



UNITÀ DI BIOSTATISTICA

Dipartimento Universitario Clinico di
Scienze Mediche Chirurgiche e della Salute

Healthcare Research and Pharmacoepidemiology

Epidemiologia transnazionale: Sistemi Integrati per le Cure Integrate

2 Dicembre 2017, Torrette di Ancona

Healthcare Research

& Pharmacoepidemiology

Experiences in monitoring of paths and evaluation of outcomes in the cardiovascular field

HRP working group* in cardiovascular diseases

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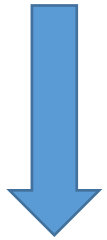
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Outline

Background & Motivations

Linking Clinical & Administrative Data for Epidemiology

*Heart Failure (HF) & «PDTA» (**P**ercorso **D**iagnostico-**T**erapeutico-**A**ssistenziale)*



Applications & Work in Progress

Prevalence and prognostic impact of noncardiac comorbidities in Heart Failure

Multi state modelling of Heart Failure care path

PDTA-HF: a multi-regional project of the Health Ministry

Chronic Heart Failure: a silently progressing disease



Perspectives



Administrative databases for epidemiological evaluation of health-care systems = widespread diffusion, low cost.

Epidemiologists today agree on validity of disease/intervention registries based on administrative databases.

Data collected for administrative purposes at time of service: registration, transactions, record-keeping, etc.

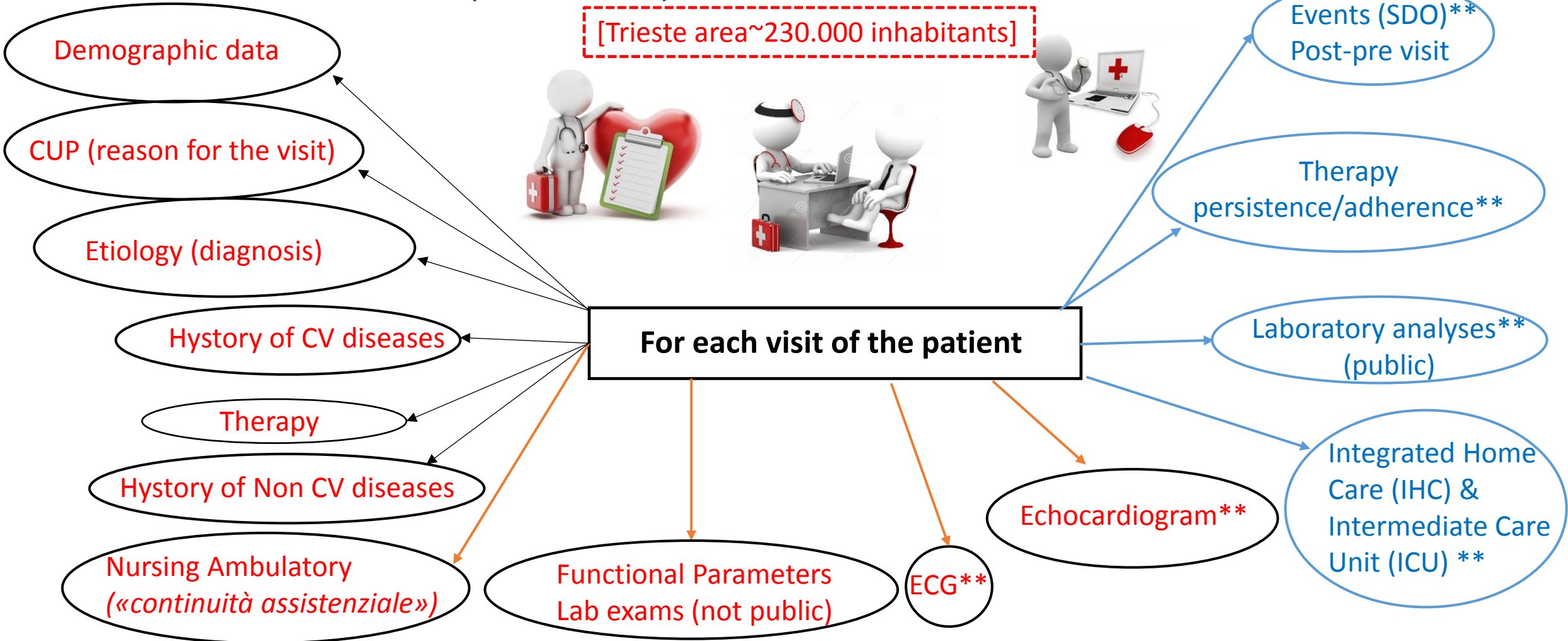


*Regional Repository of MicroData, RRMD/RER, SAS Enterprise Guide, INSIEL S.p.A.  THE POWER TO KNOW.

Clinic E-chart (Cardionet®)

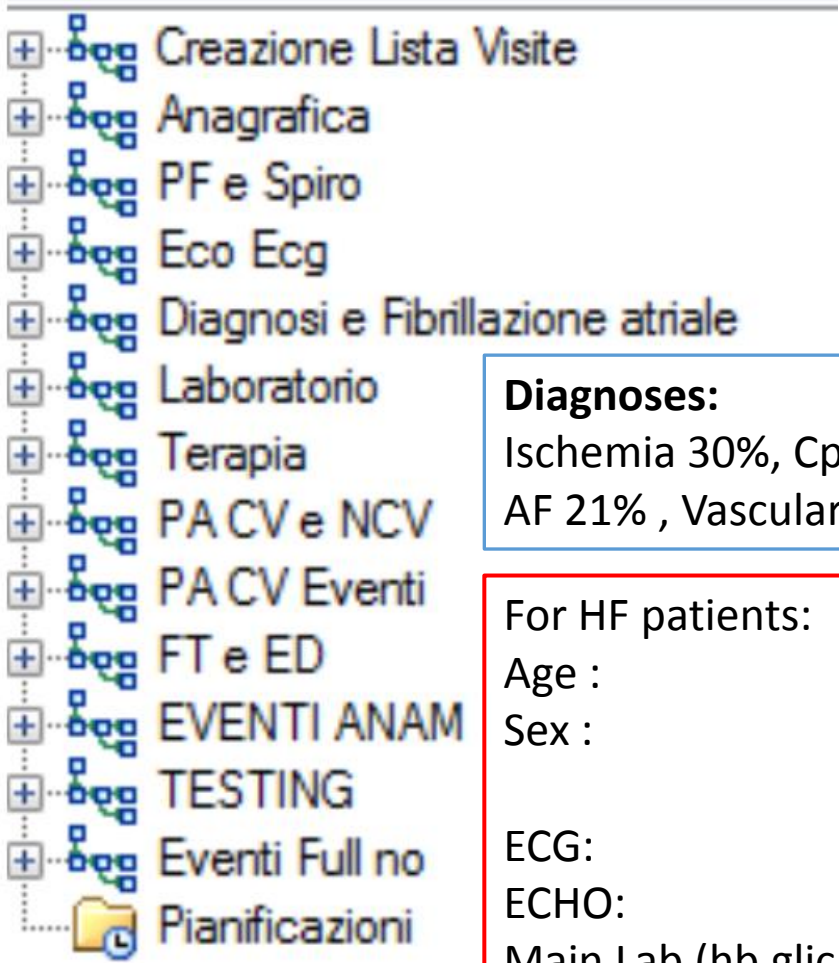
[Trieste area~230.000 inhabitants]

RRMD/RER



**Linkage with temporal rules on dates

Clinic E-chart (Cardionet®)

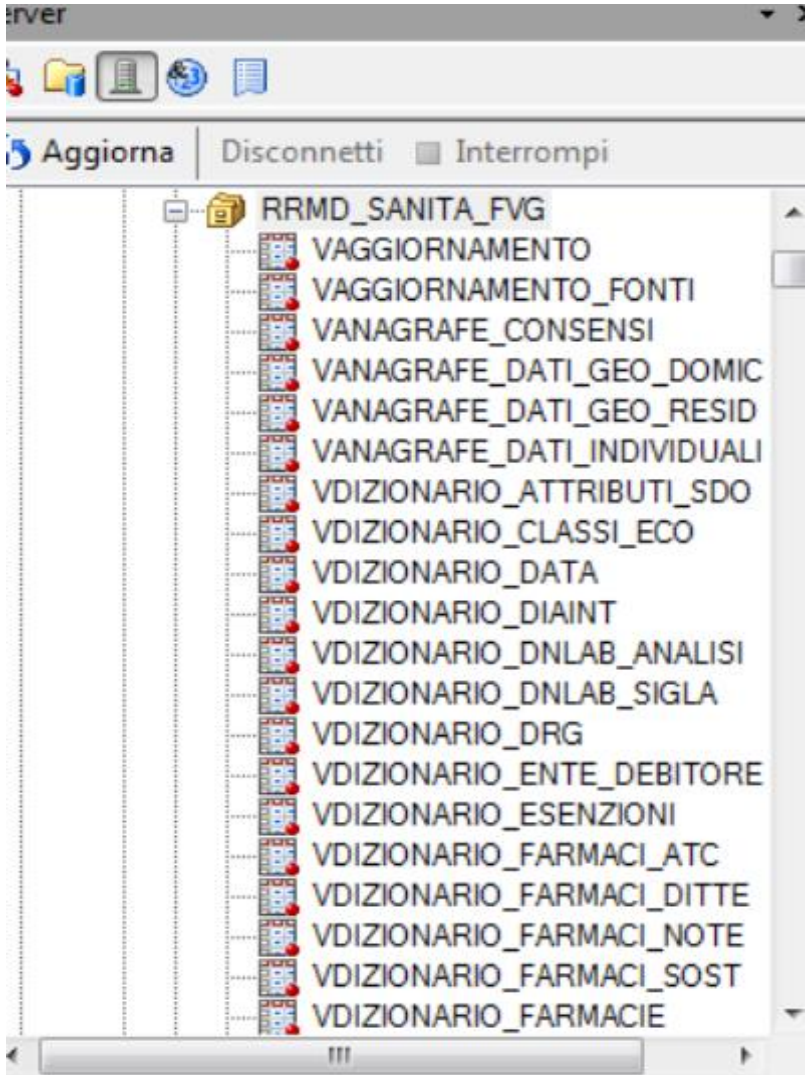


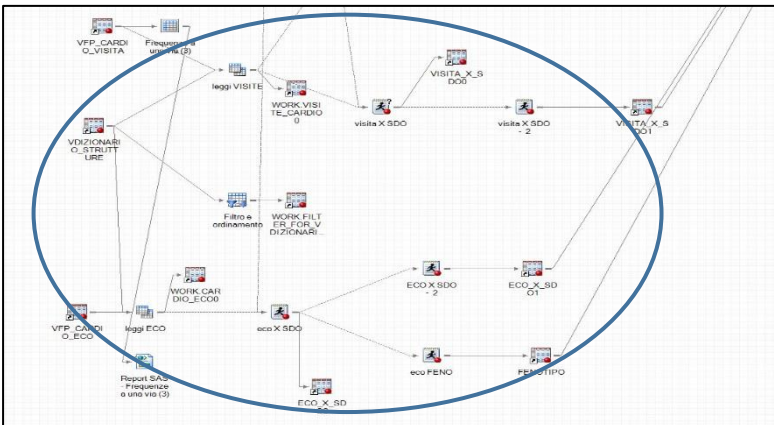
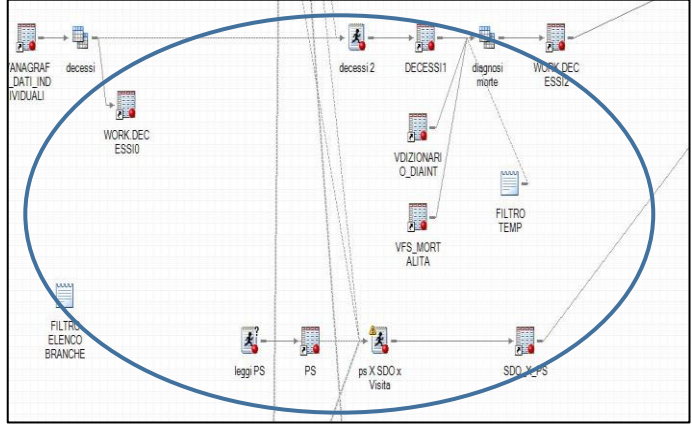
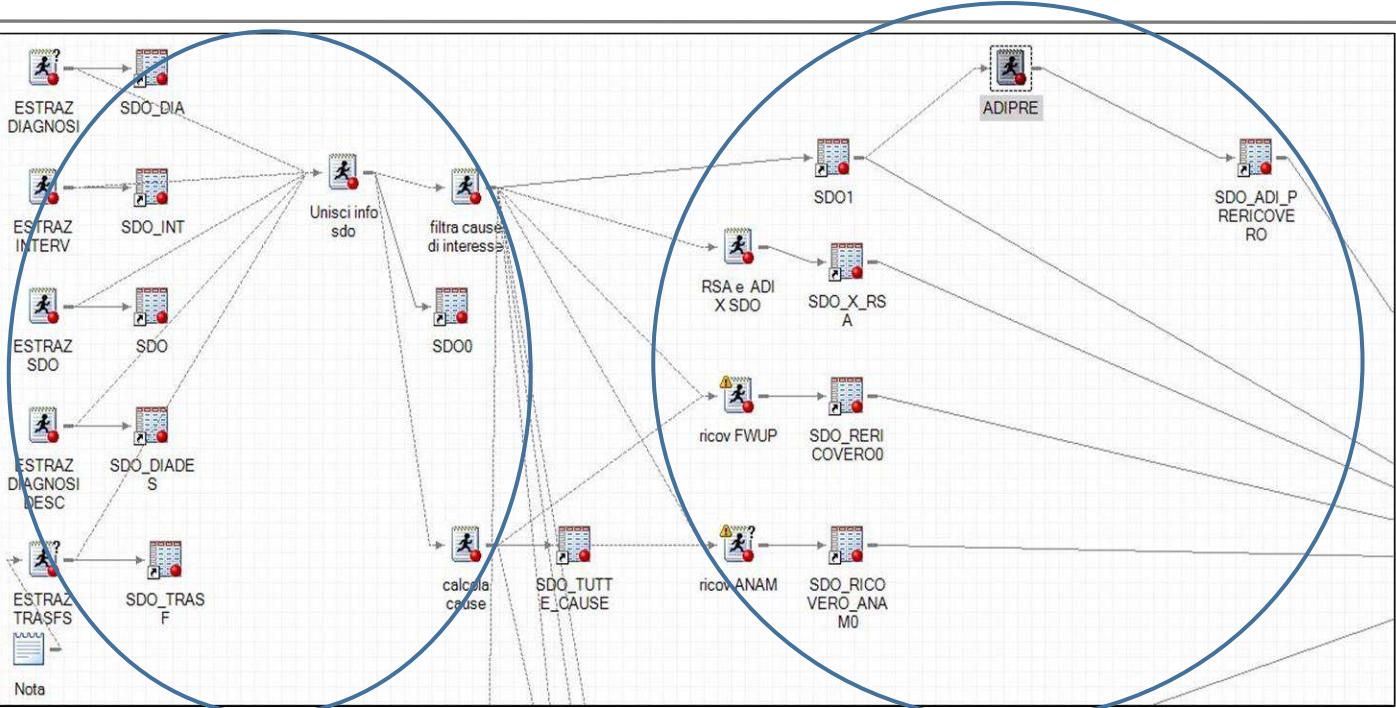
From 2009 to today:
95407 visits for 32477 pts
Mean age : 66 yrs ± 15
Sex : 49% Males

Diagnoses:
Ischemia 30%, Cpt Hypertensive 25%
AF 21% , Vascular disease 15%, **Heart Failure 10%**

For HF patients: 19885 visits for 3826 pts
Age : 76 yrs ± 10
Sex : 55% Males

ECG: linked for 98% of visits
ECHO: linked for 74% of visits
Main Lab (hb glic/creat): linked for 95-85% of visits





1. Hospitalizations for **Heart Failure (HF)**
2. Individual demographic data (sex, age, place of residence, life status...)
3. Lab tests during hospitalization [and pre/post...]
4. Drugs before/after hospitalization **[work in progress]**
5. Post-discharge path: Integrated Home Care (IHC) activations, Intermediate Care Unit (ICU)
6. Cardiological e-chart Cardionet®



IF HOSPITALIZATION IS IN CARDIOLOGICAL WARD (Trieste's area):
cardiological visits and procedures...,
like echocardiograms (i.e. quantitative
evaluation of left ventricular function, LVEF)

1. Database of the cardiological visits:



Explore prevalence and attributable fraction of noncardiac comorbidities on outcomes in pts with HFrEF (LVEF < 50%) and HFpEF (LVEF >= 50%) in a large contemporary community-based population*

- First visit of pts enrolled from October 2009 to December 2013. Follow up at December 2014.
- Inclusion: HF diagnosis, LVEF determination within 3 months from the index visit in the period.
- Exclusion: all patients who had severe primary left-sided valvular disease.



Study outcomes: death from any cause, (first) all-cause hosp, (first) HF hosp (first) noncardiovascular hosp.

(a) PAF: Population Attributable Fraction (for censored data)

PAF: % of events in a population that could be prevented by elimination of risk factor

[Several definitions and estimation methods have been proposed for survival data]**

$$PAF(t) = \frac{P(T \leq t) - P(T \leq t | Z = z^*)}{P(T \leq t)}$$

T= time to event; Z=risk factors; z*=chosen target values in order to quantify the potential impact of modifying the current distribution of Z to z* (i.e. absence of the comorbidity).

$$PAF(t) = 1 - \frac{1 - S(t)_{adj}}{1 - S(t)}$$

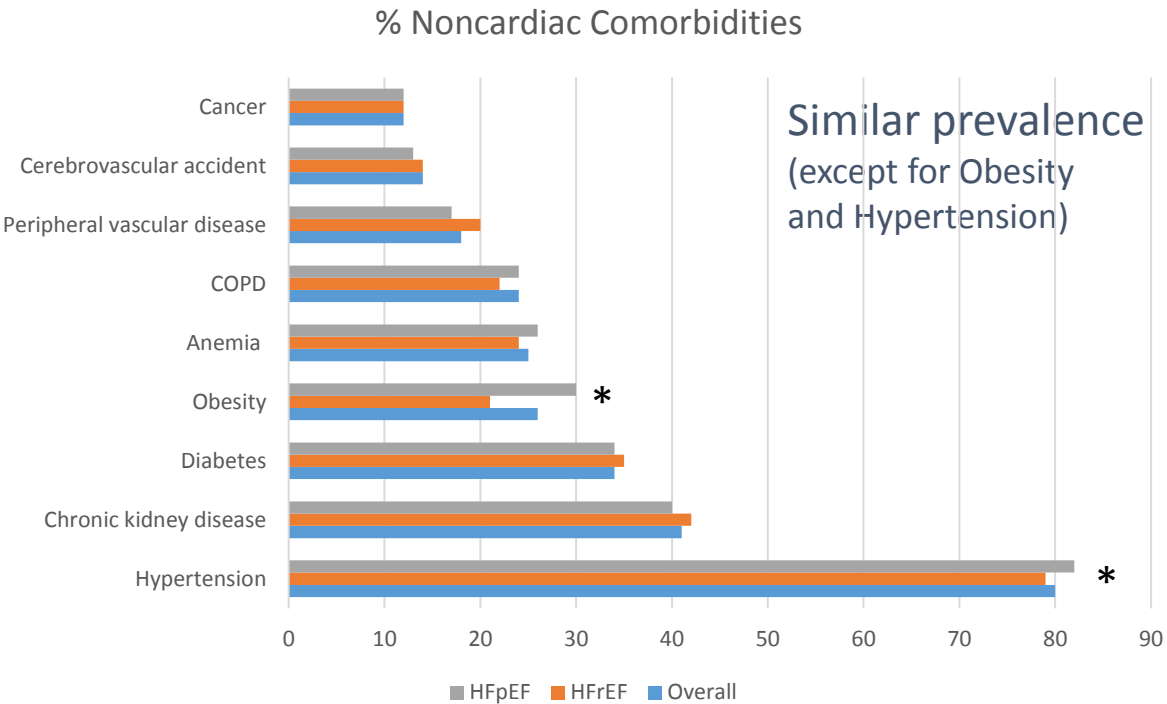
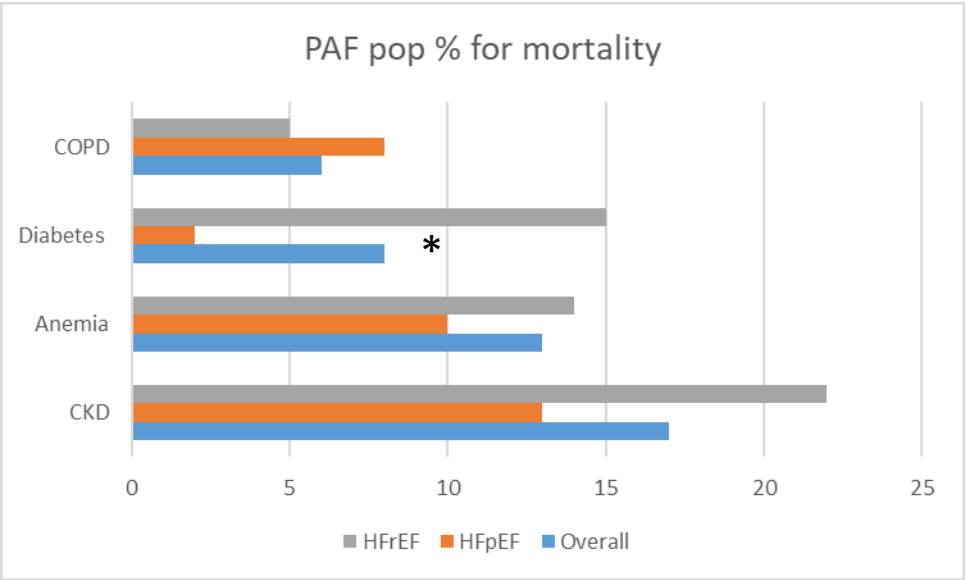
S(t) = P(T > t) : crude survival function; S(t)_{adj} = S(T > t | Z = z*): standardized survival [adjusted also for confounders age/sex]

(b) Interaction analysis [Cox model]

$$\lambda(t) = \lambda_0(t) \exp(\beta_1 * Age + \beta_2 * Sex + \beta_3 * Comorb + \beta_4 * LVEF_{group} + \beta_5 * Comorb * LVEF_{group})$$

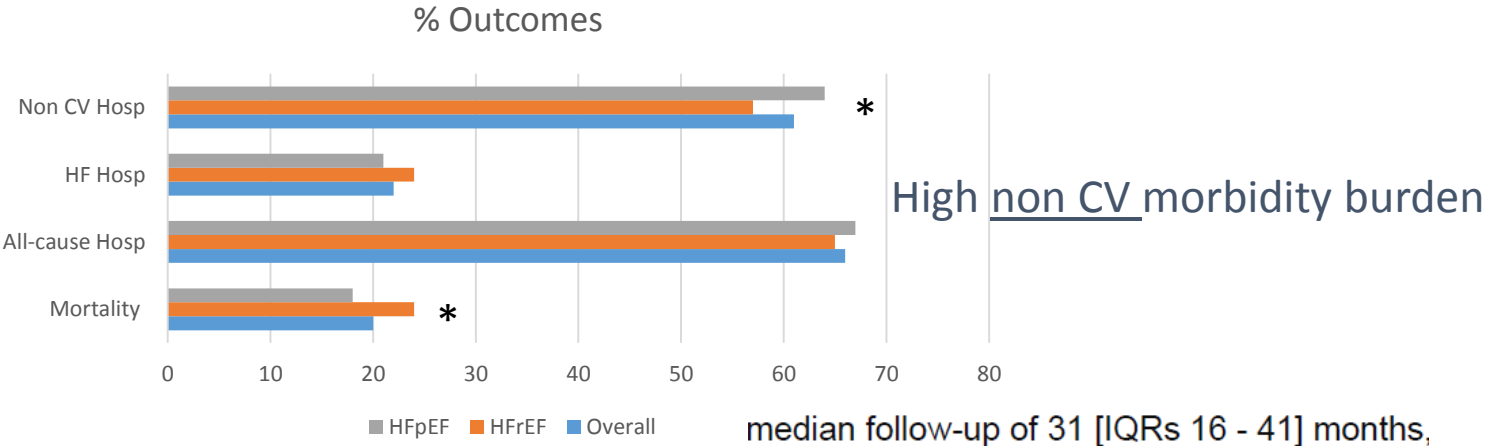
Test of significance for β_5

Applications (I)



PAF: **CKD, anemia, COPD** and **diabetes** showed the highest quantitative contribution.

Adjusting for age and sex, no significant interactions were found between LVEF groups and comorbidities (trend for diabetes).



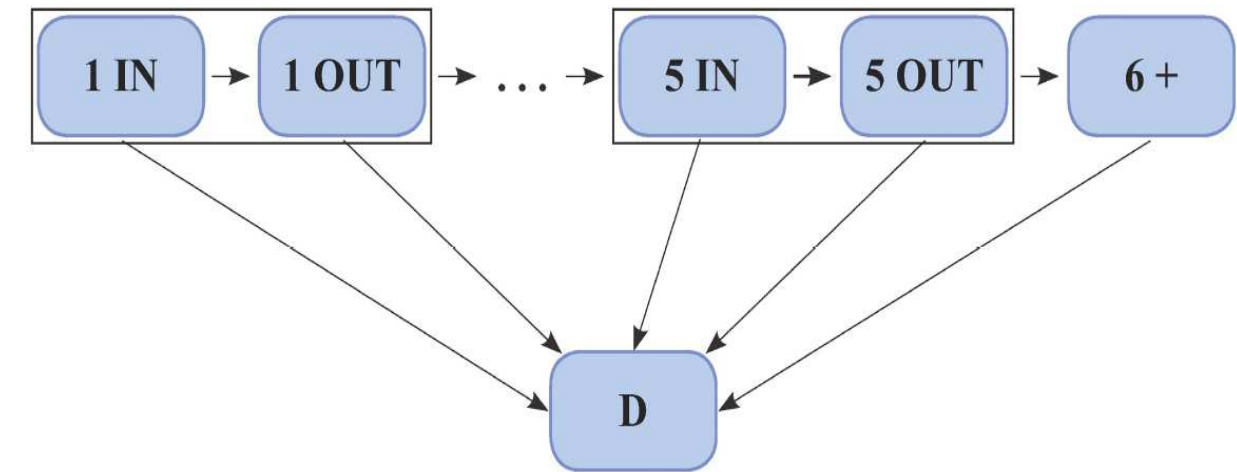
2. PDTA Database (Trieste's area):

How different risk profiles of HF patients can influence multiple readmissions and outpatient management.
Two multi-state models : one for hospital admissions, the other including Integrated Home Care (IHC) and Intermediate Care Unit (ICU) and death**.

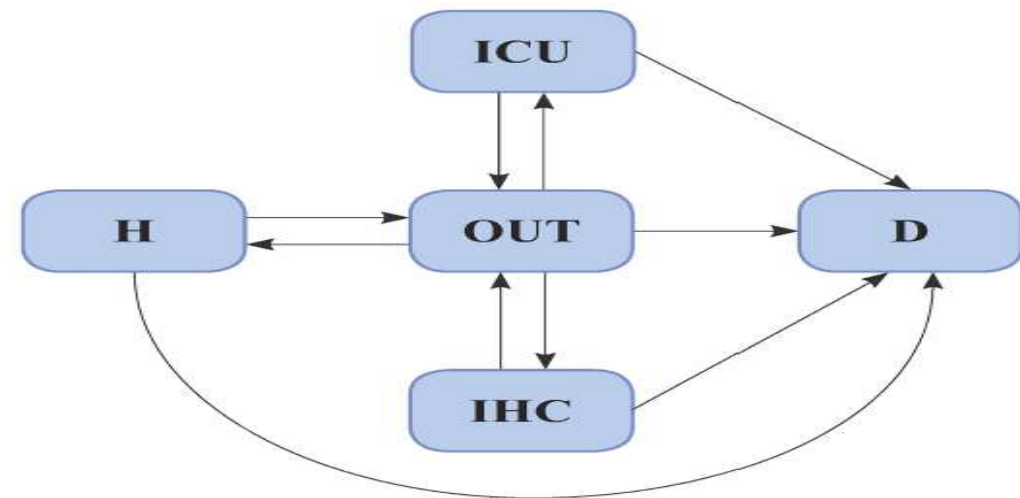
Patients hospitalized at least once for HF from 2009 to 2015. Follow up at September 2016.

Identified by ICD-9CM codes for HF (428:x) and hypertensive HF (402:01, 402:11, 402:91) according to the “*Programma Nazionale Esiti*”

Model 1: the first 5 hospitalizations are considered. No distinction has been done between rehospitalization for HF or for any cause.



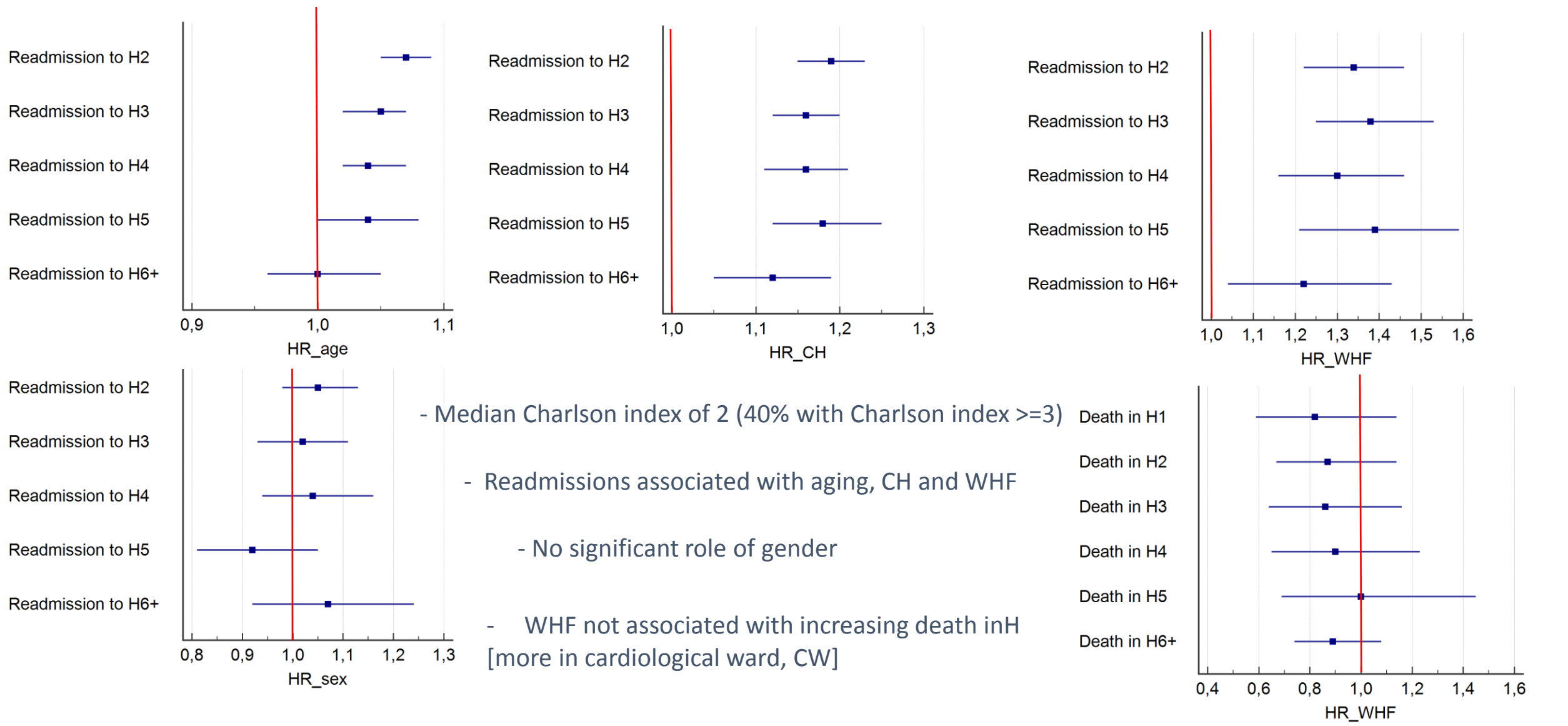
Model 2: The state space is made by: admission to hospital (H), to ICU or IHC, discharge from any state (OUT) and death.



**Gasperoni F, Ieva F, et al. Multi-state modelling of heart failure care path: A population-based investigation from Italy . [PLoS One](#). 2017 Jun 7;12(6).

Model 1: Readmissions & Death inH

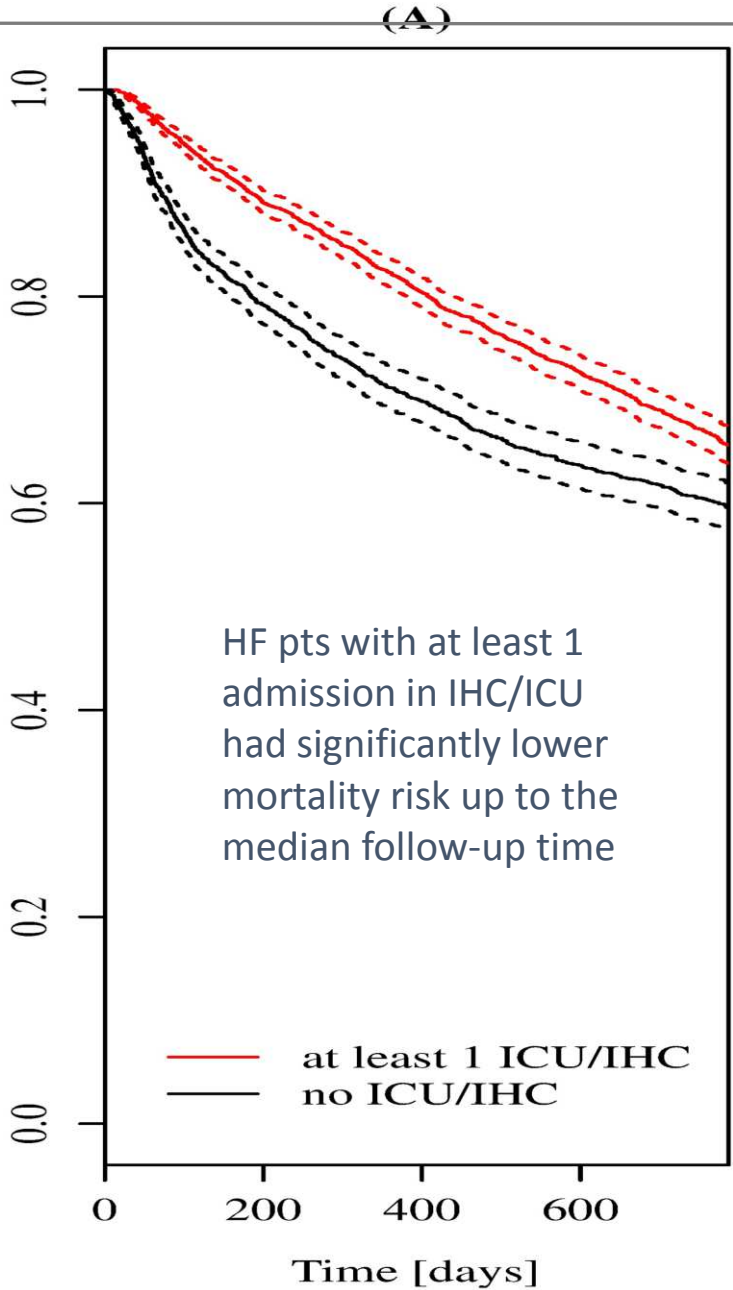
WHF=Worsening HF (i.e. previous hosp. within 5 yrs)



Model 2 : Readmission/ICU/IHC/Death

	Age (5 years)	CH index (2 points)	WHF
Readmission to H	1.04 (1.03, 1.05)	1.19 (1.17, 1.21)	1.30 (1.24, 1.36)
Readmission to ICU	1.19 (1.16, 1.22)	1.16 (1.13, 1.20)	0.92 (0.83, 1.02)
Readmission to IHC	1.05 (1.03, 1.06)	1.14 (1.12, 1.17)	1.03 (0.97, 1.10)
Discharge from H	0.98 (0.97, 0.99)	0.94 (0.93, 0.95)	
Discharge from ICU	0.98 (0.95, 1.01)	1.03 (1.00, 1.07)	
Inactivation of IHC	1.04 (1.03, 1.06)	1.18 (1.16, 1.21)	
Death in H	1.35 (1.30, 1.40)	1.20 (1.16, 1.25)	0.89 (0.79, 1.01)
Death in ICU	1.09 (0.99, 1.20)	1.53 (1.40, 1.67)	0.72 (0.51, 1.01)
Death in IHC	1.42 (1.27, 1.59)	1.15 (1.00, 1.31)	0.94 (0.62, 1.42)
Death OUT	1.44 (1.38, 1.51)	1.25 (1.18, 1.31)	0.81 (0.68, 0.96)

- Aging and higher Charlson increased the risk of re-hospitalization, ICU and IHC
- Aging increased time spent in hospital, inversely related to time spent in IHC
- WHF increased the risk of re-hospitalization, protective factor for death outside;
not associated with ICU/IHC



3. PDTA (**P**ercorso **D**iagnostico-**T**erapeutico-**A**ssistenziale) – a project of Health Ministry

How adherence to recommendations can influence all-cause mortality among heart failure patients in four Italian regions.

Patients hospitalized at least once for heart failure.

Identified by ICD-9CM codes for HF (428:x) and hypertensive HF (402:01, 402:11, 402:91)

Enrolment year to assess the care pathways in the subsequent year: 2013

Enrolment year to assess the outcomes in the subsequent year: 2014

Enrolment period to evaluate the association between pathways and outcomes in the subsequent five years: 2009-2010



3. PDTA (Percorso Diagnostico-Terapeutico-Assistenziale) – a project of Health Ministry

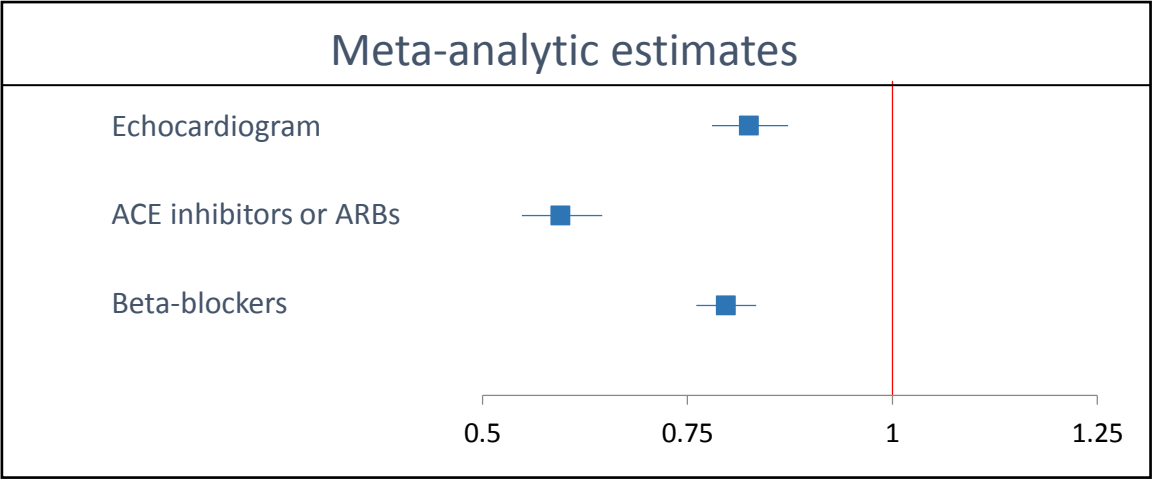
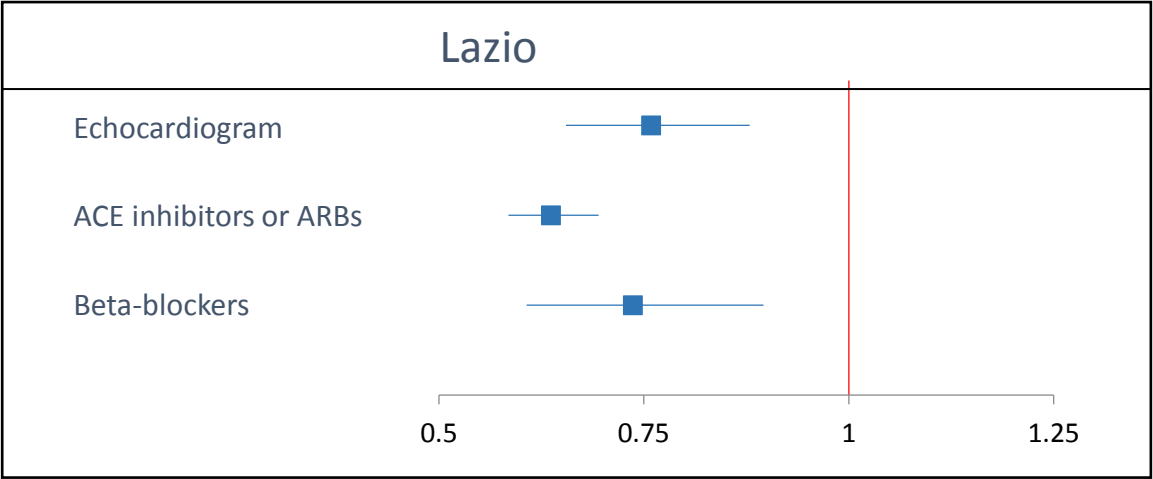
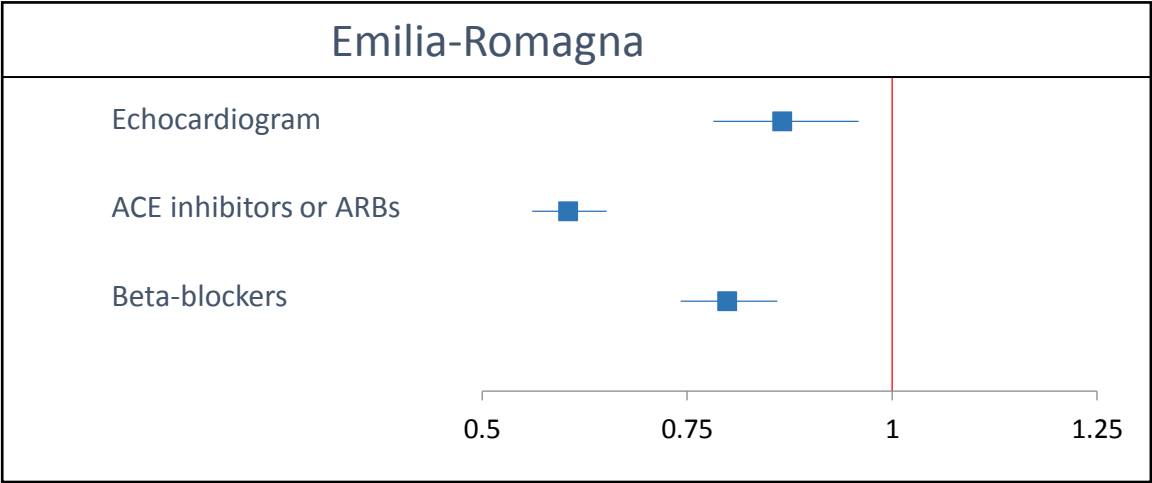
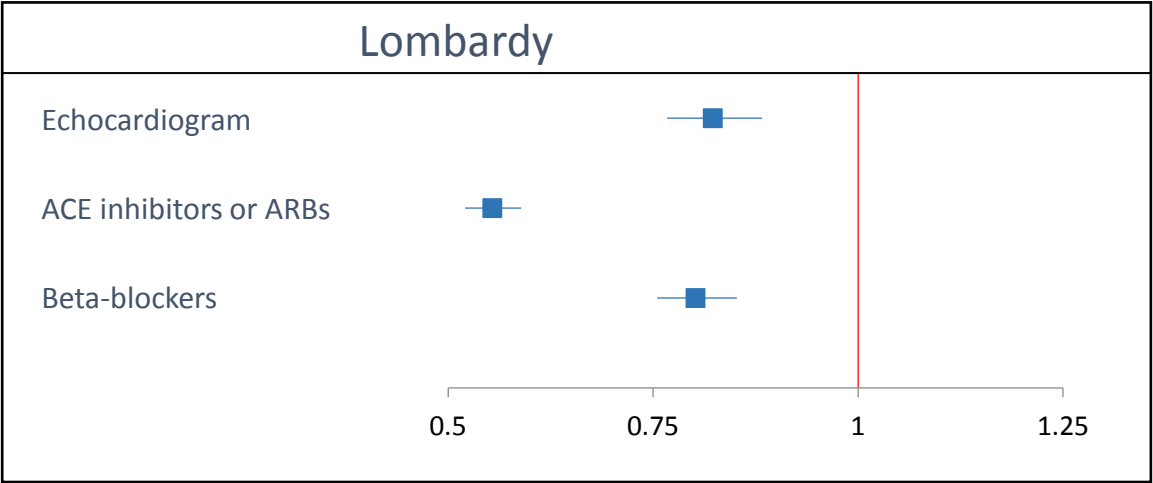
Recommendations	Lombardy	Emilia-Romagna	Lazio	Sicily
Cardiological examination ¹	30.6%	20.6%	25.0%	23.8%
Echocardiogram ²	25.9%	16.4%	10.7%	10.1%
ACE inhibitors o ARBs ³	59.7%	62.4%	64.4%	62.8%
Beta-blockers	58.1%	64.4%	56.5%	54.4%

¹ At least one visit per year; ² at least one test per year; ³ proportion of time spent under treatment ≥ 75%

Outcomes	Lombardy	Emilia-Romagna	Lazio	Sicily
Heart failure hospitalization	224.2	265.3	211.2	235.4
Death	289.7	311.1	197.9	282.6

Rate (*1,000 person-year)

3. PDTA (Percorso Diagnostico-Terapeutico-Assistenziale) – a project of Health Ministry



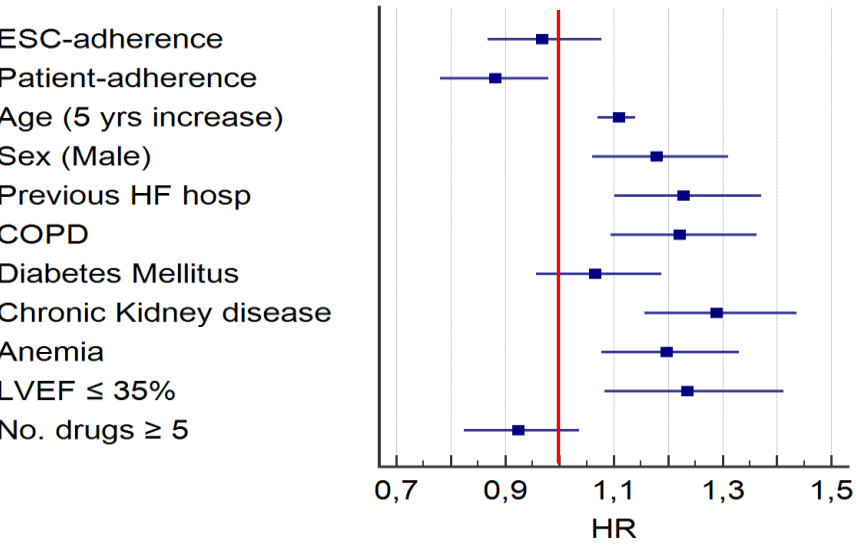
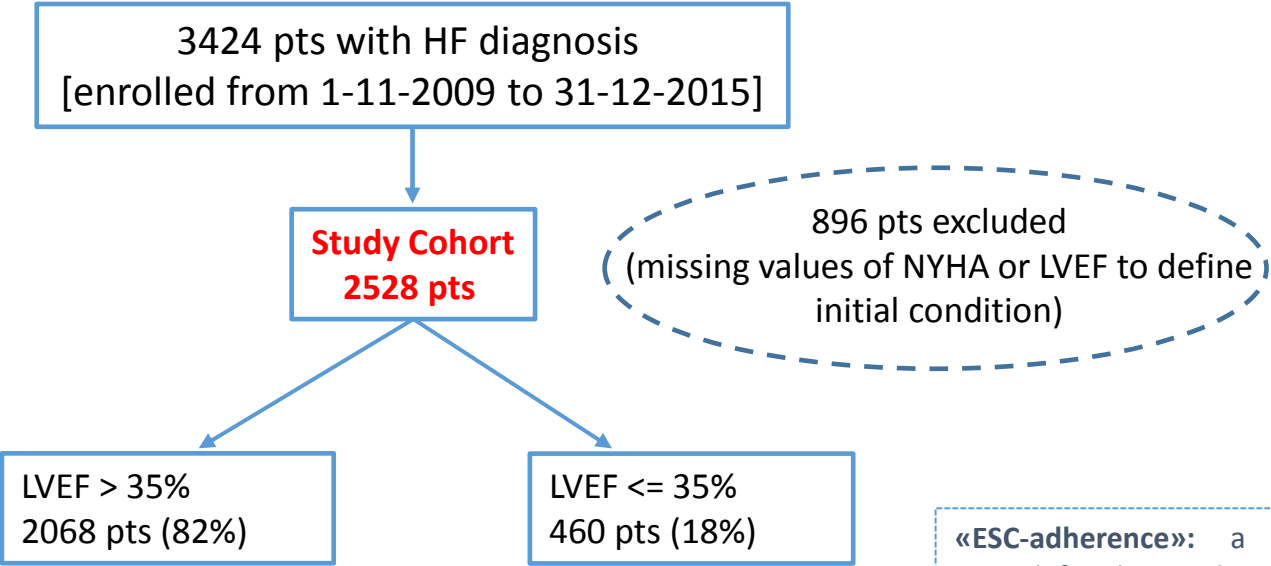
“Chronic Heart Failure: A silently progressing disease”

To evaluate rate of HF progression and factors associated with worsening. Moreover, how pharmacological treatments are adopted in clinical practice and the impact of adherence to HF treatment on HF progression (taking into account contraindications /intolerance).

Primary outcome: progression of HF
(at least one of the following criteria):

- Step up of ≥ 1 NYHA class;
 - Decrease LVEF $\geq 10\%$;
 - Association of diuretics (thiazides + furosemide) or increase $\geq 50\%$ of furosemide dosage (in any case > 25 mg)
- Or
- HF hospitalization [Death]

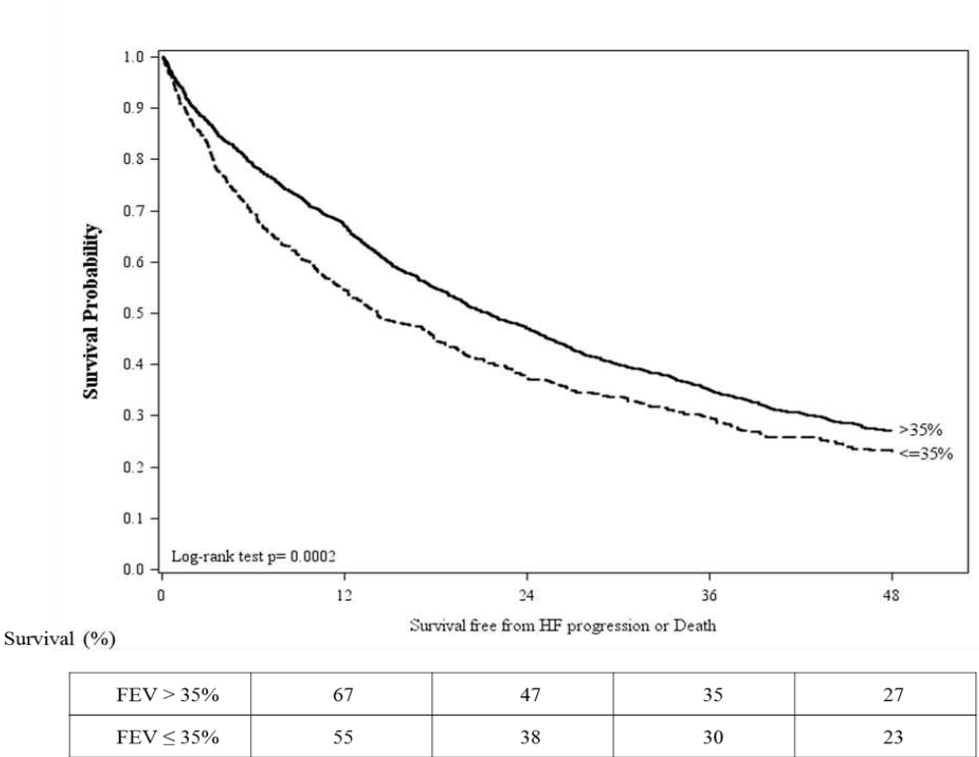




«ESC-adherence»: a subject was defined compliant to HF treatment guidelines if (s)he has at least 2 prescriptions (**if not contraindicated or intolerant**) of ACEi/ARB and Beta-Blocker and (s)he takes a **dosage at least ≥ 50% of the target dosage** for all the two drugs.
[MRAs not considered as per available guidelines at the time of cohort observation].

«Patient-adherence»: subject is defined compliant if (s)he has a PDC ≥ 75% for all the drugs prescribed by the cardiologist

Survival free from HF progression defined with at least 1 criterion (deaths included).

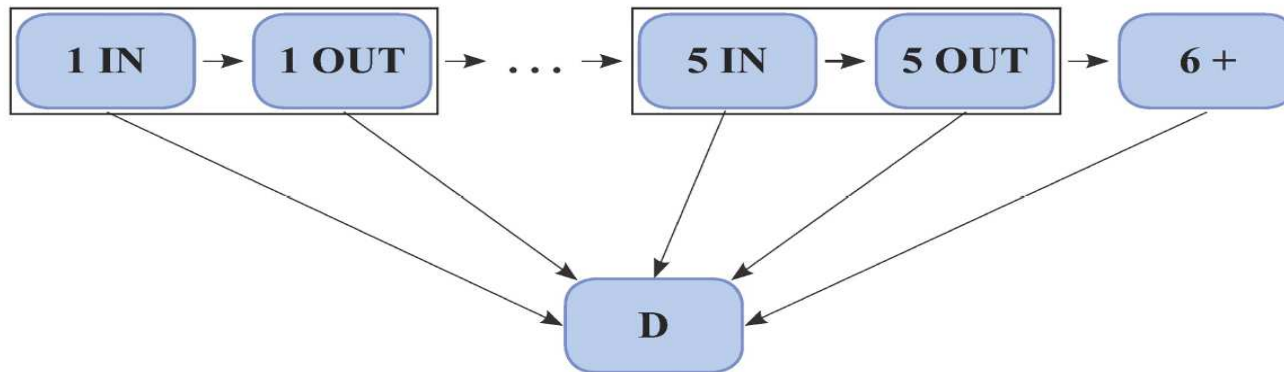


Multi State Models*

- Data collection **at a regional level** (FVG~1.216.134 inhabitants)
- Pharmacological treatment/adherence as a time-dependent covariate

Moreover: to investigate a possible relation between the admission in ICU/IHC (as a time-dependent covariate, not as a state) and the risk of re-hospitalizations at a regional level.

Statistical aspect: a nonparametric discrete frailty will be introduced, through which a probabilistic clustering technique is derived which allows to detect latent populations that could be described (spatial ? socioeconomic gradient ?...).



The Italian deprivation index at census block level (N. Caranci et al*) has been linked with a set of regional data in RER

- Nationwide deprivation index at municipality and census block level, updated at 2011 Italian General Census of Population and Housing
- 280 variables defined at census block level (371447 census tracts)
- 5 independent values selected to represent the multidimensionality of the social and material deprivation concept: **low level of education, unemployment, non-home ownership, one parent family, population density**
- The index is calculated by summing standardized indicators and it is also available categorized in quintiles of population
- General national mortality is positively correlated to the index (in particular in population up to 64 years and in larger size municipalities)
- The application of a nationwide deprivation index to a regional dataset may have some limitations requiring **adjustment or recalculation from regional data**

Linkage of individual 2011 Census data in RER:

- Type/characteristics of house
- Family informations
- Level of Education
- Job
- Commuting



Research objectives:

Impact of socio-economic indicators on cardiovascular outcomes, taking into account clinical characteristics, in order to better address local choices of health policy.