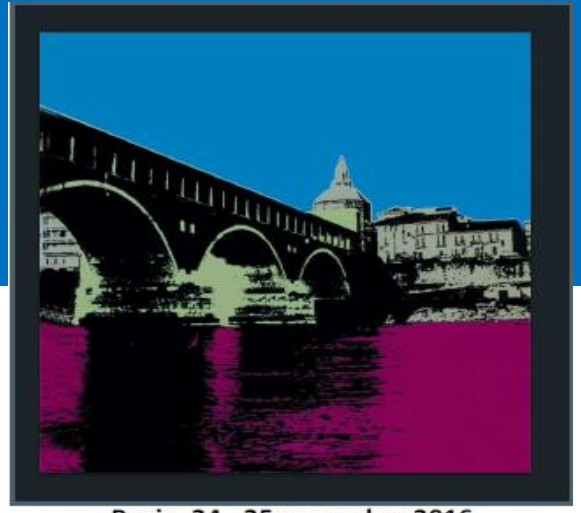

Pavia, 24 - 25 novembre 2016
Collegio Fratelli Cairoli
Piazza Cairoli 1

Banche dati sanitarie e ricerca sui percorsi assistenziali (Real World Evidence): il punto di vista della ricerca clinica

Aldo Pietro Maggioni

Centro Studi ANMCO

Firenze

Disclosures

- Director of the **ANMCO Research Center** that receives **public grants** of research from Oxford University, NIH, Canadian Government, PHRI, SID and **company grants** of research from Bayer, Sanofi-Aventis, Amgen, AstraZeneca, Menarini, Boehringer Ingelheim, DalCor.
- Scientific Coordinator of **ESC EurObservational Research** supported by unrestricted grants from Abbott Vascular, Bayer AG, Bristol Myers Squibb, Pfizer, Boehringer Ingelheim , Daiichi Sankyo, Menarini, Novartis, Sanofi-Aventis, Servier, Amgen, Boston Scientific, MSD.
- **Scientific Coordinator of CORE, supported for this analysis by Novartis, Sanofi-Aventis and AMGEN**
- **Member of Trial Committees** (SC, EC, CEC, DSMB) sponsored by Novartis, Cardiorentis, AstraZeneca, Bayer, Pfizer, Sanofi-Aventis

Twenty years ago….

"If you find that a study was not randomized, we'd suggest that you stop reading it and go on to the next article".

David Sackett. BMJ 1996;312:71

The beginning of cooperative observational clinical research in HF in Italy

Snap-shots (1995-1996)	**SEOSI:** 3,921 in-outpatients **with HF** enrolled in 12 days **EARISA:** 6,030 in-patients **with heart disease** (1090 with HF) enrolled in 12 days
LongTerm Registry: (1995 → ...)	**IN-HF:** ~25,000 in-out-patients with HF
Outcome studies: (1998-2001)	**OSCUR, TEMISTOCLE:** performed in both **cardiology and internal medicine** wards (3000 pts) **BRING-UP 1 and 2:** to induce an appropriate use of beta-blockers in chronic HF (4690 pts)

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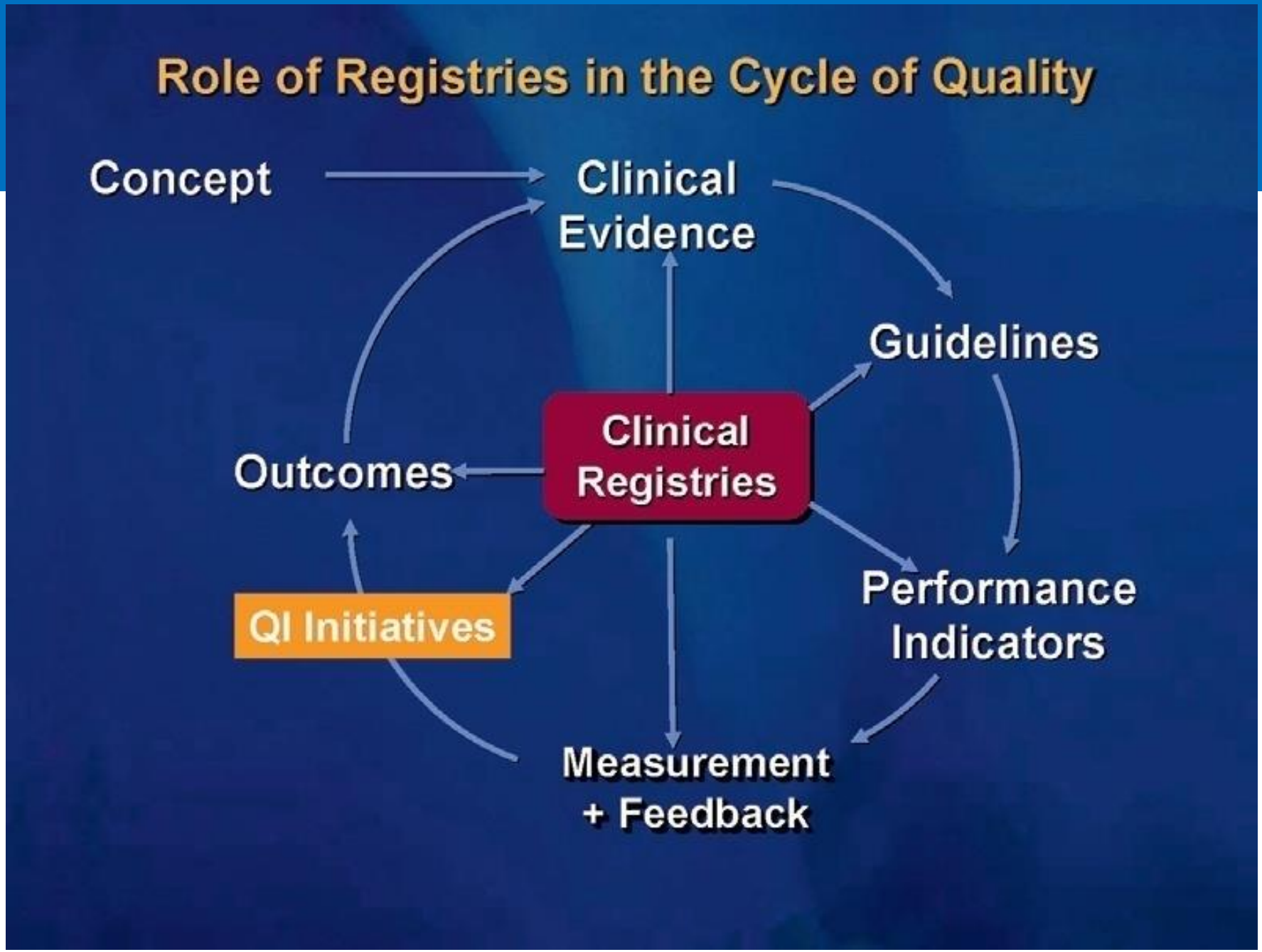
http://dx.doi.org/10.1016/j.jacc.2015.07.010

PERFORMANCE MEASURES

ACC/AHA/STS Statement on the Future of Registries and the Performance Measurement Enterprise

A Report of the American College of Cardiology/American Heart Association Task Force on Performance Measures and The Society of Thoracic Surgeons

Bhatt DL, et al. JACC 2015; 66: 2230-2245



Bhatt DL et al. (ACC, AHA, STS) JACC 2015; 66: 2230

Deep current changes across the world

- ✓ **Globalisation** (associated with potentially immediate penetration of new knowledge across the world, diffuse benchmarking and competition)
- ✓ Spreading of **Information Technology** (individually and by networks)
- ✓ Progressive (still incomplete) understanding that an erratic **Health Governance** does not meet the subjects' needs and is no longer acceptable
- ✓ In essence, **need to know and interpreting the real world**, thereby need for observational research and big data

Perchè abbiamo bisogno (anche) di studi di Real World Evidence

- Le differenze nei diversi scenari di ricerca sono molto rilevanti:
  - Il trial clinico randomizzato (TRAP 2-TIMI 50)
  - Il registro degli specialisti (MANTRA)
  - I flussi amministrativi (ARNO)

Caratteristiche di base in pazienti con Sindrome Coronarica Acuta

	ARNO 2008 (n. 7082)	MANTRA 2009 (n. 6394)	TRAP 2 2012 (n. 26449)
Età >70 anni, %	61	42	18
Donne, %	36	30	24
Ipertensione trattata, %	77	58	68
Diabete, %	25	27	25
BPCO, %	9	9	NA
Depressione, %	14	-	NA

SCA:terapie prescritte per la prevenzione secondaria

	ARNO 2008 (n. 6592)	MANTRA 2009 (n. 6185)	TRAP 2 2012 (n. 26449)
Antiaggreganti %	79.0	97.9	98.2
Ace-Inibitori %	56.7	63.4	74.2
Statine %	55.4	89.8	91.0
Betabloccanti %	45.0	77.0	80.0
Omega 3 %	11.7	25.7	NA

Forze e debolezze

Registri specialistici/RCT	Registri amministrativi
Migliore definizione diagnostica	Diagnosi basate su diagnosi di dimissione o su pattern prescrittivi
Ricchezza di variabili cliniche	Povertà di variabili cliniche
Presenza di dati strumentali che consentono di valutare end-point fisiologici	Assenza di informazioni su misure ricavate da dati di laboratorio e/o strumentali
Follow-up spesso incompleti	*Completezza di informazioni su prescrizioni, ospedalizzazioni nel follow-up*
Punto di vista limitato agli specialisti coinvolti=scarsa rappresentatività	*Universalità delle popolazioni oggetto di valutazione*
Outcome in genere più favorevoli	Outcome più sfavorevoli data la eterogeneità delle popolazioni incluse

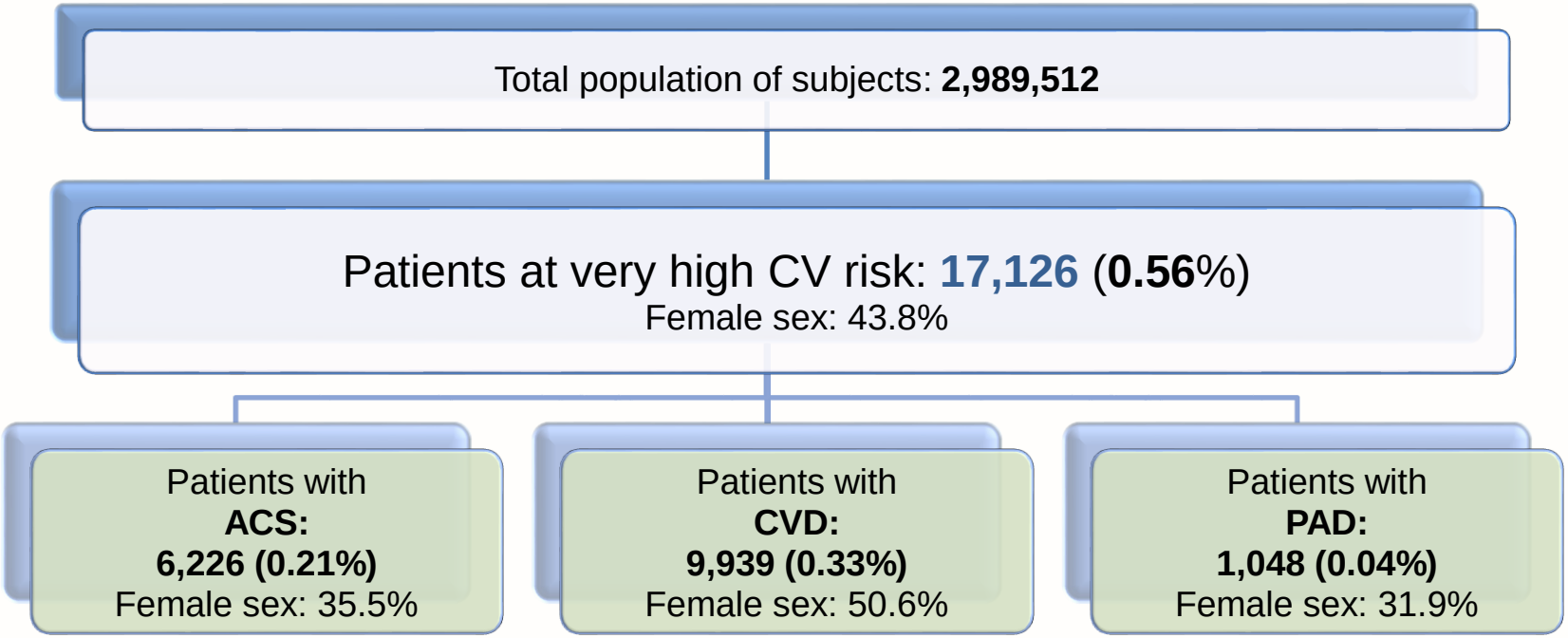
Perchè abbiamo bisogno (anche) di studi di Real World Evidence

- Le differenze nei diversi scenari di ricerca sono molto rilevanti:
  - Il trial clinico randomizzato (TRAP 2-TIMI 50)
  - Il registro degli specialisti (MANTRA)
  - I flussi amministrativi (ARNO)

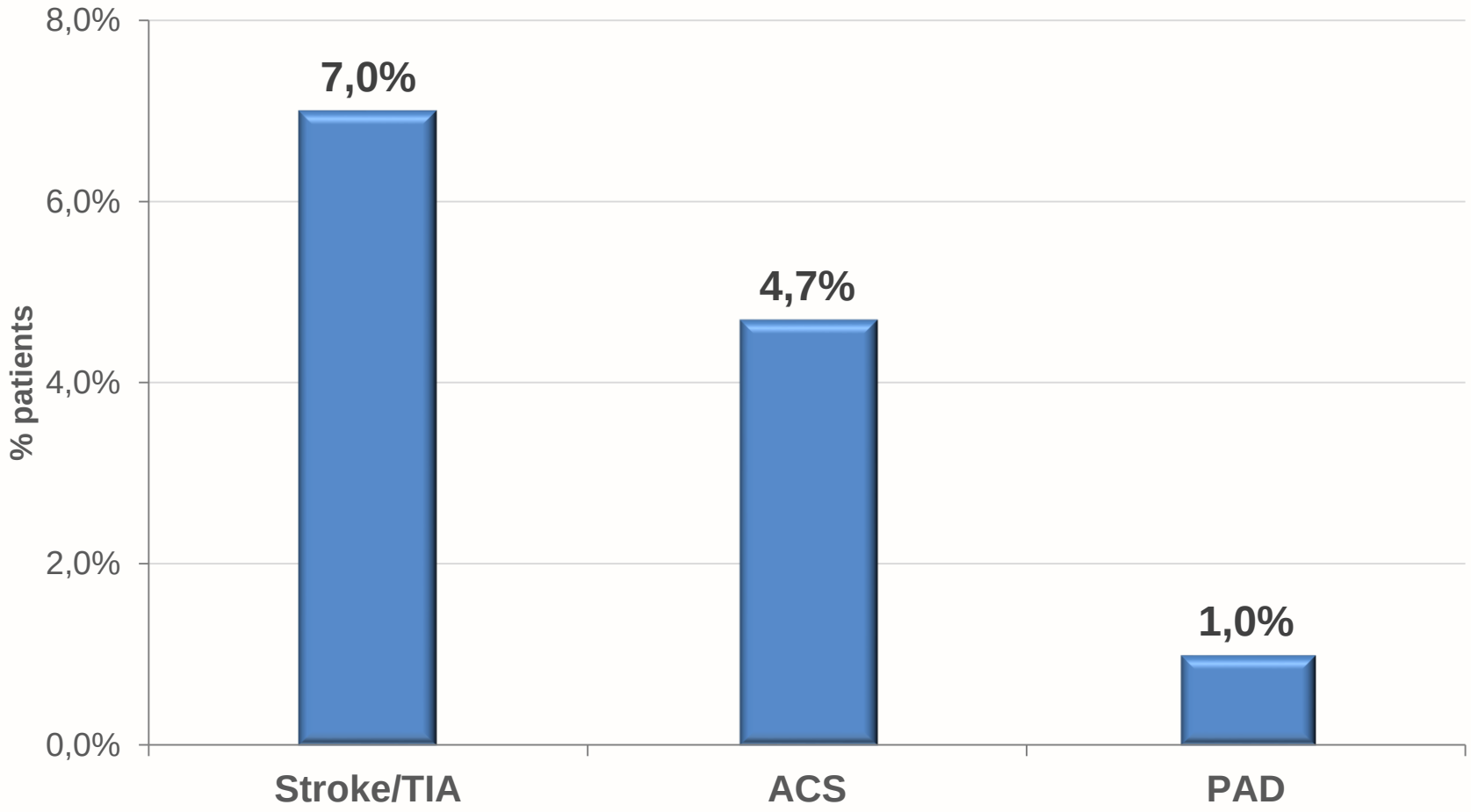
- Un paio di esempi clinici:
  - le sindromi coronariche acute
  - lo scompenso cardiaco

Therapeutic strategies and health costs of patients admitted for an atherothrombotic cardiovascular event in a community setting of nearly 3,000,000 subjects

Patient population (Year 2011)



In-hospital all-cause mortality

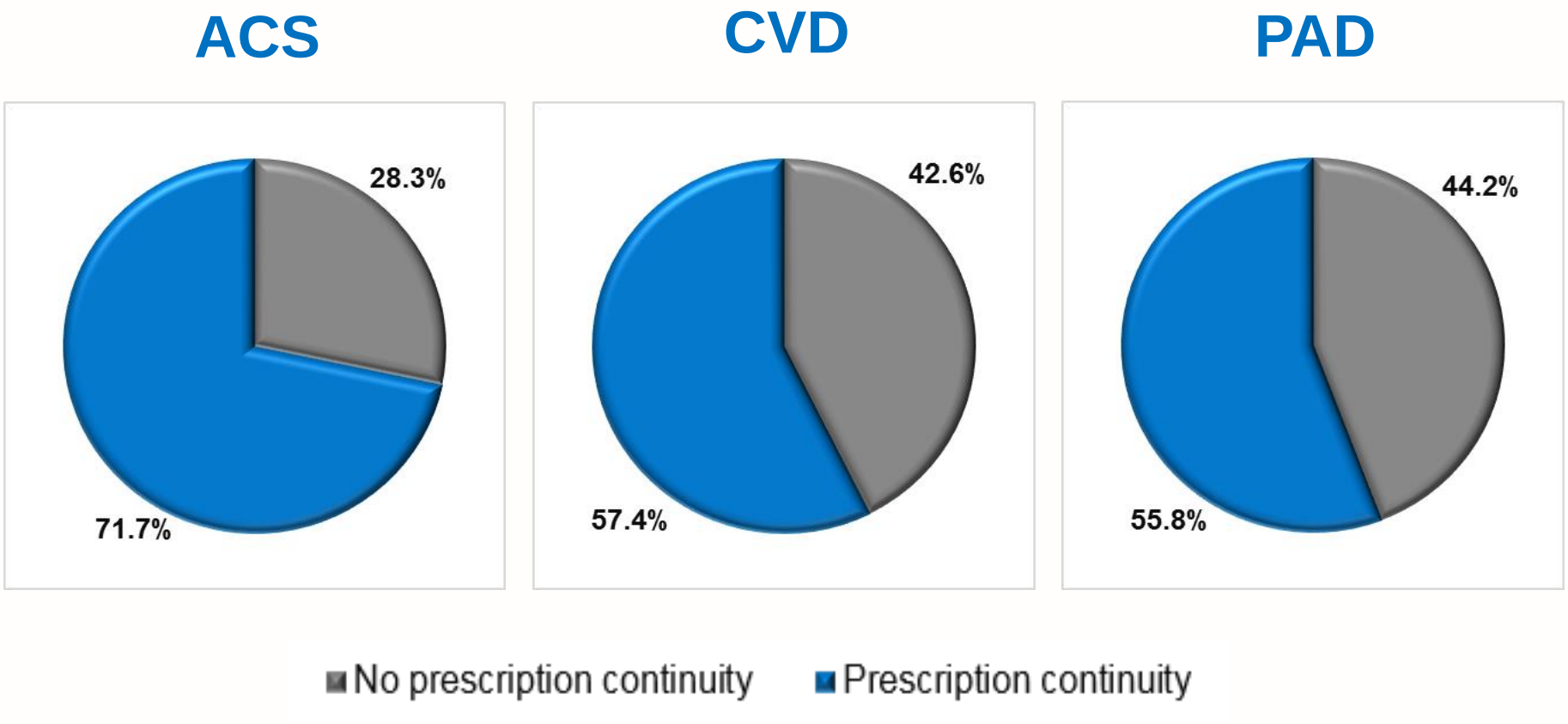


Lipid lowering therapy in patients discharged alive

In the first month after discharge	ACS	CVD	PAD
	n. 5,937	n. 9,251	n. 1,038
Statin (alone or in association with exetimibe)	4.148 (69.9%)	2.684 (29.0%)	388 (37.4%)

In the 1 year after discharge	ACS	CVD	PAD
	n. 5,937	n. 9,251	n. 1,038
Statin (alone or in association with exetimibe)	4.933 (83.1%)	4.119 (44.5%)	663 (63.9%)

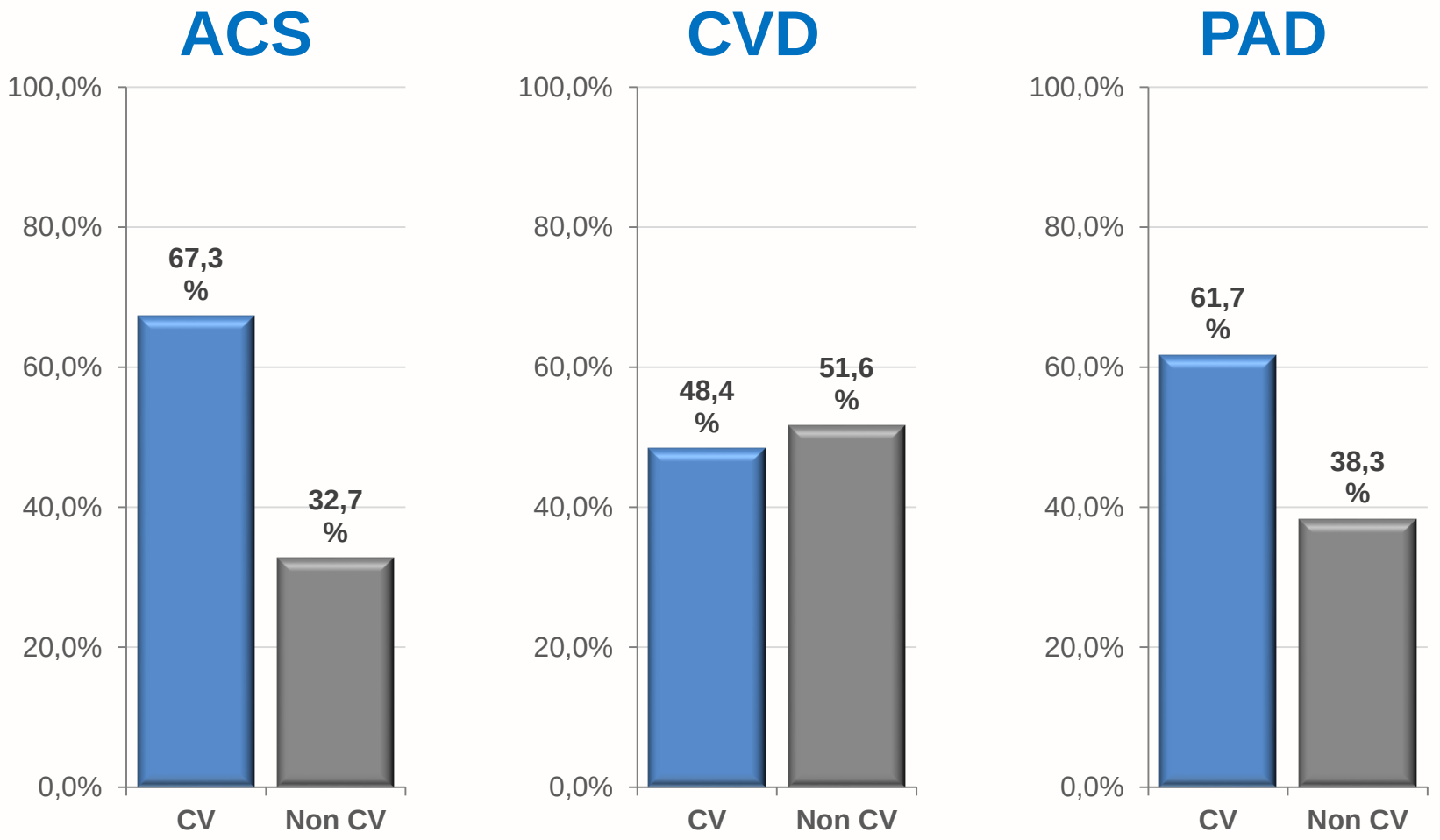
1-year Prescription Continuity of Statins



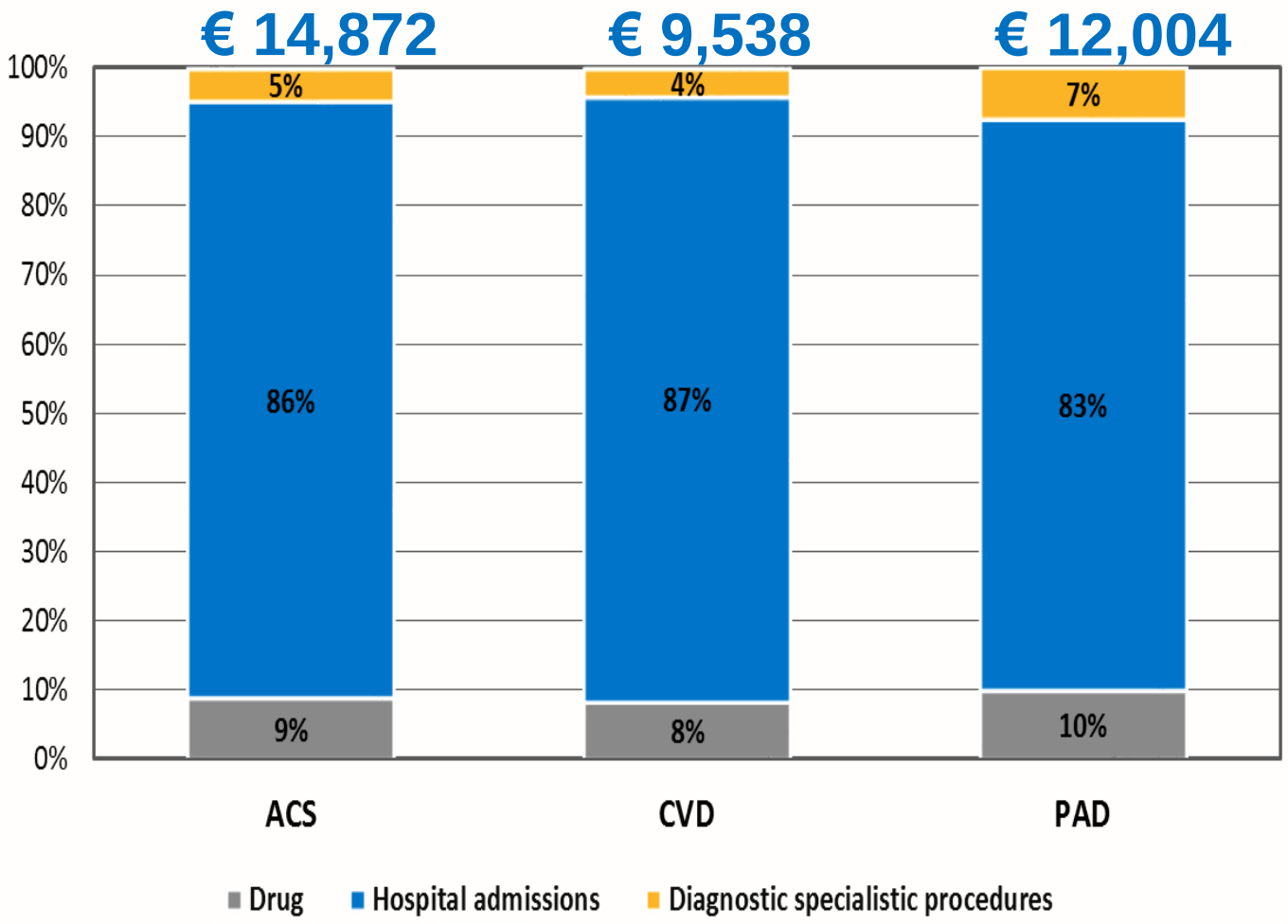
1-year Re-hospitalizations

	ACS (n. 5,937)	CVD (n. 9,251)	PAD (n. 1,038)
Pts with at least 1 readmission, %	**63.3**	**49.1**	**57.6**
Total readmissions, n.	8,201	8,564	1,298
N. of readmission per patient	2.18	1.89	2.17
CV readmission, n. (%)	**5,524 (67.3)**	**4,145 (48.4)**	**801 (61.7)**
ACS, % PCI/CABG, % HF, % CVD, % PAD, % Other, %	30.9 8.7 11.5 3.6 0.03 45.3	4.2 0.9 8.9 45.1 - 40.9	6.1 1.1 7.4 5.9 0.1 79.4
Non CV readmission, n. (%)	**2,677 (32.7)**	**4,419 (51.6)**	**497 (38.3)**

1-year rehospitalizations



1-year overall costs for the NHS



European Journal of Heart Failure (2016)
doi:10.1002/ejhf.471

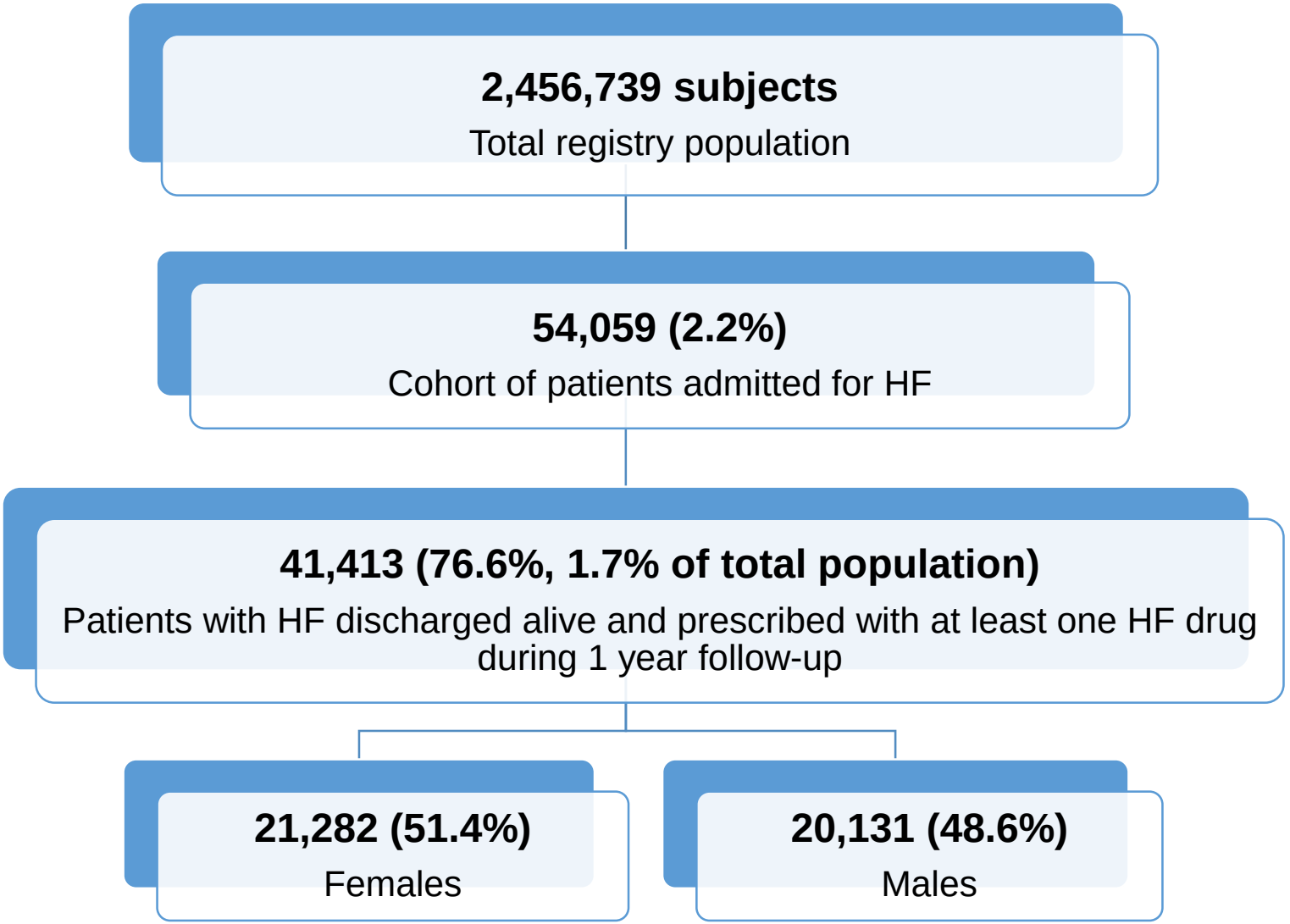
The real-world evidence of heart failure: findings from 41 413 patients of the ARNO database

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[†]

[1]ANMCO Research Center, Florence, Italy; [2]Azienda Ospedaliero-Universitaria Careggi, Department of Geriatrics, Section of Geriatric Medicine and Cardiology, Florence, Italy; [3]CORE, Collaborative Outcome Research, Bologna, Italy; [4]CINECA Interuniversity Consortium, Casalecchio di Reno, Bologna, Italy; [5]Azienda Ospedaliero-Universitaria Careggi, Department of Heart and Vessel, Section Internal Medicine and Cardiology, Florence, Italy; and [6]Accademia Nazionale di Medicina, Rome, Italy

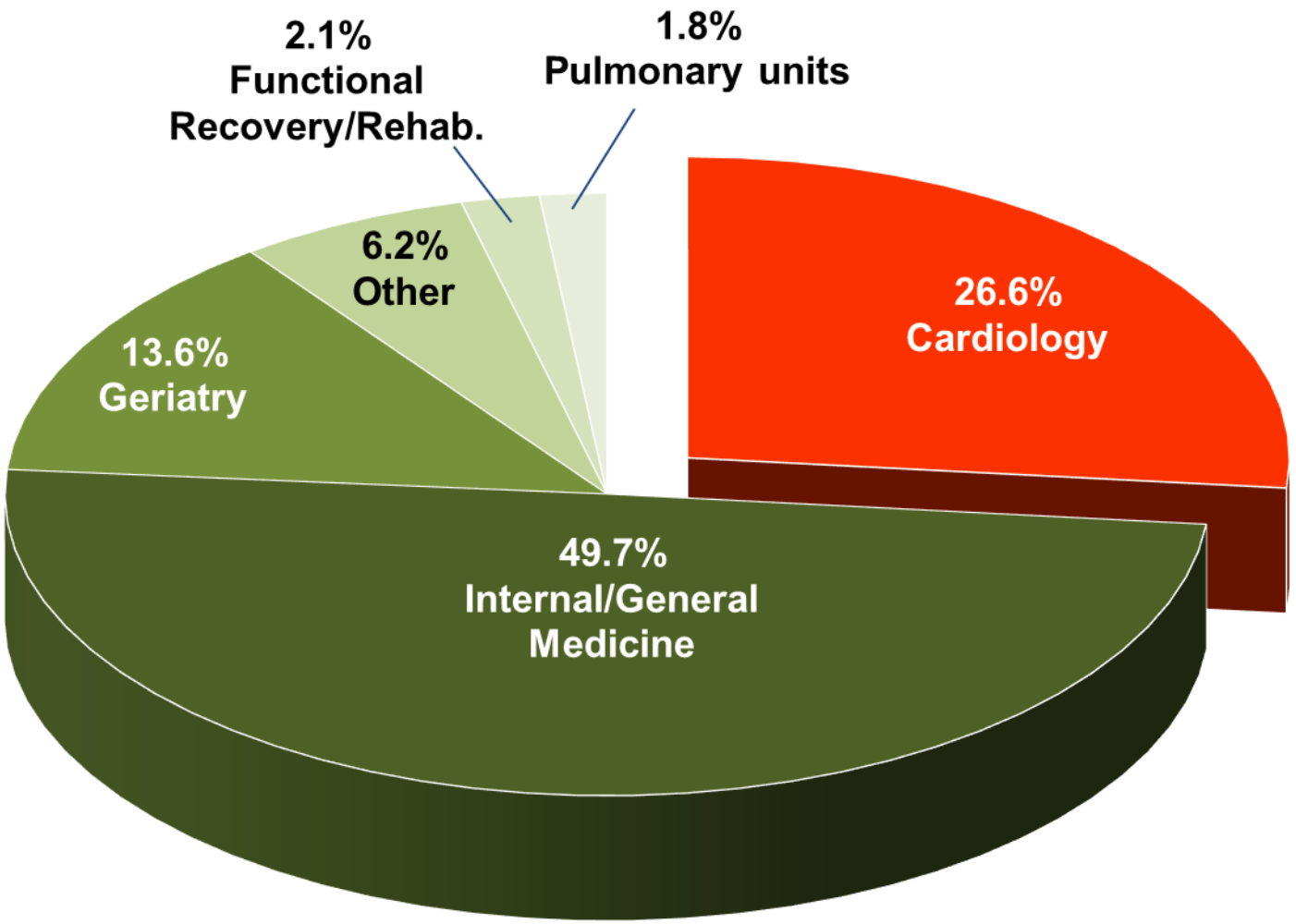
Received 17 July 2015; revised 24 November 2015; accepted 27 November 2015

Patients' disposition



HF=heart failure

Where are the patients with AHF admitted?



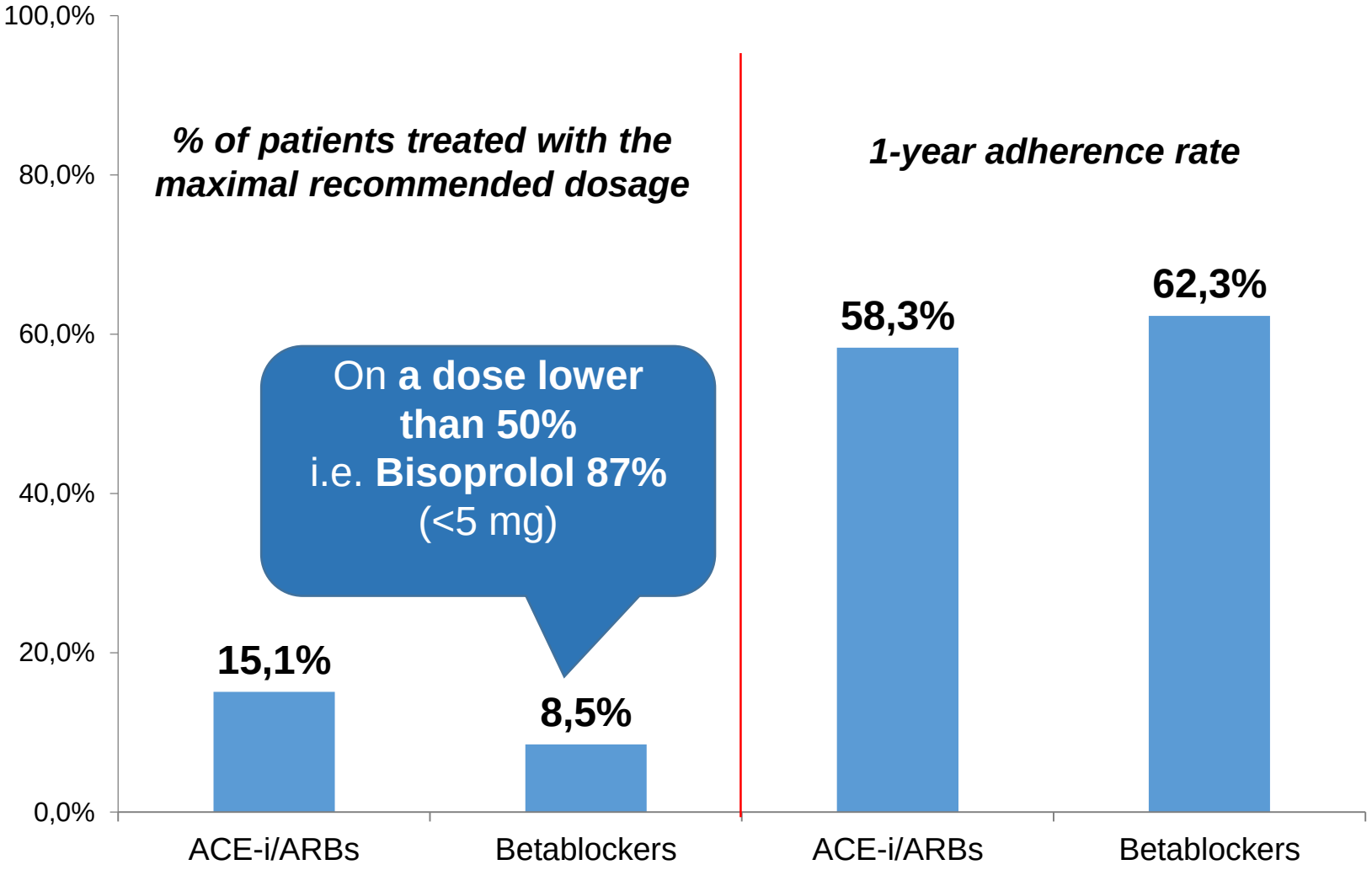
Baseline characteristics

	ARNO 2008-2012 (n. 41,413)	RELAX-AHF 2013 (n. 1,161)	ESC-HF LT 2015 (n. 12,440)
Mean age (yrs)	78	72	71
Female (%)	51	38	37
Co-morbidities			
COPD (%)	30.5	15.5	20.2
CKD (%)	4.3	NR	26.4
Depression (%)	21.0	NR	7.9

Pharmacological Treatments

	ARNO 2008-2012 (n. 41,413)	RELAX-AHF 2013 (n. 1,116)	ESC-HF LT 2015 (n. 12,440)
Treatments			
ACE-I/ARBs (%)	65.8	72.0	77.0
Betablockers (%)	52.3	68.5	71.8
MRAs (%)	42.1	31.5	55.3
Diuretics (%)	84.2	99.9	83.6
Digitalis (%)	26.8	20.0	26.4
Ivabradine (%)	1.5	NR	3.2

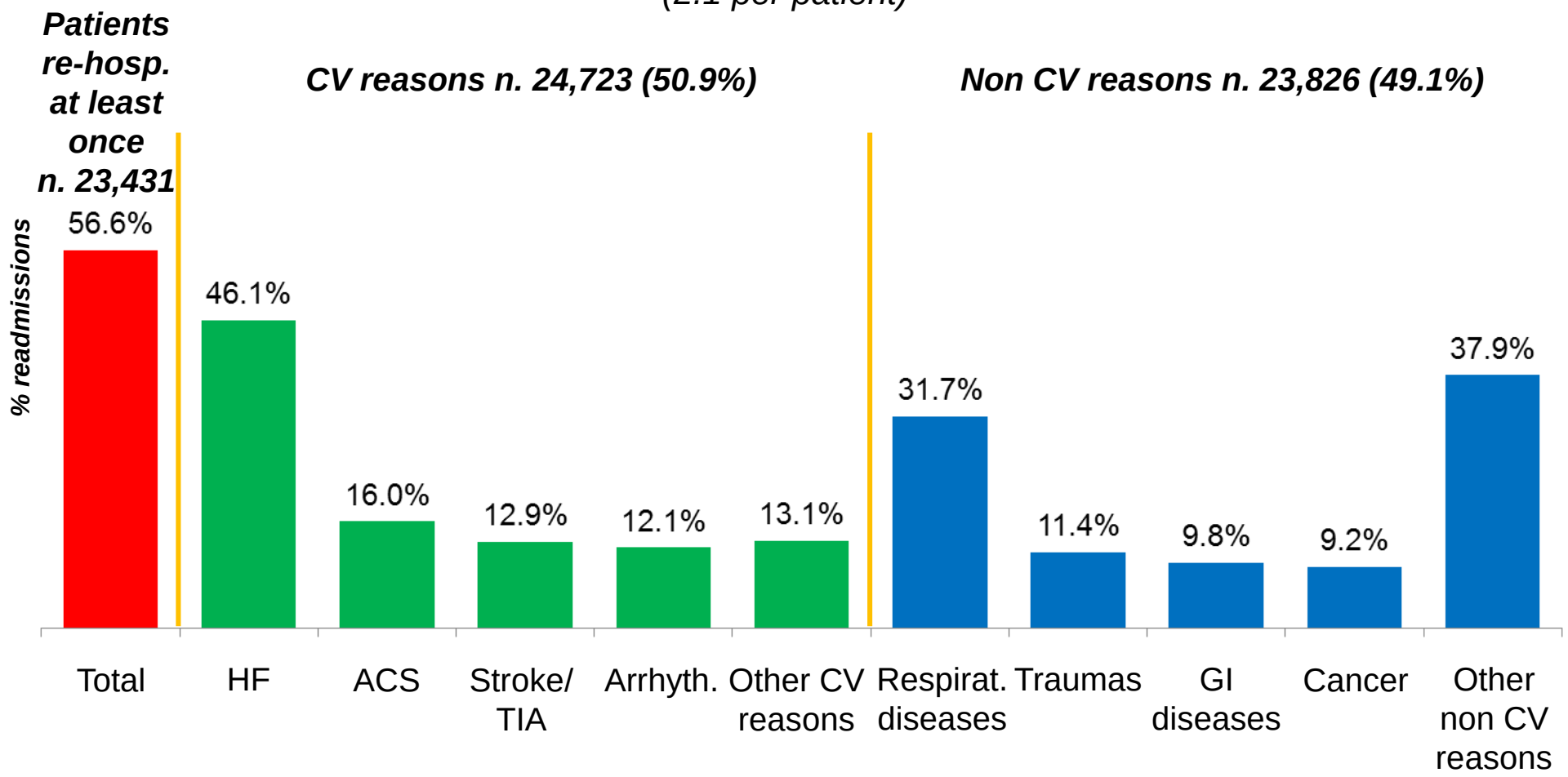
Dosages and 1-year adherence to 1A recommended treatments



Rate and causes of hospital re-admissions

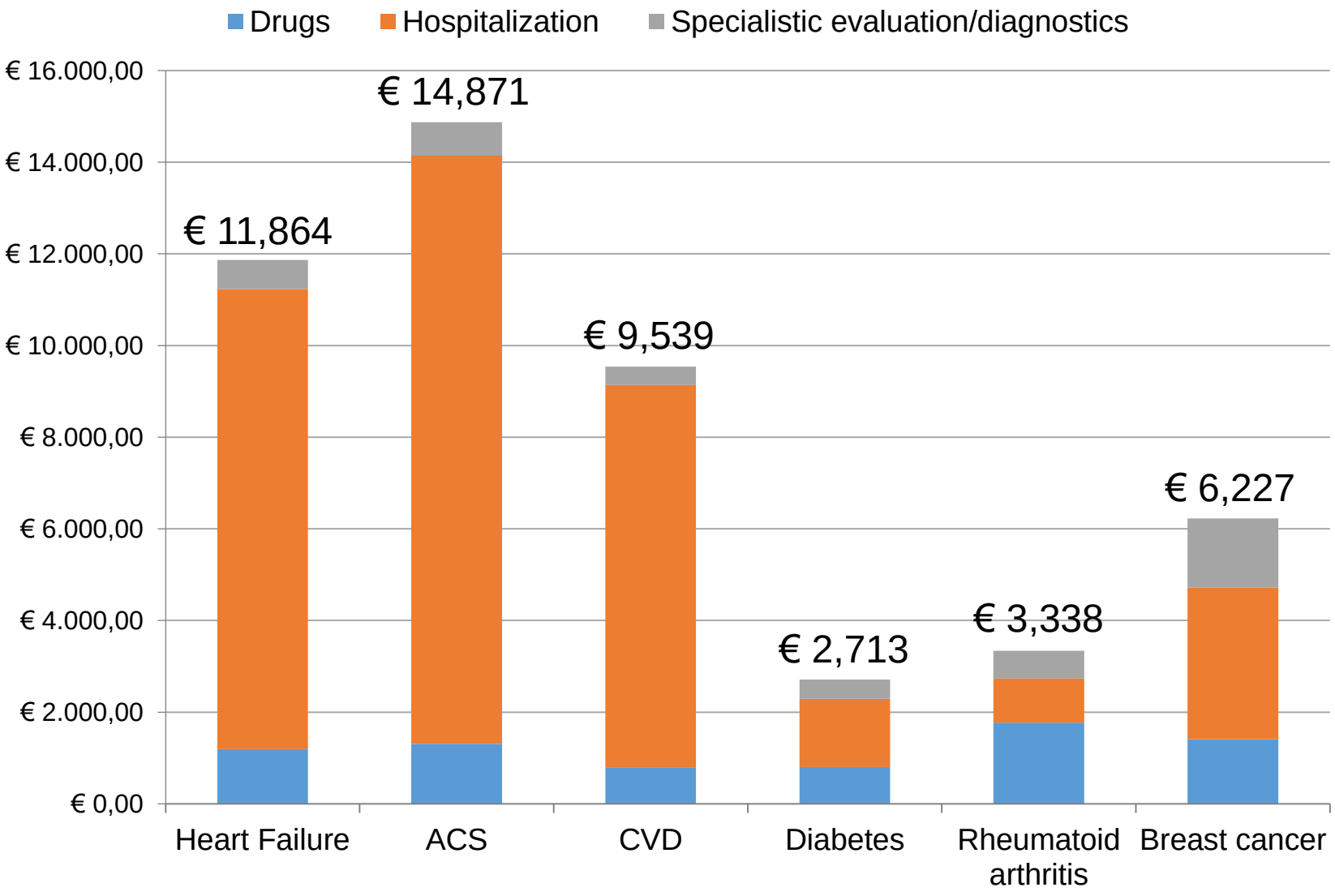
Total number of re-admissions = 48,549

(2.1 per patient)



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

Costs per patient per year



Perchè abbiamo bisogno di *Real World Evidence*

- ✓ Per valutare l'applicabilità e la applicazione della *Evidence Based Medicine*
- ✓ Per identificare le aree nelle quali i trattamenti della pratica clinica sono sub-ottimali
- ✓ Per identificare le aree nelle quali è necessario pianificare progetti formativi
- ✓ Per avere riferimenti affidabili circa il carico economico determinato dalle diverse componenti assistenziali
- ✓ Per generare ipotesi di ricerca

EHR system in the USA

- So far, >$40 billion have been allocated to a federal initiative of **mandatory**, **universal implementation** of an Information Technology network across the public Health system (Medicare, Medicaid [*447,832 hospitals]*, Veterans, Pentagon), covering > 100 million people: ***the Electronic Health Recording (EHR) system.***
- The federal process of implementation is strictly and **continuously monitored**. Should be completed by 2017.
- *>$500 million in* ***penalties*** expected on 2018-2020.

The key factor for EHR success

- **Cooperation and integration of Health Systems with Research Institutions**

- In USA besides **>$40 billion** allocated to implement the **EHR** system, a parallel integrated investment of **>$30 billion** to the **NIH** to support innovative basic and clinical research and using the EHR system for research.

Use of EHR. Is the Research 2.0 ?

- ✓ Big data will probably transform medicine
- ✓ However, these data by themselves can be useless
- ✓ Collaboration between data scientists and clinical scientists is necessary
- ✓ To be useful, data must be analyzed, interpreted, reproduced and, finally, applied