing to bleeding
N pts 27560 (73,6%)
240.000 patients potentially underdosed
Apixaban
≥80 years AND "impaired renal function"
<80 years OR "normal renal function"
2.5 mg bid
N pts 13412 (92,2%)
5 mg bid
N pts 1134 (7,8%)
2.5 mg bid
N pts 103293 (38,2%)
5 mg bid
N pts 167401 (61,8%)
At least 1 of the following:
N pts 5126 (38,2%)
1) Liver impairment
N pts 334 (6,5%)
2) Previous major bleeding or bleeding predisposition
N pts 2856 (55,7%)
3) Medications predisposing to bleeding
N pts 2604 (50,8%)
At least 1 of the following:
N pts 409 (36,1%)
1) Liver impairment
N pts 70 (17,1%)
2) Previous major bleeding or bleeding predisposition
N pts 180 (44,0%)
3) Medications predisposing to bleeding
N pts 213 (52,1%)
At least 1 of the following:
N pts 32479 (31,4%)
1) Liver impairment
N pts 1143 (3,5%)
2) Previous major bleeding or bleeding predisposition
N pts 18696 (57,6%)
3) Medications predisposing to bleeding
N pts 17481 (53,8%)
At least 1 of the following:
N pts 38695 (23,1%)
1) Liver impairment
N pts 1272 (3,3%)
2) Previous major bleeding or bleeding predisposition
N pts 17161 (44,3%)
3) Medications predisposing to bleeding
N pts 25420 (65,7%)
Edoxaban
"impaired renal function"
"normal renal function"
30 mg od
N pts 5485 (89.5%)
60 mg od
N pts 641 (10.5%)
30 mg od
N pts 35311 (42.0%)
60 mg od
N pts 48792 (58.0%)
At least 1 of the following:
N pts 1915 (34.9%)
1) Liver impairment
N pts 126 (6,6%)
2) Previous major bleeding or bleeding predisposition
N pts 951 (49,7%)
3) Medications predisposing to bleeding
N pts 1061 (55,4%)
At least 1 of the following:
N pts 233 (36.3%)
1) Liver impairment
N pts 51 (21,9%)
2) Previous major bleeding or bleeding predisposition
N pts 86 (36,9%)
3) Medications predisposing to bleeding
N pts 141 (60,5%)
At least 1 of the following:
N pts 8505 (24.1%)
1) Liver impairment
N pts 307 (3,6%)
2) Previous major bleeding or bleeding predisposition
N pts 4723 (55,5%)
3) Medications predisposing to bleeding
N pts 4760 (56,0%)
At least 1 of the following:
N pts 8791 (18.0%)
1) Liver impairment
N pts 263 (3,0%)
2) Previous major bleeding or bleeding predisposition
N pts 3579 (40,7%)
3) Medications predisposing to bleeding
N pts 6117 (69,6%)

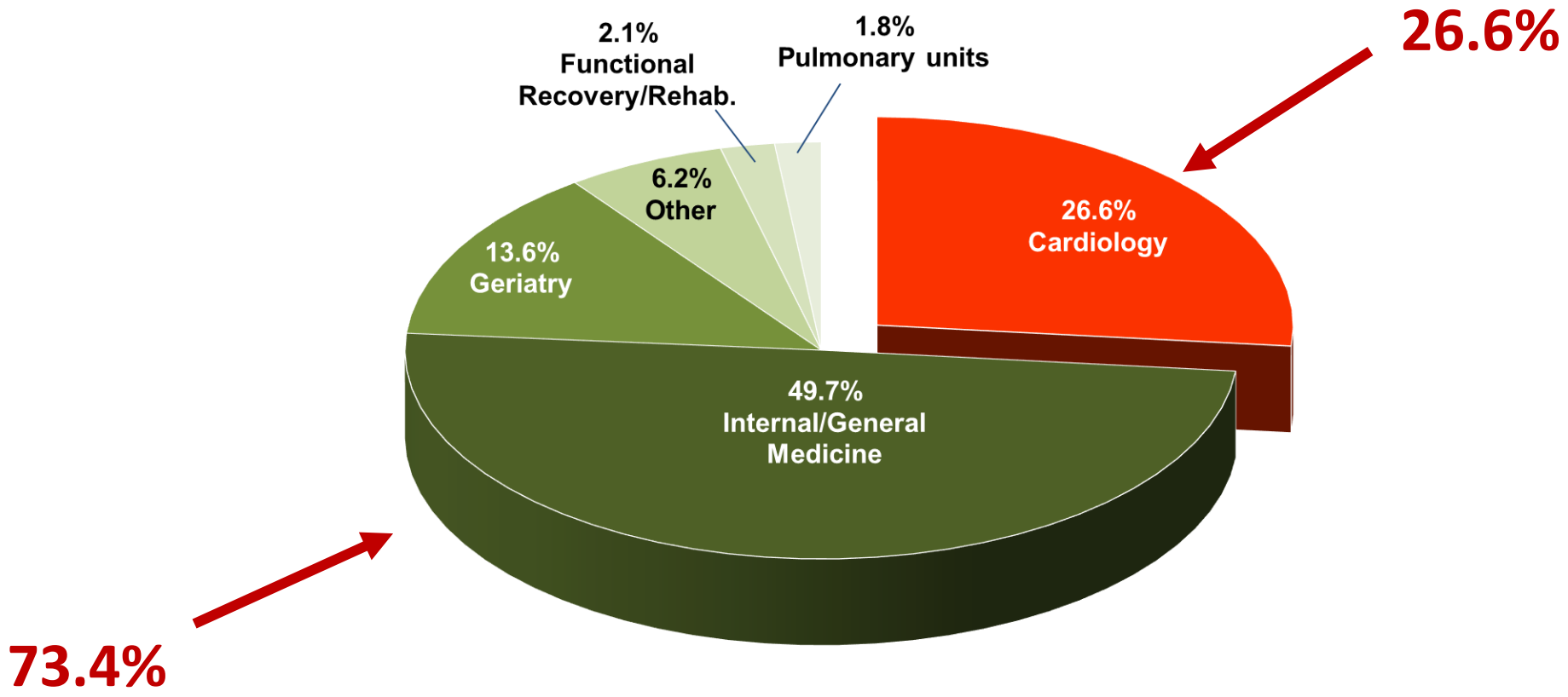
Agenda
(3 examples)

- Lipid profile, treatment and CV risk
- Atrial fibrillation and NOAC treatment
- Heart failure patients, multimorbidity, treatment and outcome

The real-world evidence of heart failure: findings from 41 413 patients of the ARNO database

Aldo P. Maggioni[1,*], Francesco Orso[1,2], Silvia Calabria[3], Elisa Rossi[4], Elisa Cinconze[4], Samuele Baldasseroni[5], and Nello Martini[6], on behalf of the ARNO Observatory[†]

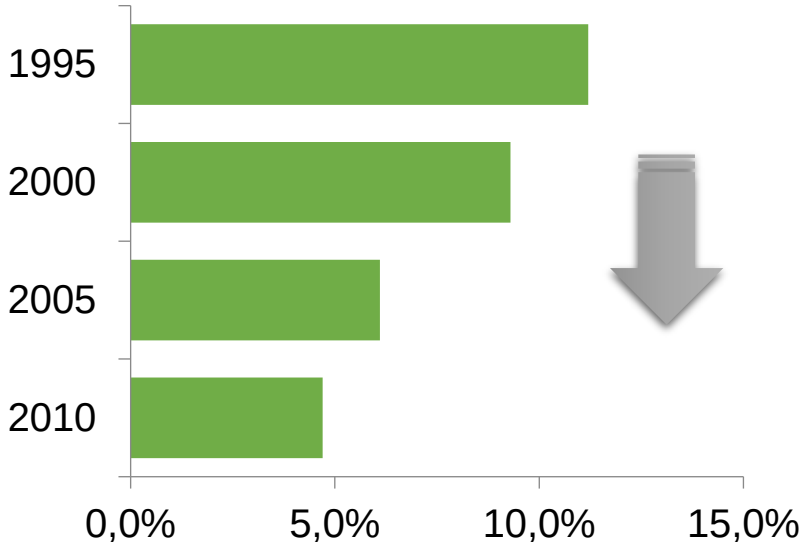
Where are the patients with AHF admitted?



Results on patients' outcomes
ANMCO Trial – Registries and RWE

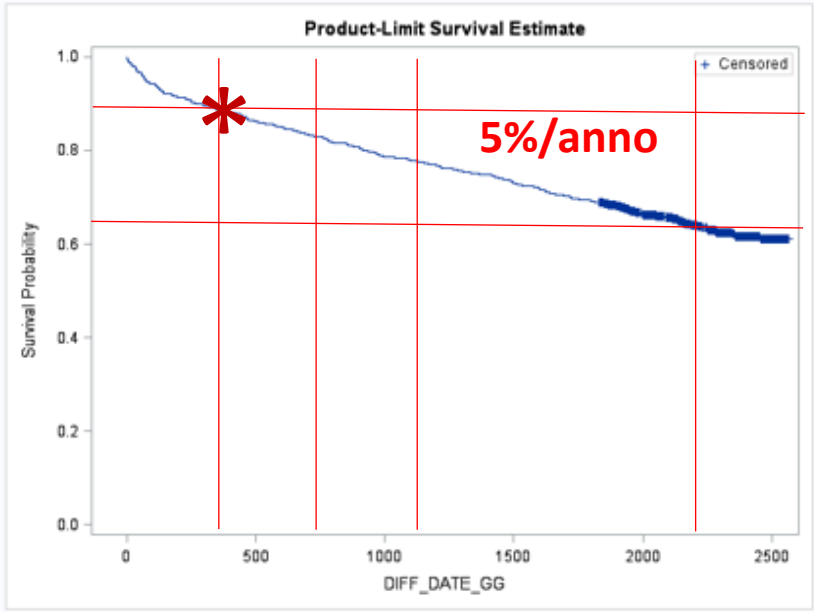
IN-HF Cardiology Registry

Chronic HF – 1y mortality

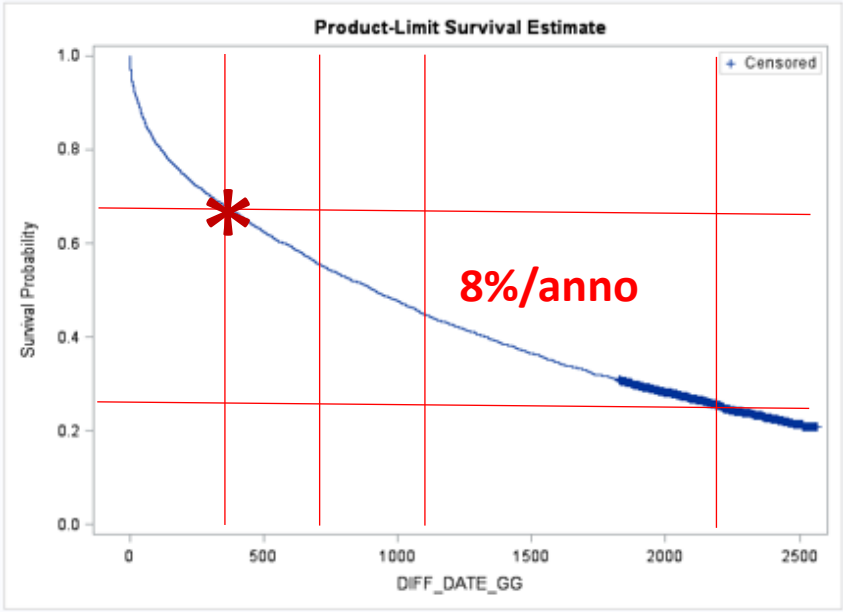


5963 new HF patients; cohort 2009-2010; FVG region

HF patients <70 yo



HF patients ≥70 yo



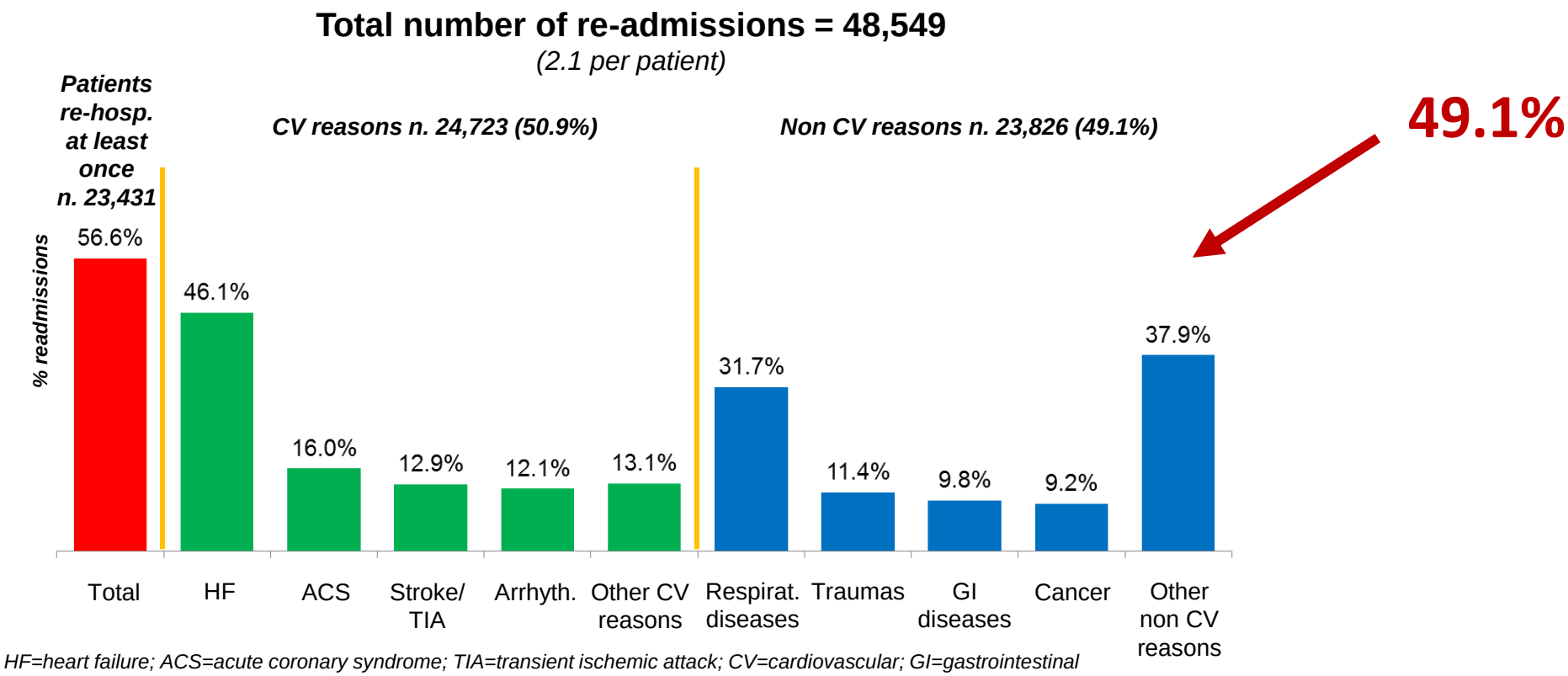
1y mortality <5%!

1y mortality ≈10%!

1y mortality >30%!

The real-world evidence of heart failure: findings from 41 413 patients of the ARNO database

Aldo P. Maggioni[1,*], Francesco Orso[1,2], Silvia Calabria[3], Elisa Rossi[4], Elisa Cinconze[4], Samuele Baldasseroni[5], and Nello Martini[6], on behalf of the ARNO Observatory[†]



HF=heart failure; ACS=acute coronary syndrome; TIA=transient ischemic attack; CV=cardiovascular; GI=gastrointestinal

European Journal of Heart Failure (2018)
doi:10.1002/ejhf.1202

RESEARCH ARTICLE

Prevalence and prognostic impact of non-cardiac co-morbidities in heart failure outpatients with preserved and reduced ejection fraction: a community-based study

Annamaria Iorio[1,2], Michele Senni[1]*, Giulia Barbati[2], Stephen J. Greene[3], Stefano Poli[2], Elena Zambon[2], Concetta Di Nora[2], Giovanni Cioffi[4], Luigi Tarantini[5], Antonello Gavazzi[6], Gianfranco Sinagra[2], and Andrea Di Lenarda[7]

Mean age 77 yo

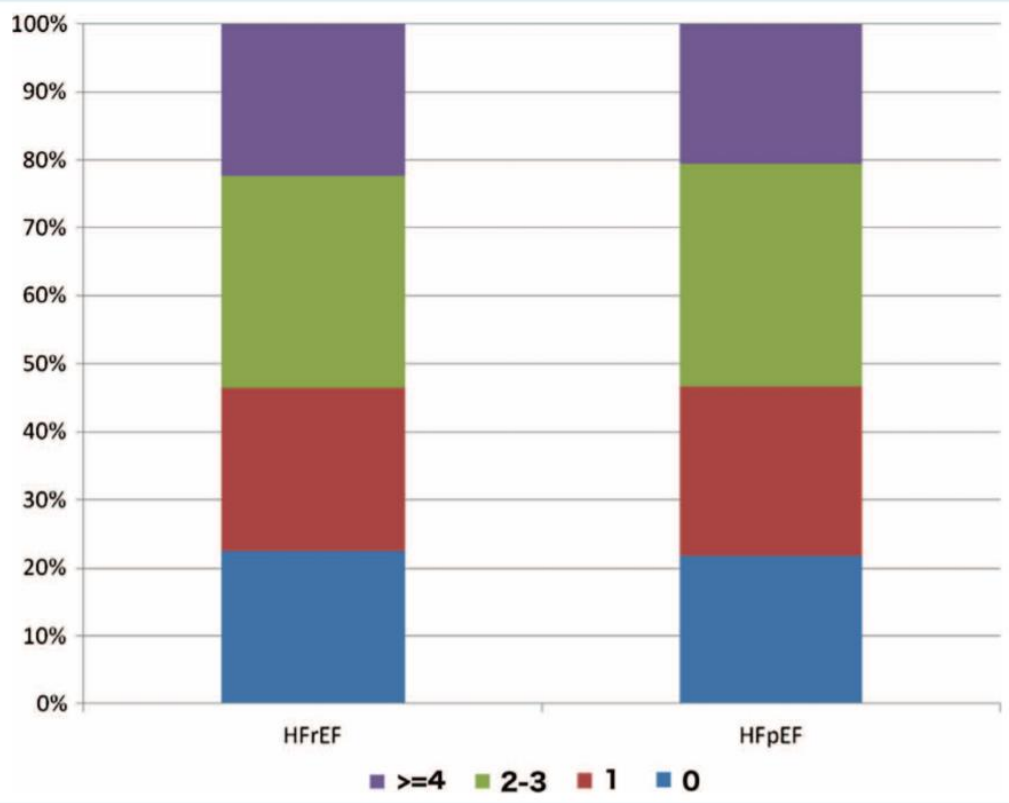


Figure 2 Co-morbidity load (0, 1, 2, 3, ≥4 co-morbidities) according to left ventricular ejection fraction groups. HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction.

European Journal of Heart Failure (2018)
doi:10.1002/ejhf.1202

RESEARCH ARTICLE

Prevalence and prognostic impact of non-cardiac co-morbidities in heart failure outpatients with preserved and reduced ejection fraction: a community-based study

Annamaria Iorio[1,2], Michele Senni[1]*, Giulia Barbati[2], Stephen J. Greene[3], Stefano Poli[2], Elena Zambon[2], Concetta Di Nora[2], Giovanni Cioffi[4], Luigi Tarantini[5], Antonello Gavazzi[6], Gianfranco Sinagra[2], and Andrea Di Lenarda[7]

Mean age 77 yo

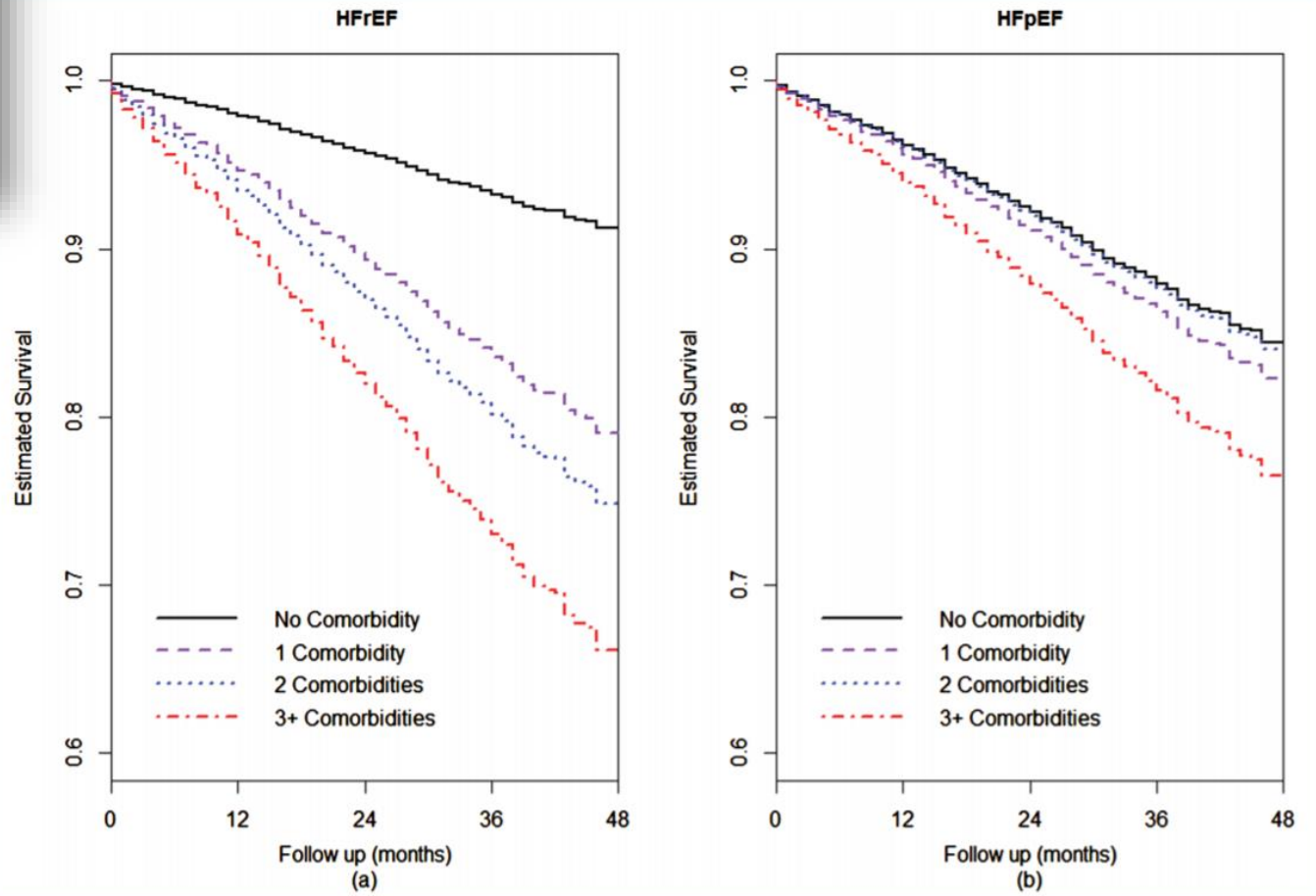


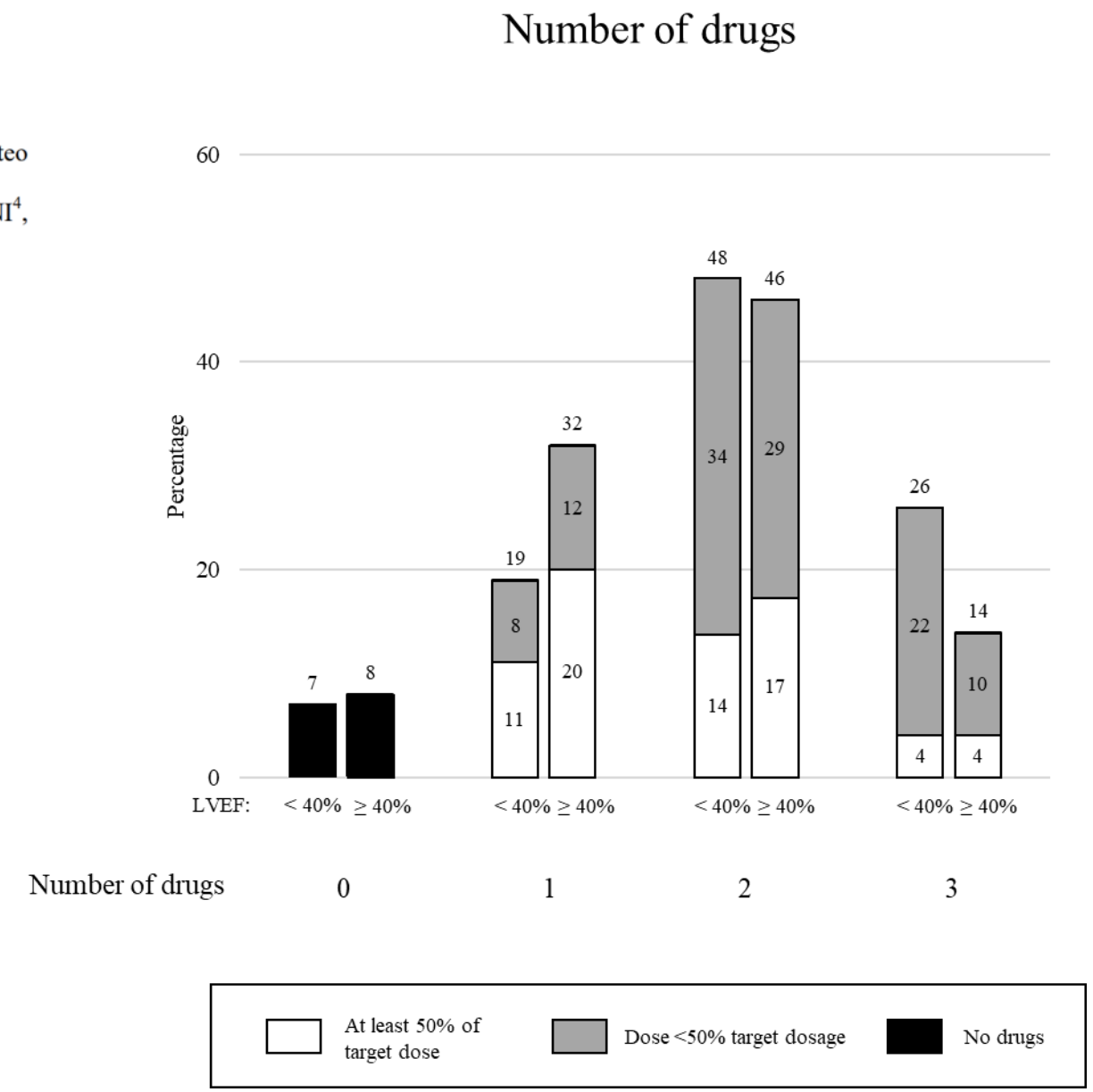
Figure 3 Estimated survival curves from the Cox model according to co-morbidity load (0, 1, 2, ≥3 co-morbidities) in patients with heart failure with reduced (HFrEF, *A*) and preserved ejection fraction (HFpEF, *B*).

Patients' adherence to disease modifying treatment in a community based-sample of patients with chronic heart failure

*Federico REA[1,2], *Annamaria IORIO[3,4], Giulia BARBATI[5,1], Riccardo BESSI[3], Matteo CASTRICHINI[3], Vincenzo NUZZI[3], Arjuna SCAGNETTO[5], Elena PERUZZI[6], Michele SENNI[4], Giovanni CORRAO [1,2], Gianfranco SINAGRA[3], Andrea DI LENARDA[3]

Eur Heart J 2020, submitted

In a prospective, observational community registry, 2528 outpatients with HF (median age 76, 58% men) were examined.
Of those, 609 had a LVEF < 40%.



…machine learning approaches are, essentially, black boxes,
in which you can't really inspect
"how the algorithm is accomplishing what it is accomplishing"

- Non linearities (Simple scores vs more complex models)
- Interactions/association
- Number of events/variables