

Il cross-talk cuore-rene: fisiopatologia ed aspetti clinici

Catania, 4 novembre 2019

Cross-talk rene-cuore: Effetti della CKD sull'apparato cardiovascolare

Diapositiva preparata da ANDREA NATALI e ceduta alla Società Italiana di Diabetologia.
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Andrea Natali

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Università di Pisa**

Disclosure

Fee for lectures/advisory board:

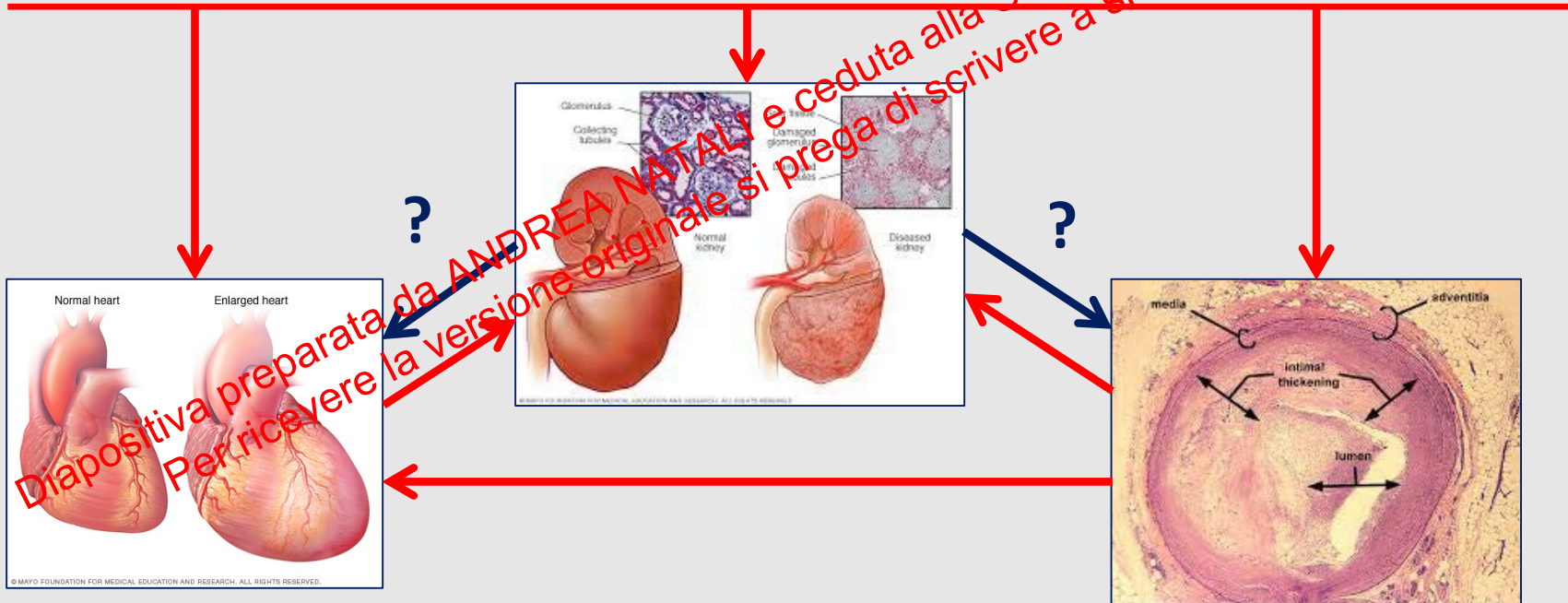
Eli Lilly, Amgen, Servier, Boheringer Ingelheim, Astra Zeneca

Research support:

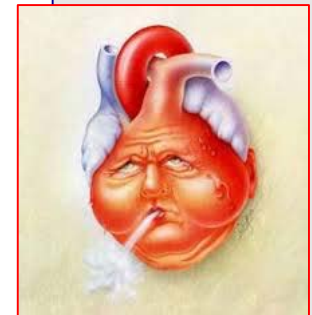
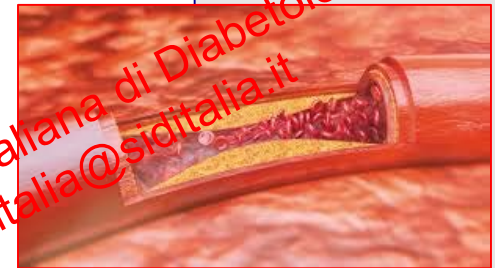
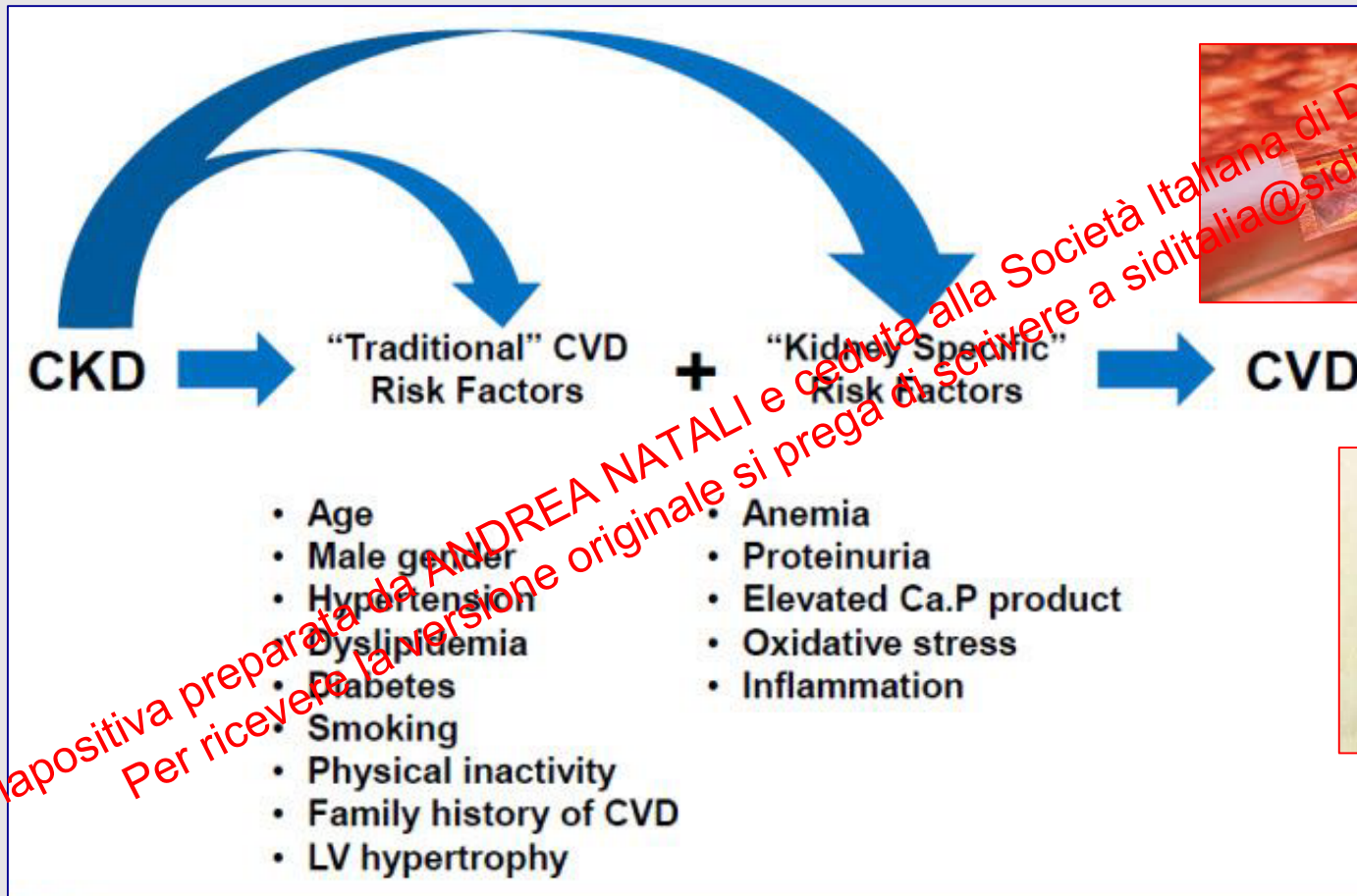
Eli Lilly, Boheringer Ingelheim, Sanofi Aventis

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Contesto



Modello fisiopatologico



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CKD e coronarie



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Impact of mild to moderate reductions of glomerular filtration rate on coronary artery disease severity

A. Natali ^{a,*}, B. Boldrini ^a, S. Baldi ^a, M. Rossi ^a, P. Landi ^b, S. Severi ^c, A. Solini ^a, E. Ferrannini ^a

Nutrition, Metabolism & Cardiovascular Diseases (2014) 24, 681–688

Table 1 Clinical characteristics of the study population according to either eGFR class or deviation

	105+	90+	75+	60+	45+	p°
N	118	443	547	452	192	
Age (yrs)	42 ± 6	52 ± 8	53 ± 8	59 ± 9	62 ± 7	<0.001
Female (%)	17.0	17.9	16.3	20.4	26.1	0.03
BMI (kg/m ²)	26.3 ± 3.7	26.1 ± 3.1	26.3 ± 3.1	26.4 ± 3.0	26.1 ± 3.0	ns
Effort angina (%)	43.2	55.9	55.8	57.1	56.2	ns
Stress ischemia (%)	33.1	43.1	49.9	51.8	52.1	<0.001
Rest ischemia (%)	16.1	27.3	27.4	30.1	25.2	0.048
Any ischemia (%)	41.5	56.3	62.7	63.5	61.1	0.007
Previous MI (%)	37.6	36.5	37.7	35.9	44.3	ns
Smoking N/F/C (%)	19/53/28	22/50/28	18/60/22	28/53/19	29/56/15	<0.001
Hypertension (%)	22.0	30.0	39.1	45.3	50.0	<0.001
SBP (mmHg)	121 ± 11	126 ± 13	127 ± 13	131 ± 15	131 ± 15	<0.001
DBP (mmHg)	79 ± 7	80 ± 7	80 ± 8	81 ± 8	81 ± 8	0.012
Pl. Glucose (mM)	4.72 ± 0.65	4.78 ± 0.66	4.79 ± 0.60	4.78 ± 0.65	4.83 ± 0.70	ns
T-Cholesterol (mM)	5.64 ± 1.65	5.51 ± 1.24	5.59 ± 1.28	5.63 ± 1.22	5.67 ± 1.20	ns
Triglycerides (mM)	1.76 ± 0.89	1.79 ± 0.87	1.85 ± 0.92	1.82 ± 0.99	1.89 ± 0.98	ns
eGFR (ml/min/1.73 m ²)	110 ± 5	97 ± 4	82 ± 4	68 ± 4	53 ± 4	<0.0001
Dipstik = trace (%)	10.3	7.2	9.0	5.8	9.4	ns
Hct (%)	40.5 ± 3.7	40.0 ± 3.9	40.4 ± 3.6	40.2 ± 3.8	40.0 ± 4.2	ns
ESR (mm)	10.1 ± 9.7	11.8 ± 12.2	11.6 ± 11.8	12.7 ± 10.7	17.9 ± 16.2	<0.0001

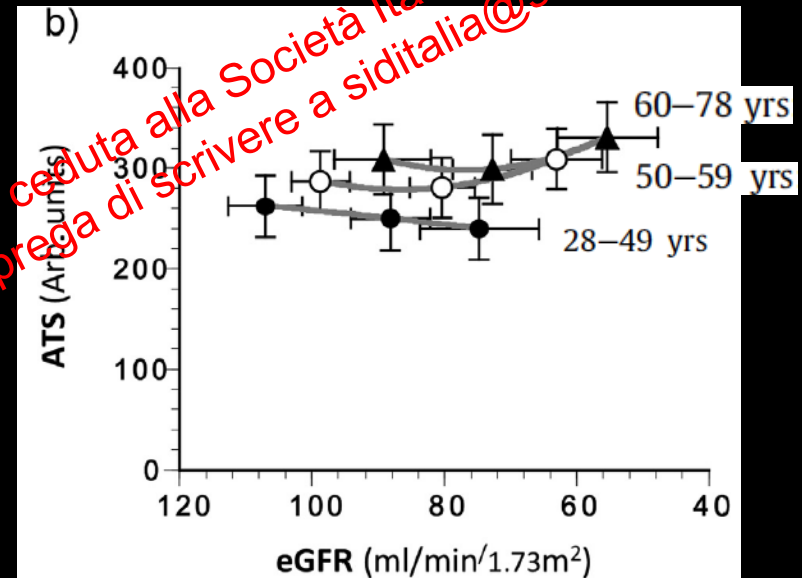
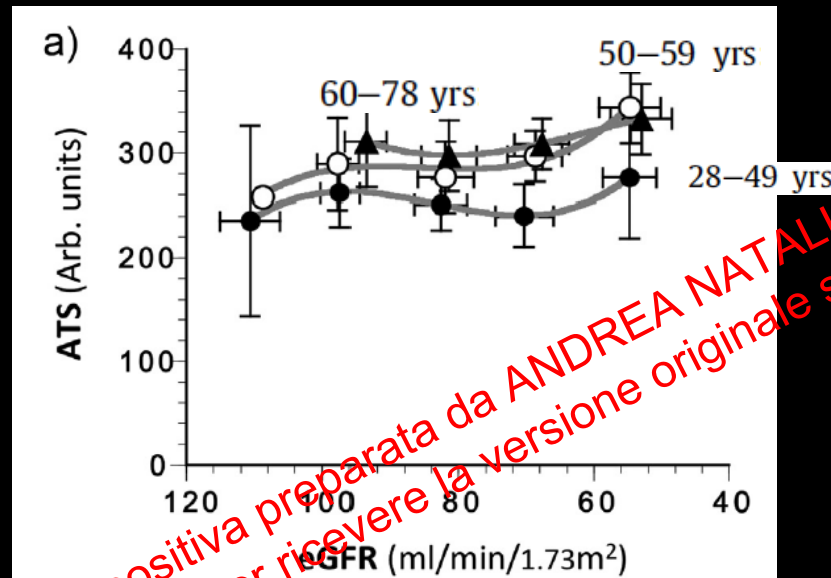
BMI = body mass index, MI = myocardial infarction, N/F/C = never/former/current smokers, SBP = systolic blood pressure, Dipstik = trace = protein <15 mg/dl in morning urine sample by Dipstick, ESR = eritrocyte sedimentation rate. °p values refer to ANOVA test for the variable “Age” and t-test for the other variables. All variables were analyzed by age- and gender-adjusted ANCOVA (continuous variables) or logistic regression (categorical variables).

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Is mild CKD associated with more severe coronary ATS ?

Impact of mild to moderate reductions of glomerular filtration rate on coronary artery disease severity

A. Natali ^{a,*}, B. Boldrini ^a, S. Baldi ^a, M. Rossi ^a, P. Landi ^b, S. Severi ^c, A. Solini ^a, E. Ferrannini ^a



(105+, 90+, 75+, 60+, and 45+)

HypoF, NormoF and HyperF

Is **Diabetes** associated with more severe coronary ATS ?

Rapid communication

Coronary atherosclerosis in Type II diabetes: angiographic findings and clinical outcome

A. Natali, S. Vichi, P. Landi, S. Severi, A. L'Abbate, E. Ferrannini

Coronary Division and Metabolism Unit of the C.N.R. Institute of Clinical Physiology, and the Department of Internal Medicine of the University of Pisa School of Medicine, Pisa, Italy

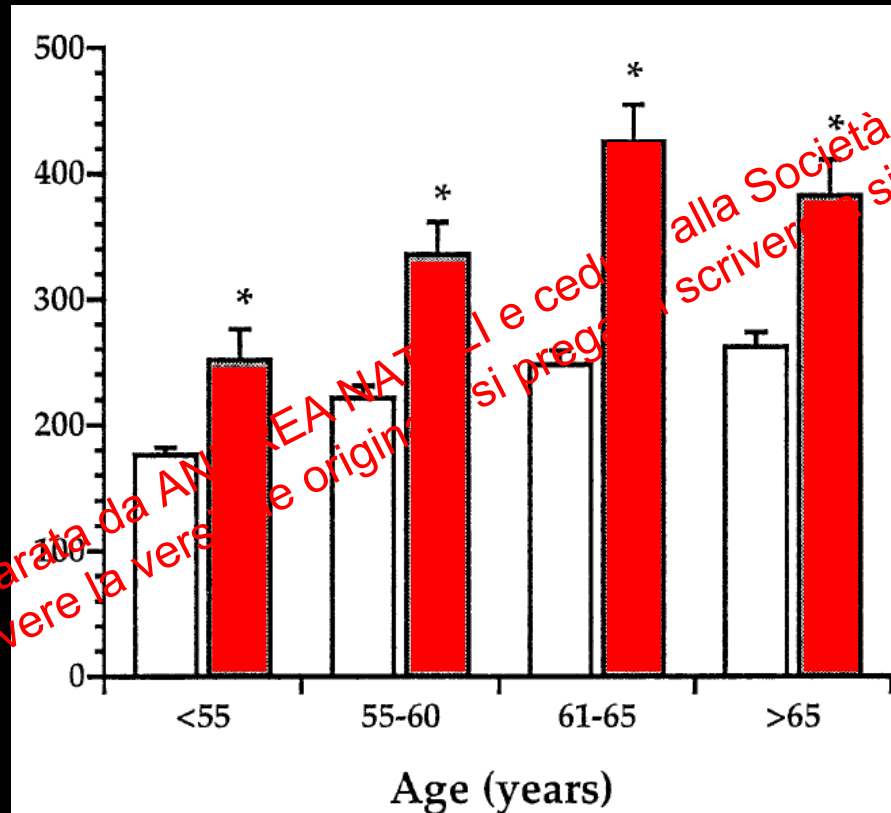
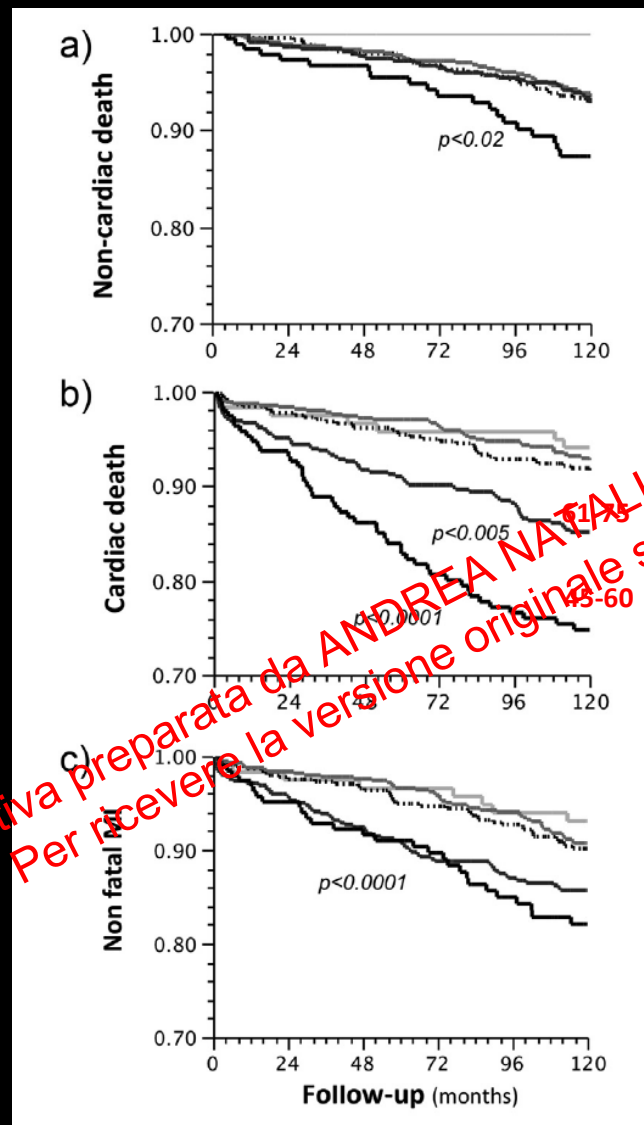


Fig.2. Sum of all atherosclerotic narrowings detected by angiography in any segment of the coronary tree (ATS score) in 1984 non-diabetic and 269 diabetic patients stratified by age. □, Non-diabetic subjects; ■, diabetic patients

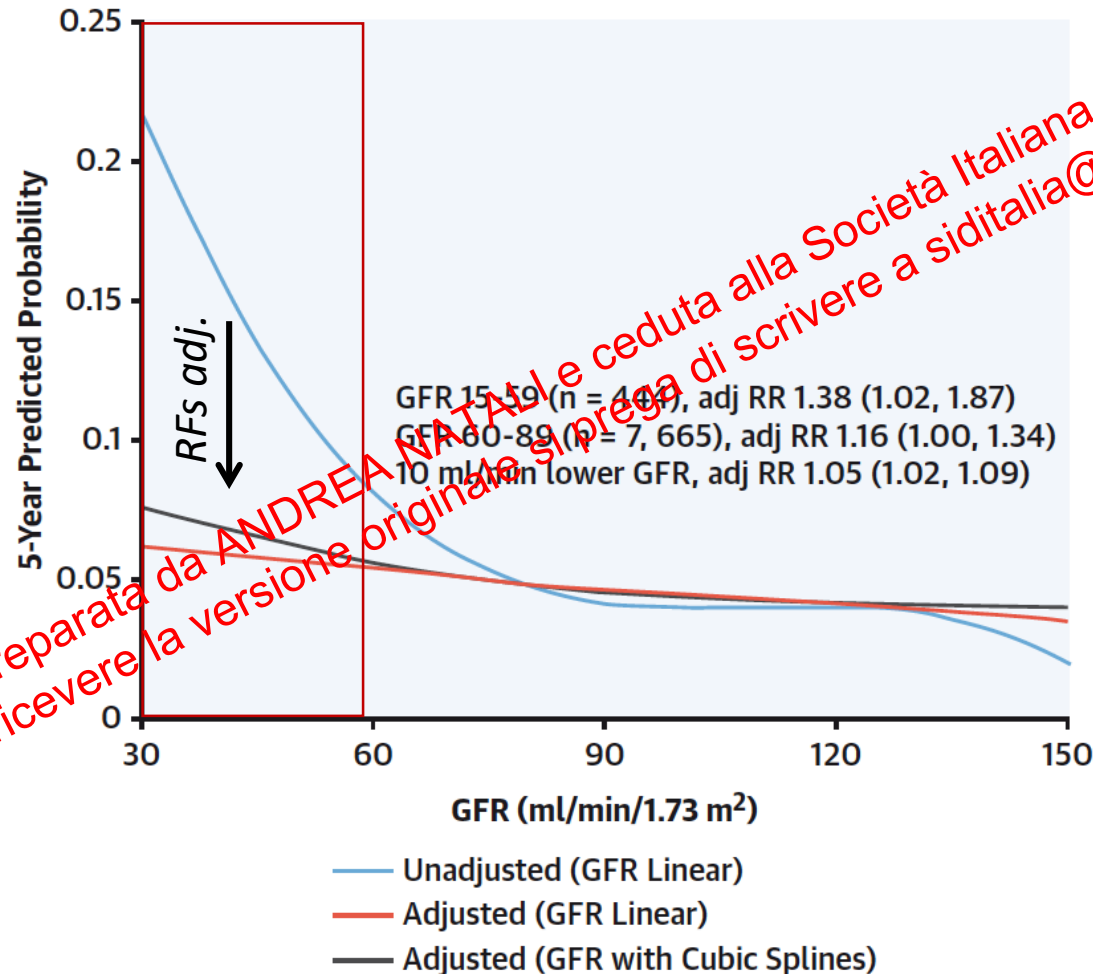
Impact of mild to moderate reductions of glomerular filtration rate on coronary artery disease severity

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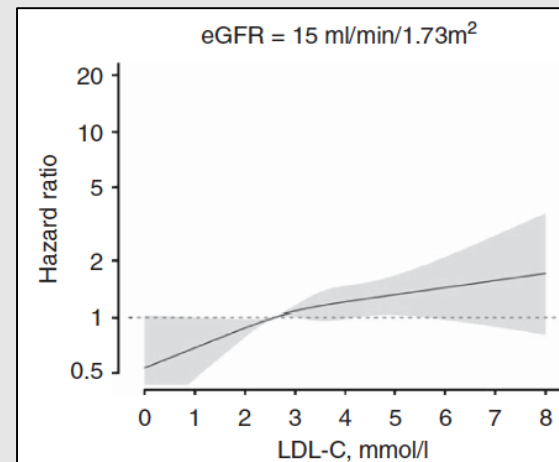
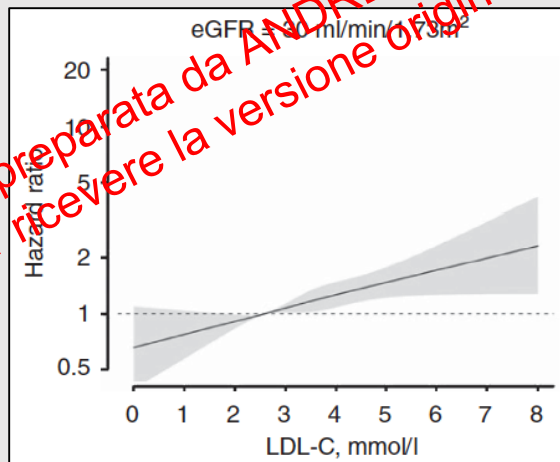
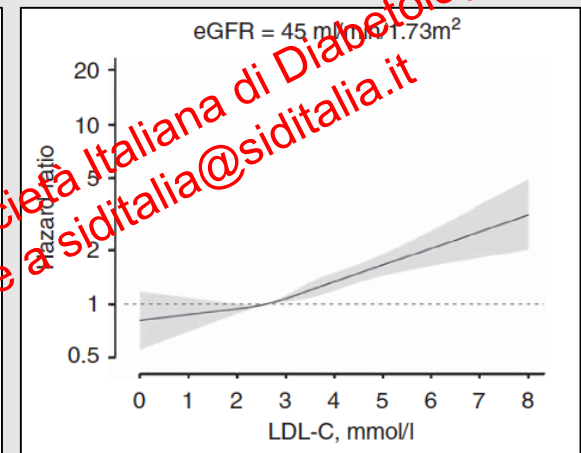
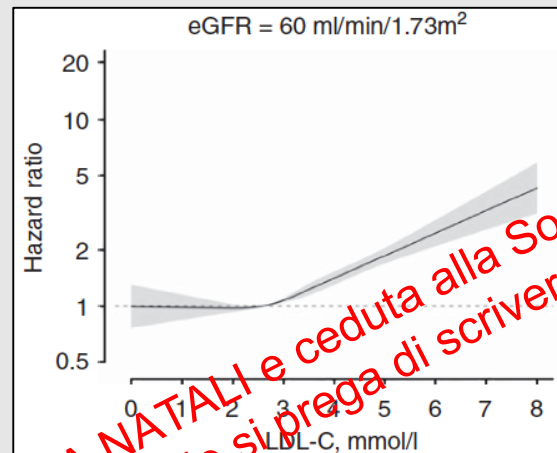
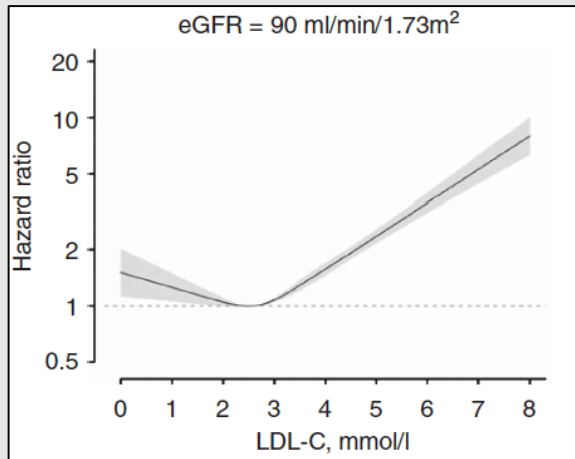
eGFR and ASCVD risk

FIGURE 1 Probability of Developing ASCVD in the ARIC Study



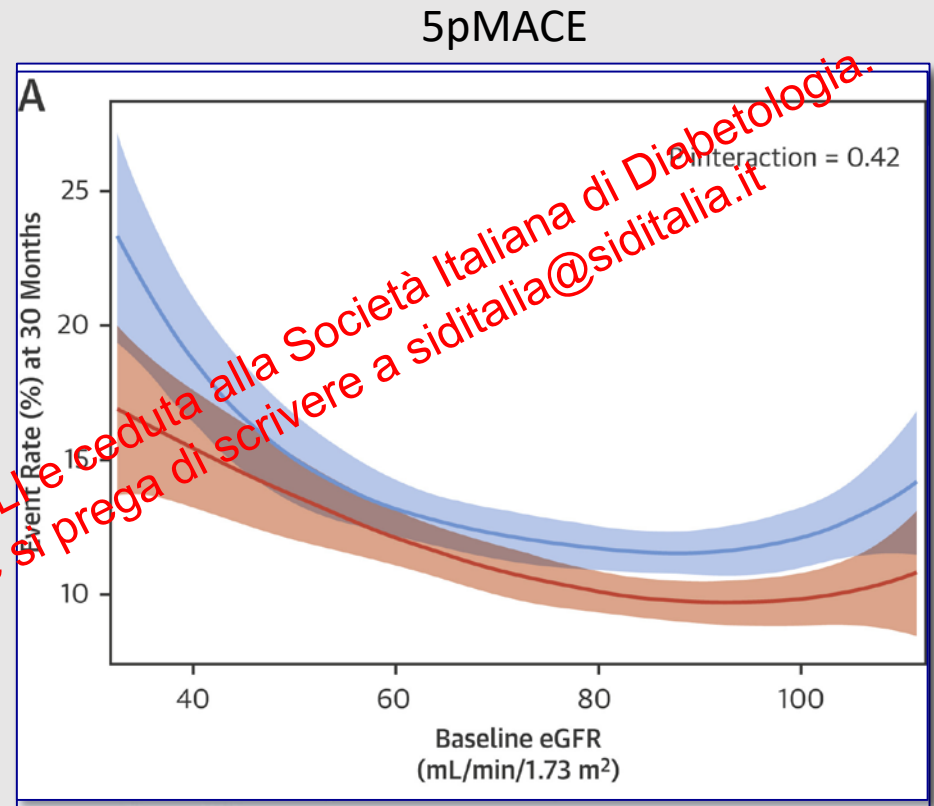
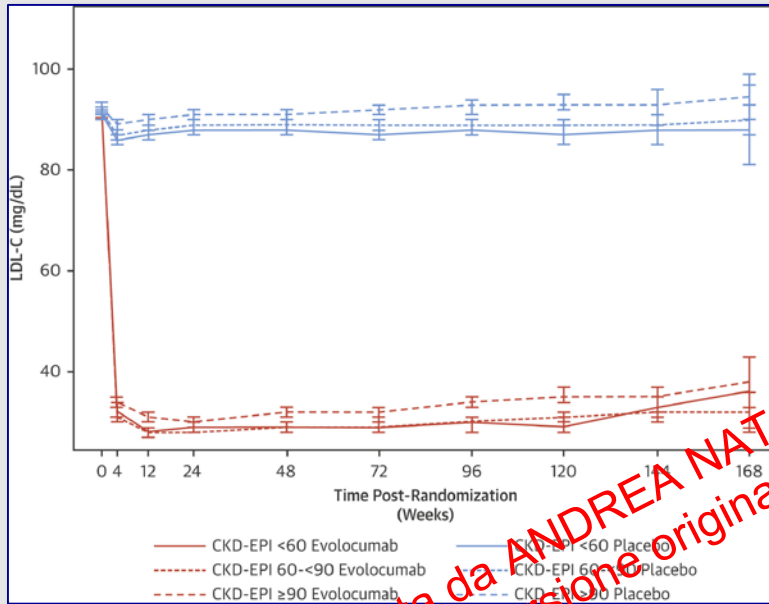
LDLc and adj. HR of MI

836,060 participants in the Alberta Kidney Disease cohort



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PCSK9 Ab (FOURIER/EVOLOCUMAB)



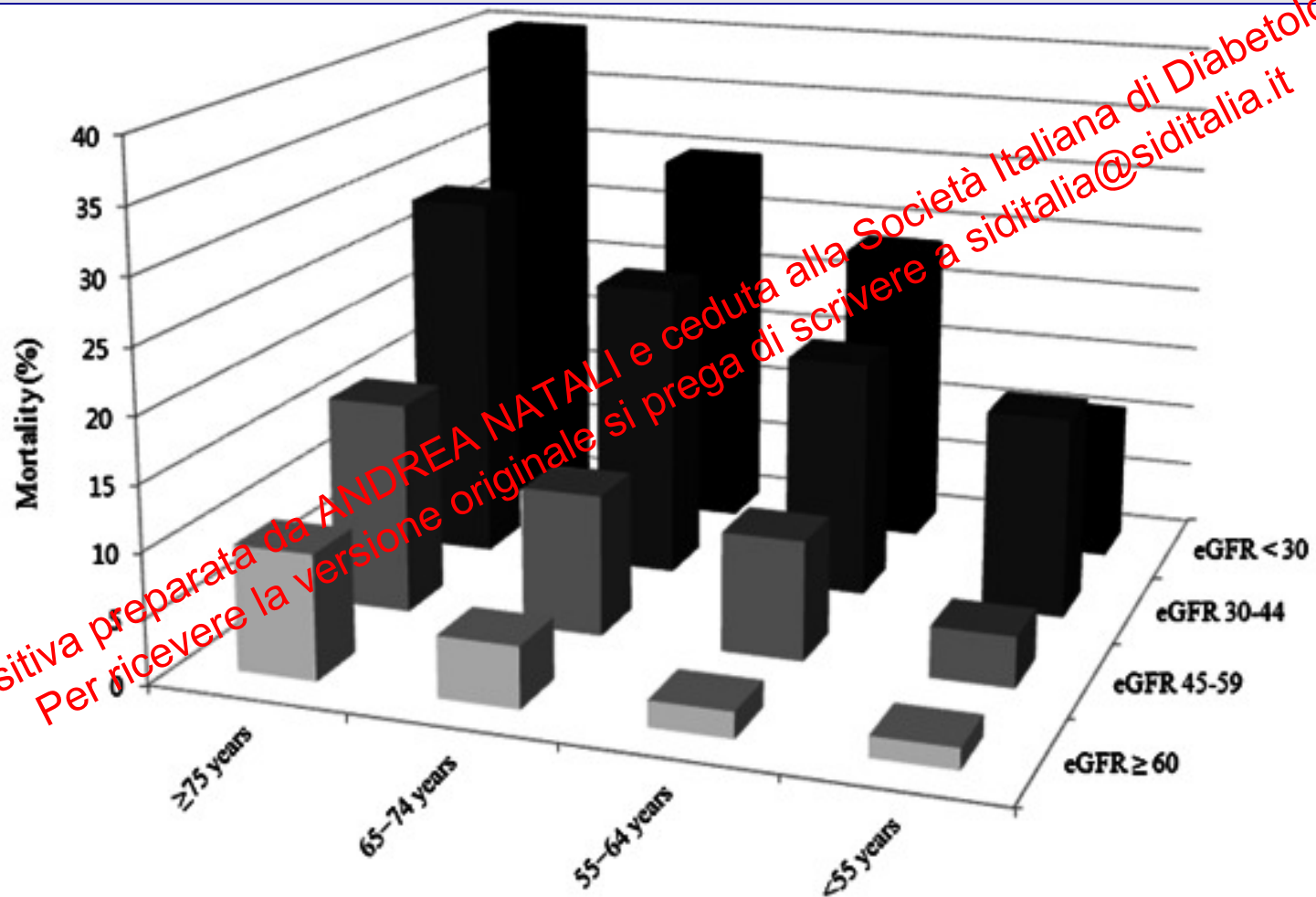
eGFR

eGFR	51	67	97
	44-56	69-84	93-102

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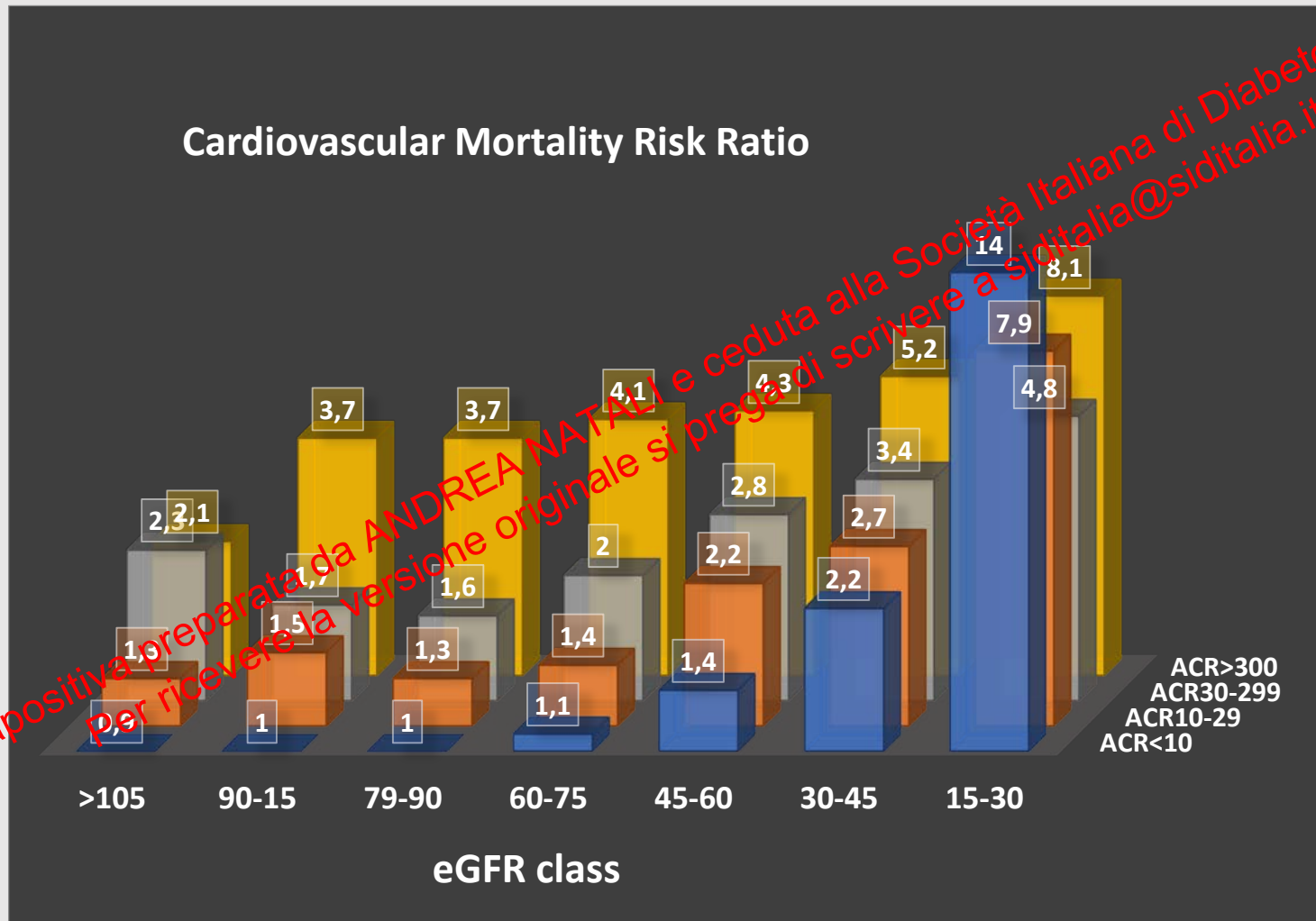
CKD = Fragility

Korean Acute Myocardial Infarction Registry, 13,898 consecutive MI



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eGFR vs albU in CV Mortality risk



Perché la proteinuria ?

A. Natali et al.: Type II diabetes and coronary atherosclerosis

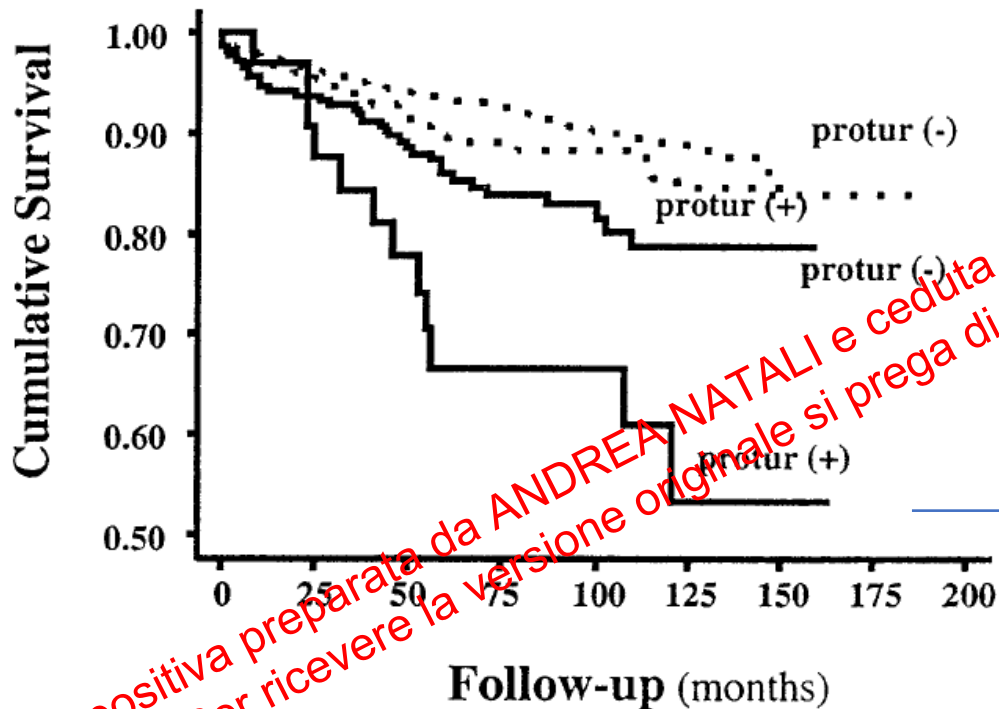


Fig.5. Kaplan-Meier survival curves for cardiac death in 2253 patients according to the presence of clinical grade proteinuria (*protur*) and diabetes. - - - Non-diabetic subjects, — diabetic patients

= serum creatinine
= age
= Coronary ATS
> HbA1c
> Diuretics

Albuminuria e CHF

Albuminuria in Congestive Heart Failure.

By GEORGE A. RACE, M.D., CHARLES H. SCHEIFLEY, M.D., AND JESSE E. EDWARDS, M.D.

Albuminuria may be an integral part of the picture of congestive heart failure. Of 161 patients in whom the histologic renal findings were considered to be either normal or to be of such a nature as not to be responsible in themselves for albuminuria, and in whom clinically obvious causes for albuminuria had been eliminated, 141, or 88 per cent, had albuminuria. The incidence of albuminuria was about equal among the various types of heart disease when heart failure existed. A trend existed for the grade of albuminuria to parallel the grade of heart failure. Based on a

TABLE 1.—The Incidence and Grades of Albuminuria in Group 1 According to the Type of Heart Disease

Type of heart disease	All cases	Patients with albuminuria					
		Grade					% of all cases
		1	2	3	4	Total	
Mitral-valve disease with or without aortic stenosis	26	8	11	4	1	24	92
Coronary-artery disease with or without hypertension	76	22	37	5	2	66	87
Isolated aortic-valve disease	26	5	11	3	3	22	85
Hypertensive heart disease	17	1	9	3	3	16	94
Myocardial hypertrophy; etiology unknown	11	2	5	1	0	8	73
Miscellaneous	5	2	2	1	0	5	100
Total	161	40	75	17	9	141	88

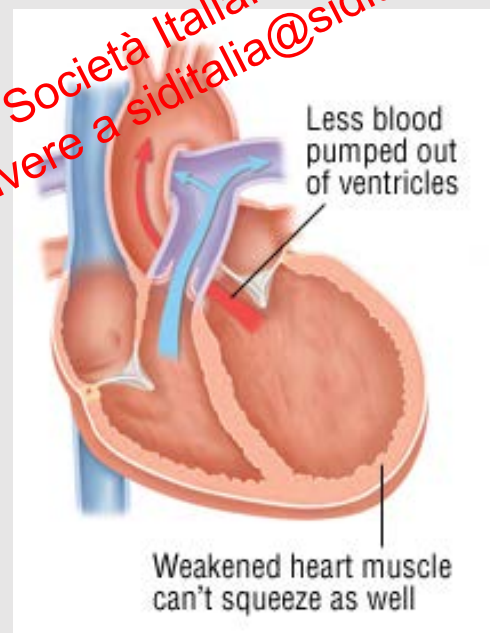
Circulation, Volume 13, March 1956

88%

CKD e scompenso cardiaco



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Modello fisiopatologico

KDIGO executive conclusions

www.kidneyinternational.org

Heart failure in chronic kidney disease: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference

Check for updates

OPEN

Kidney International (2019) **95**, 1304–1317;

Pathophysiology of heart failure in CKD progressing to ESKD

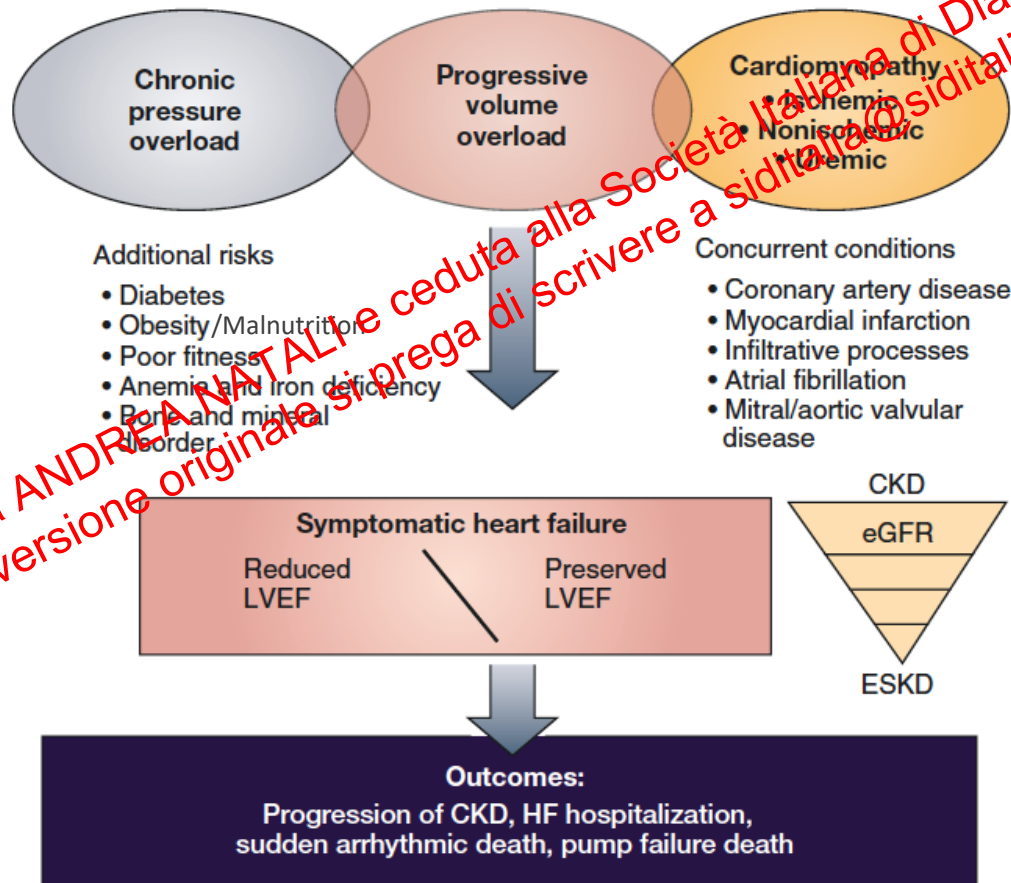
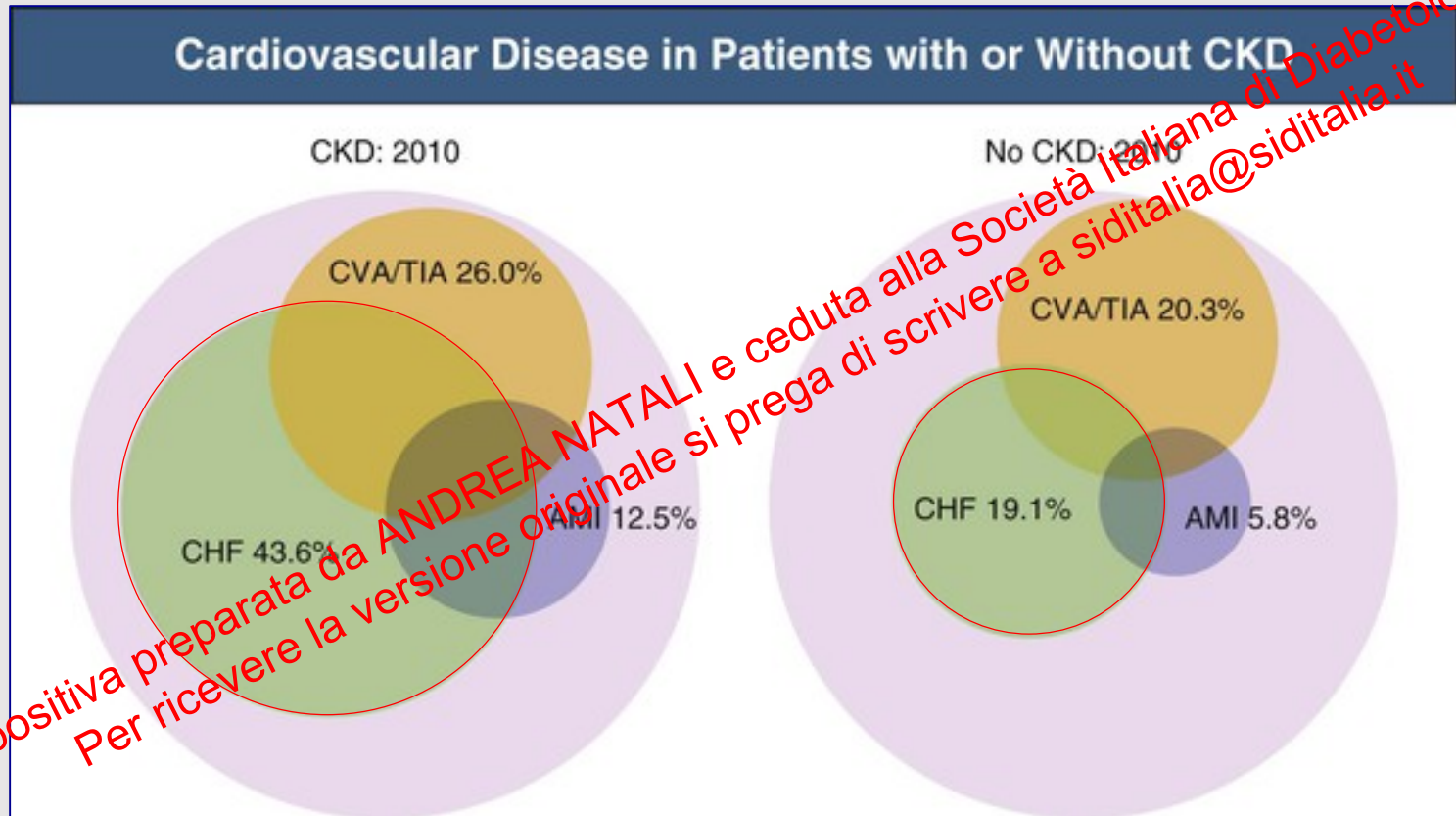
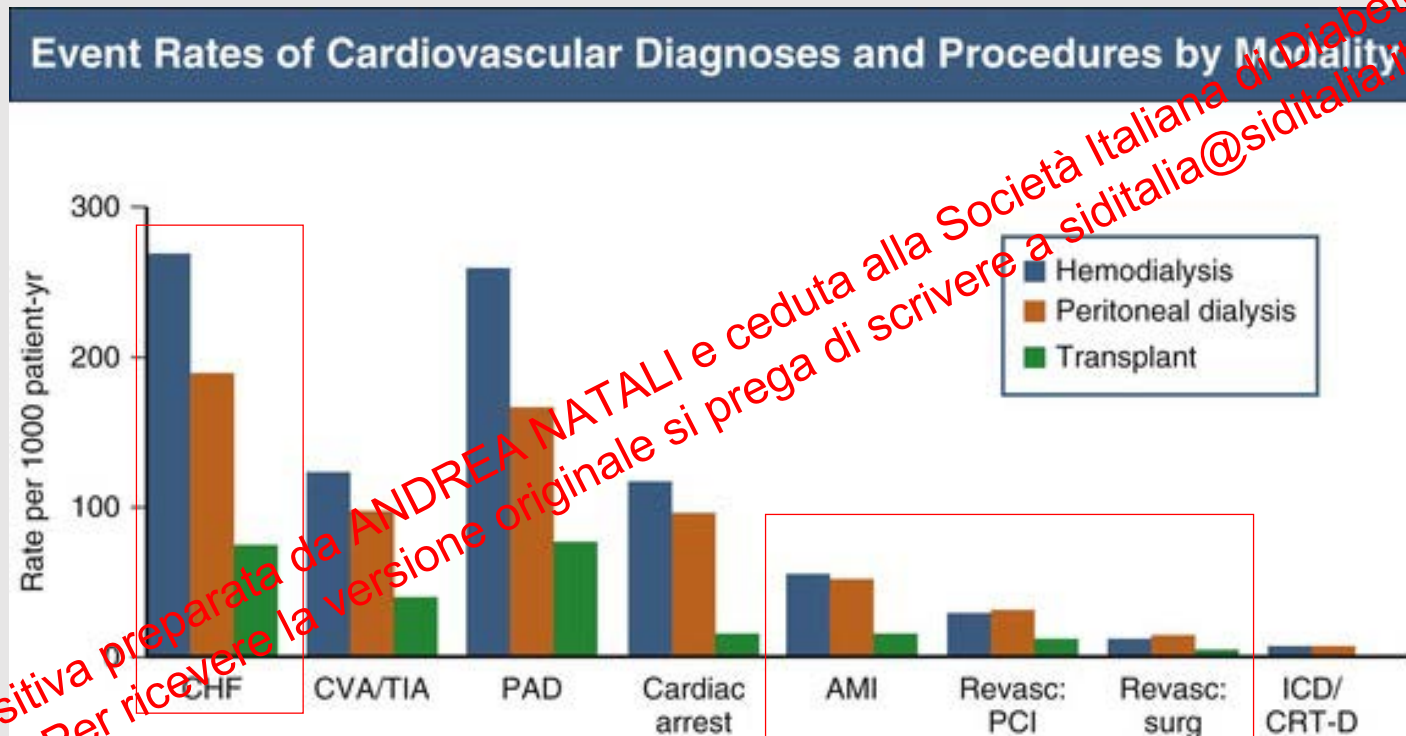


Figure 2 | Pathophysiology of heart failure (HF) in chronic kidney disease (CKD) progressing to end-stage kidney disease (ESKD). Pressure overload implies systemic hypertension. eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction.

Prevalenza



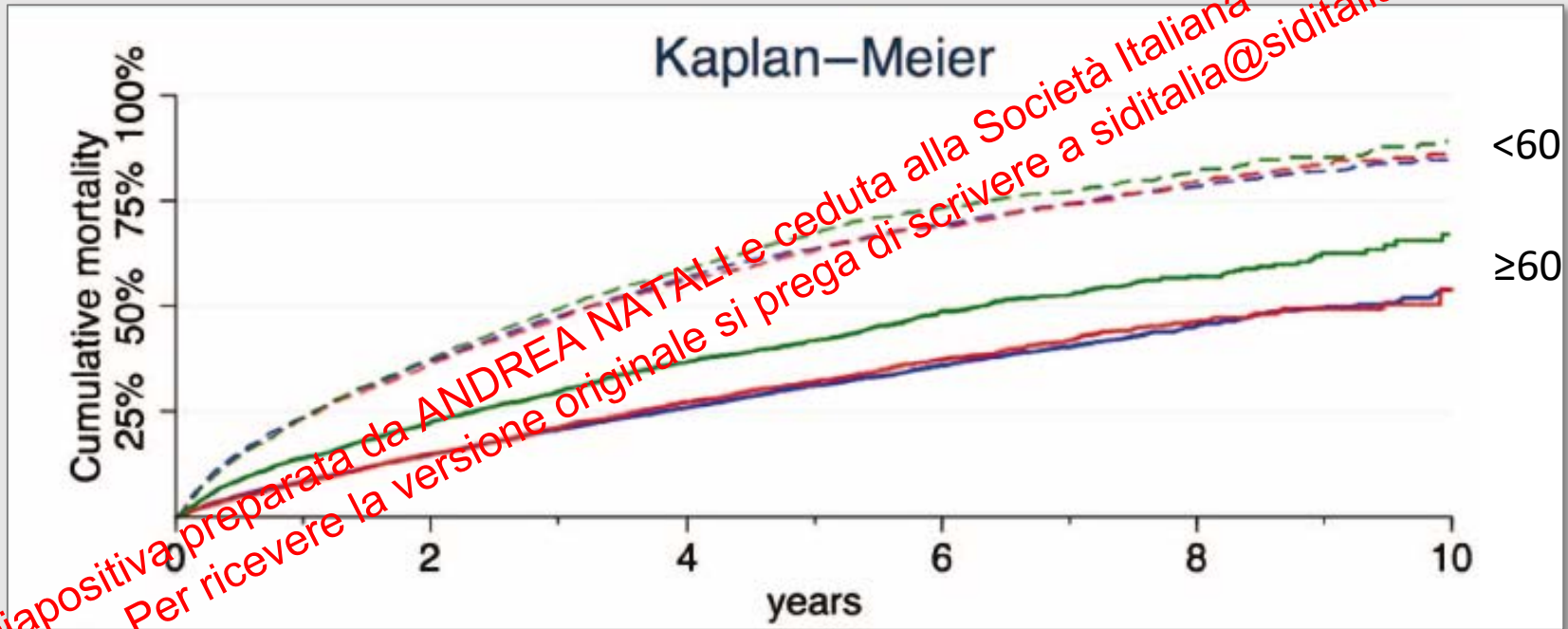
CKD ed incidenza di HF vs CHD



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eGFR e prognosi in HF

	HFpEF (n= 8860)		HFmrEF (n= 8350)		HFrEF (n= 22 953)	
	eGFR ≥60	eGFR <60	eGFR ≥60	eGFR <60	eGFR ≥60	eGFR <60
1-year mortality	13.4%	22.6*	7.8%	22.4*	8.0%	23.0*
5-year mortality	41.8%	67.1%	32.0%	63.1%	31.1%	63.7%
Deaths/100 patient-years, n	2.79	4.41	2.23	4.79	2.04	4.49



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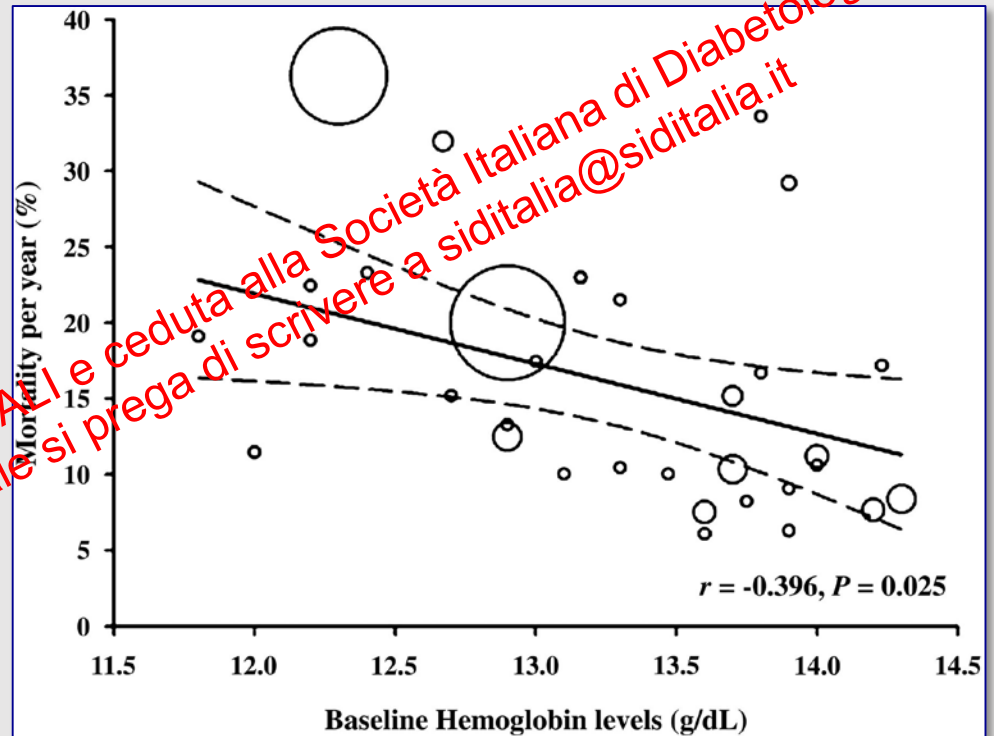
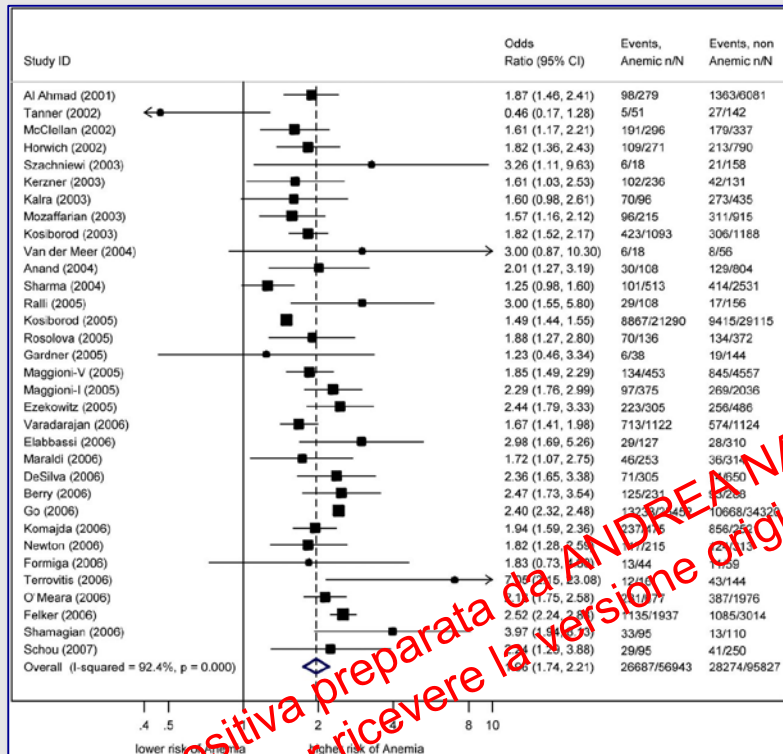
— HFrEF, eGFR ≥60	- - - HFrEF, eGFR <60
— HFmrEF, eGFR ≥60	- - - HFmrEF, eGFR <60
— HFpEF, eGFR ≥60	- - - HFpEF, eGFR <60

HR: **1.49** [1.42–1.56]

HR: **1.51** [1.40–1.63]

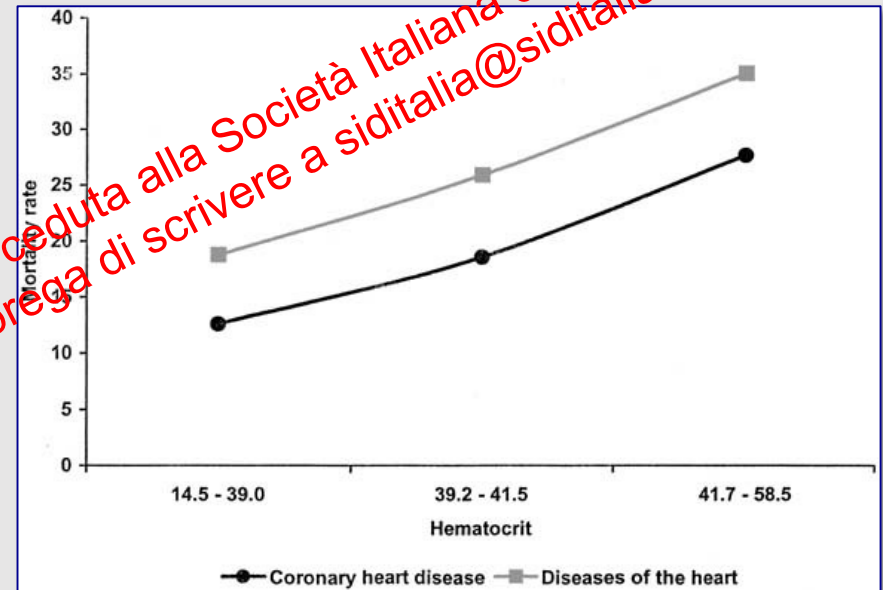
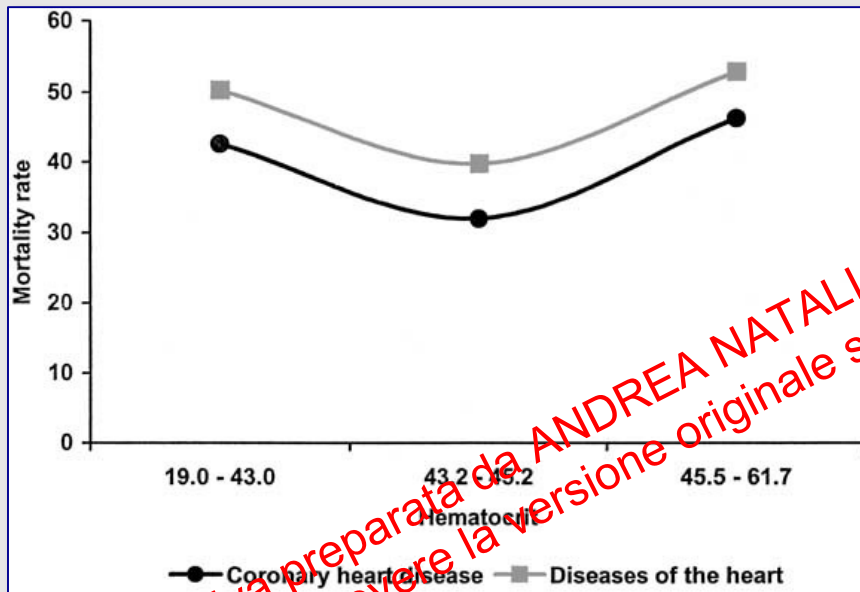
HR: **1.32** [1.24–1.42]

Anemia e prognosi in HF



Does anemia protect from CAD ?

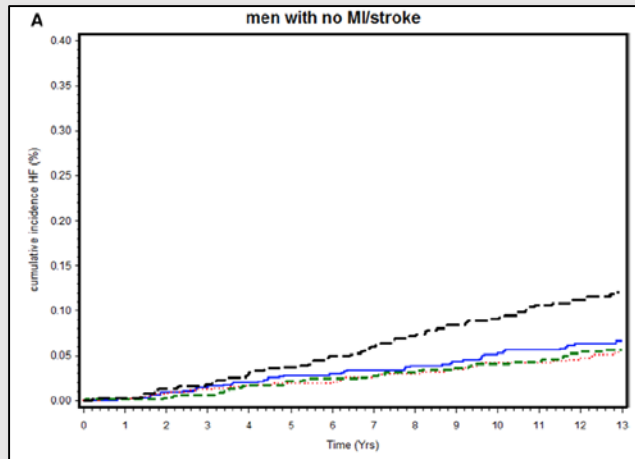
Second National Health and Nutrition Examination Survey (NHANES II) Mortality Study (1976-1992)



Brown DW, Am Heart J 2001

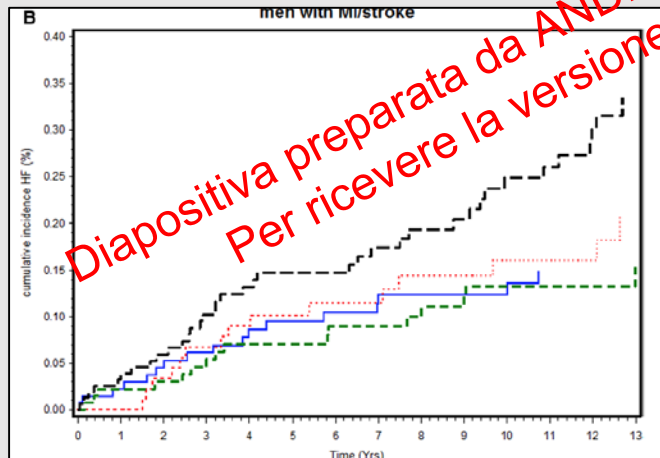
PTH and incident HF

3,731 men aged 60 to 79 years, 1 GPs 24 towns England



PTH ≥ 55.6 pg/ml

1.70 (1.25–2.30)

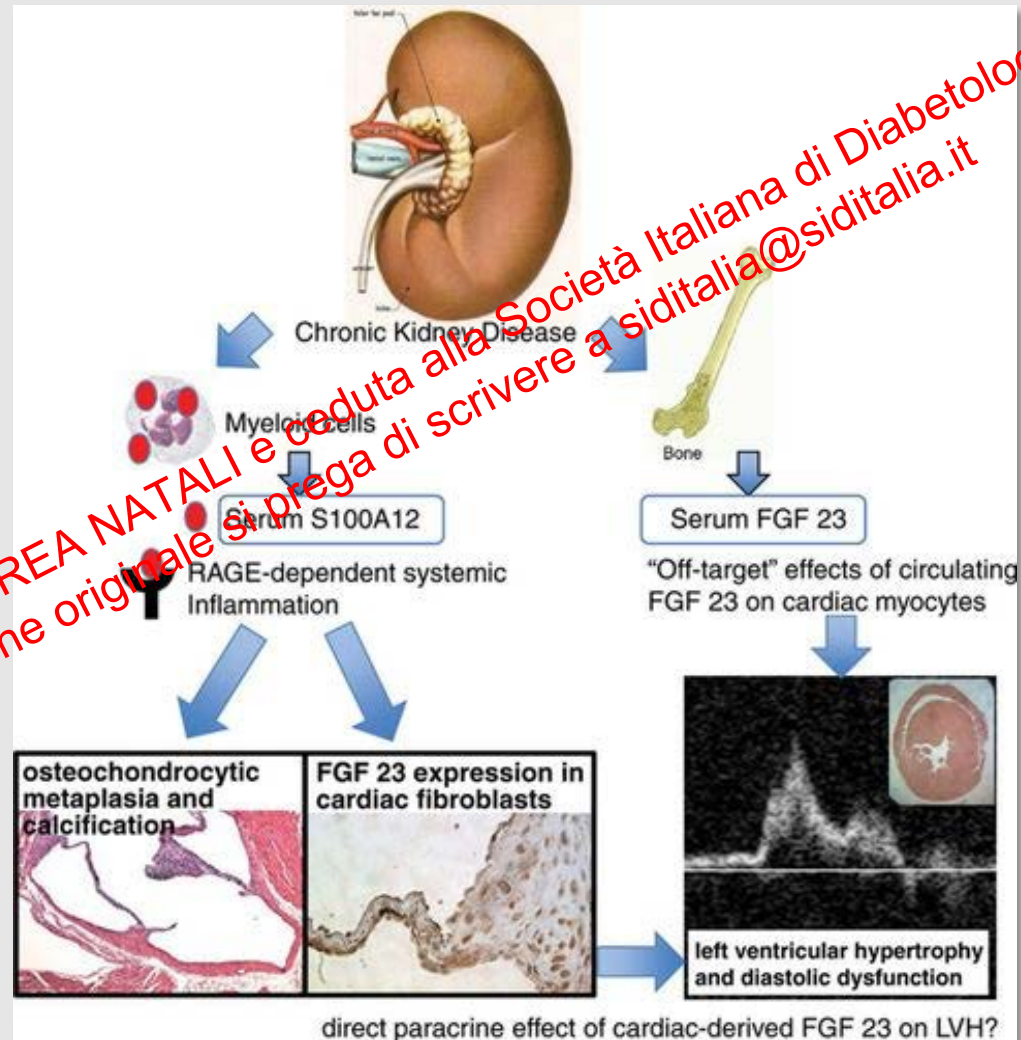
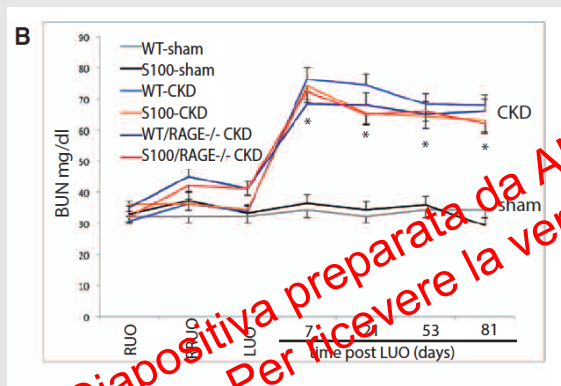
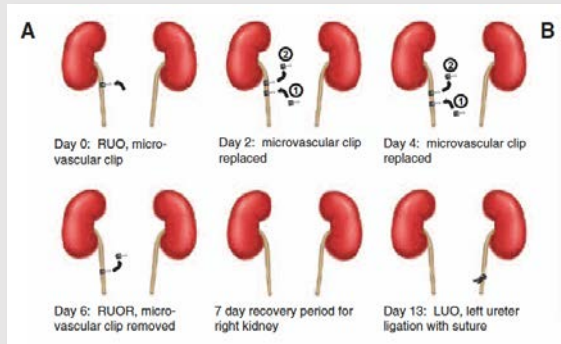


1.72 (1.07–2.76)

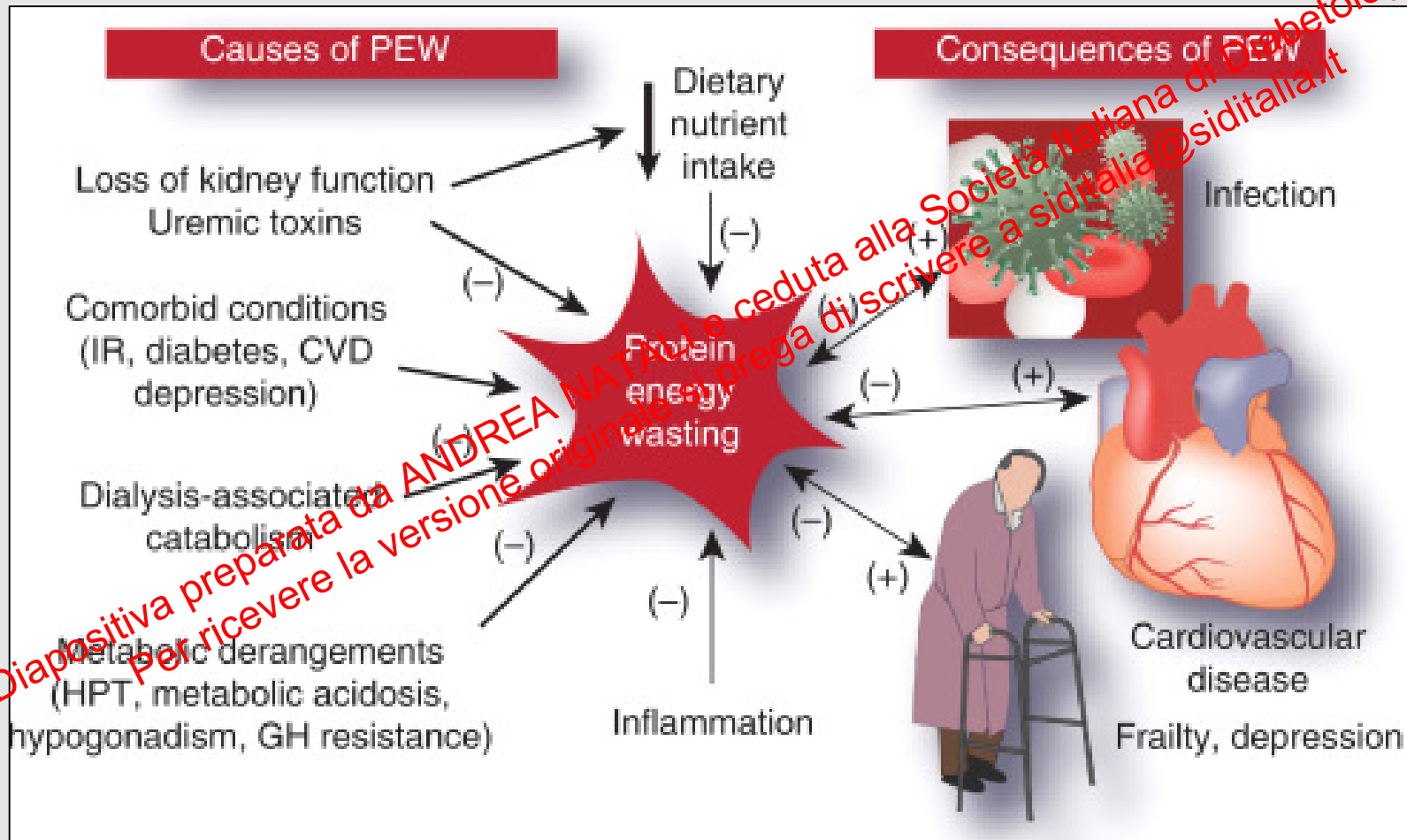
Adjusted for:

Age, smoking, social class,
alcohol intake, phys. activity,
BMI, HDL-c, diabetes
pre-existing MI/stroke, atrial
fibrillation, eGFR, heart rate
LVH, SBP, antihyp. drugs
FEV1, C-reactive protein
incident MI

Meccanismi CKD - HF



Malnutrition



In conclusione

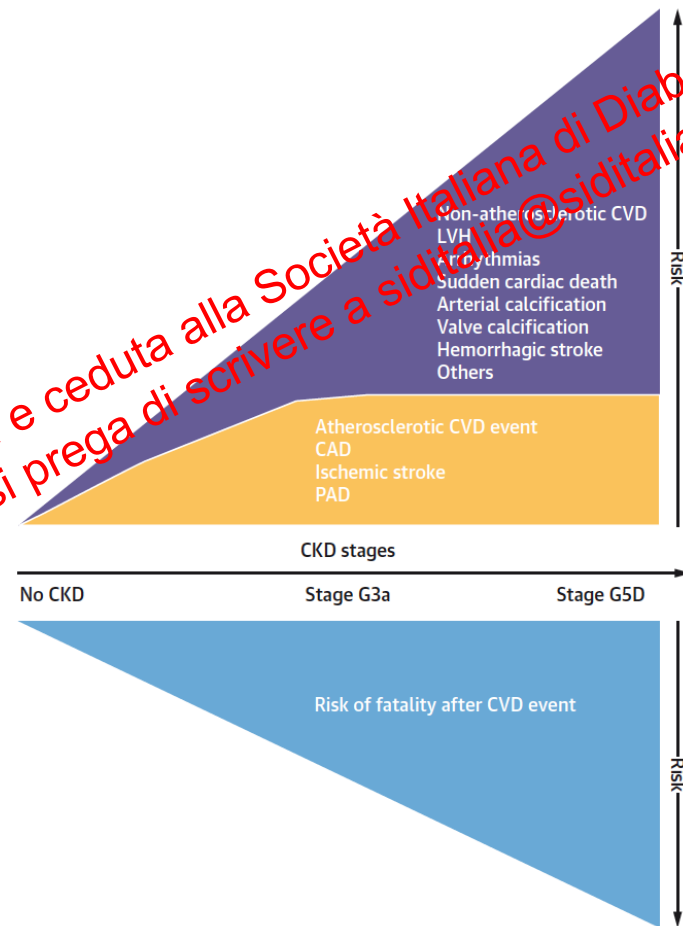
Chronic Kidney Disease and Coronary Artery Disease

JACC State-of-the-Art Review

(J Am Coll Cardiol 2019;74:1823-38)

- Sovraccarico volume
- Anemia
- Alterato metabolismo Ca/P
- Infiammazione/Malnutrizione
- Resistenza diuretici/AKI

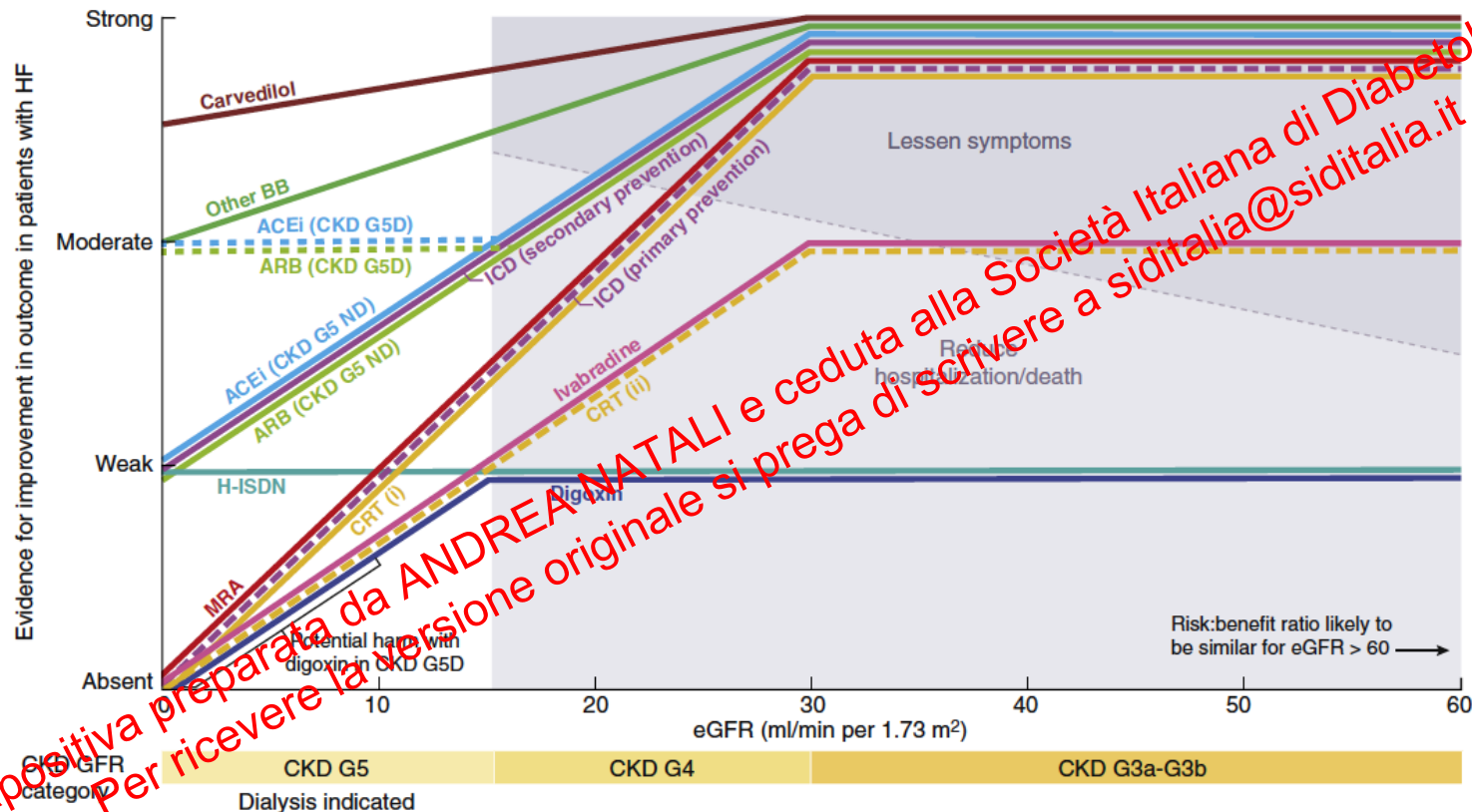
CENTRAL ILLUSTRATION Changes in Cardiovascular Disease Risk During Chronic Kidney Disease Progression



Sarnak, M.J. et al. J Am Coll Cardiol. 2019;74(14):1823-38.

Cardiovascular disease (CVD) event (upper triangle); contributions of atherosclerotic CVD (yellow); nonatherosclerotic CVD (purple), and risk of fatality after CVD event (blue). Reproduced with permission from Wanner et al. (10). CAD = coronary artery disease; LVH = left ventricular hypertrophy.

Le terapie sono meno efficaci

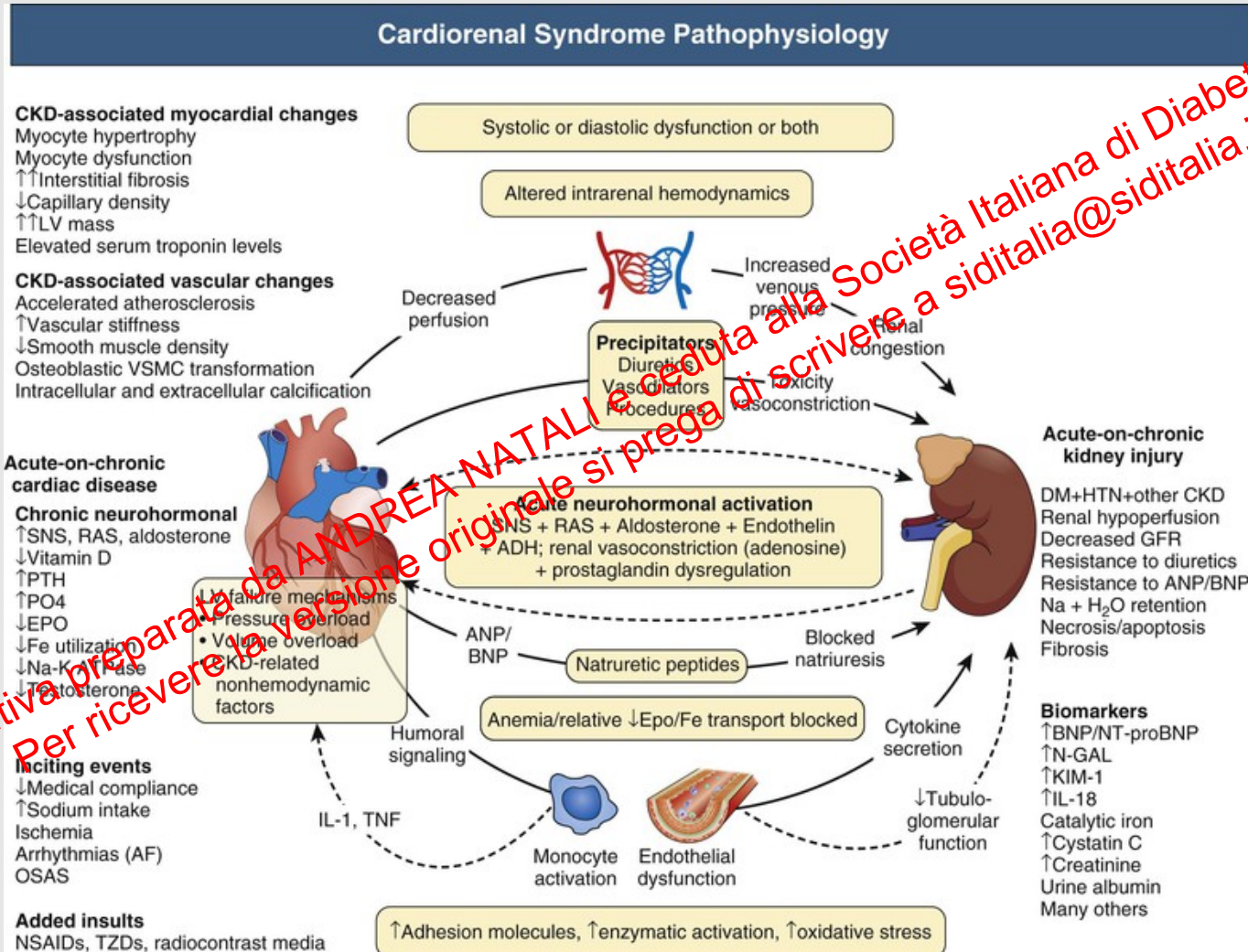


CRT (i) = QRS > 120 ms, LBBB QRS morphology, EF ≤ 35%
or QRS > 130 ms, EF ≤ 30%
CRT (ii) = QRS > 150 ms

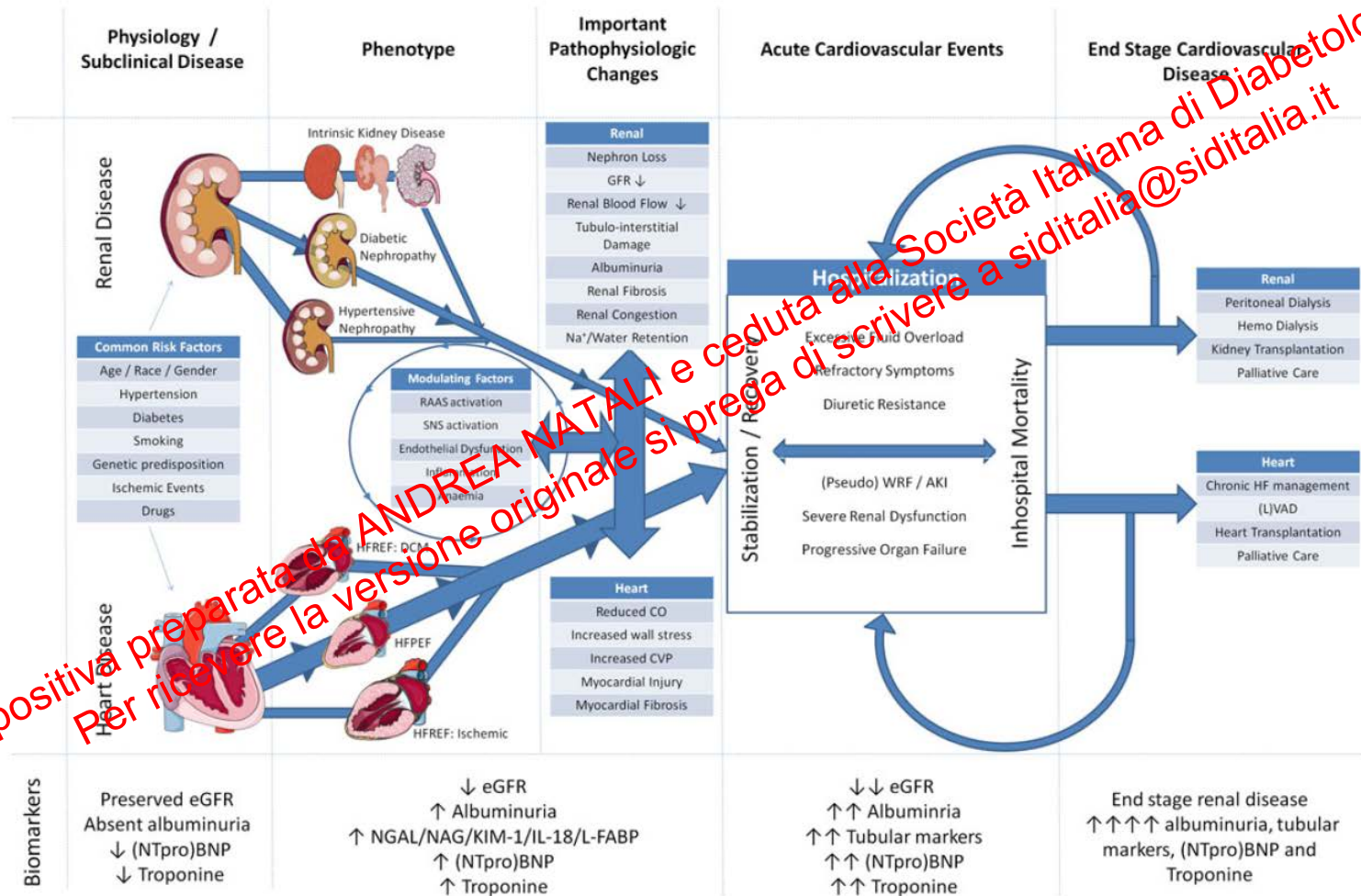
Loop diuretics (p.o./i.v.) (furosemide, bumetanide, torsemide)
and thiazide diuretics (metolazone [p.o.], chlorothiazide [i.v.])
= benefit uncertain

Figure 5 | Positioning of heart failure (HF) therapies according to left ventricular ejection fraction and renal filtration function. ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; BB, β -blocker; CKD G5D, chronic kidney disease glomerular filtration rate category 5 patient on dialysis; CKD G5 ND, chronic kidney disease glomerular filtration rate category 5 patient not on dialysis; CRT, cardiac resynchronization therapy; EF, ejection fraction; eGFR, estimated glomerular filtration rate; GFR, glomerular filtration rate; H-ISDN, hydralazine-isosorbide dinitrate; ICD, implantable cardioverter-defibrillator; LBBB, left bundle branch block; MRA, mineralocorticoid receptor antagonist.

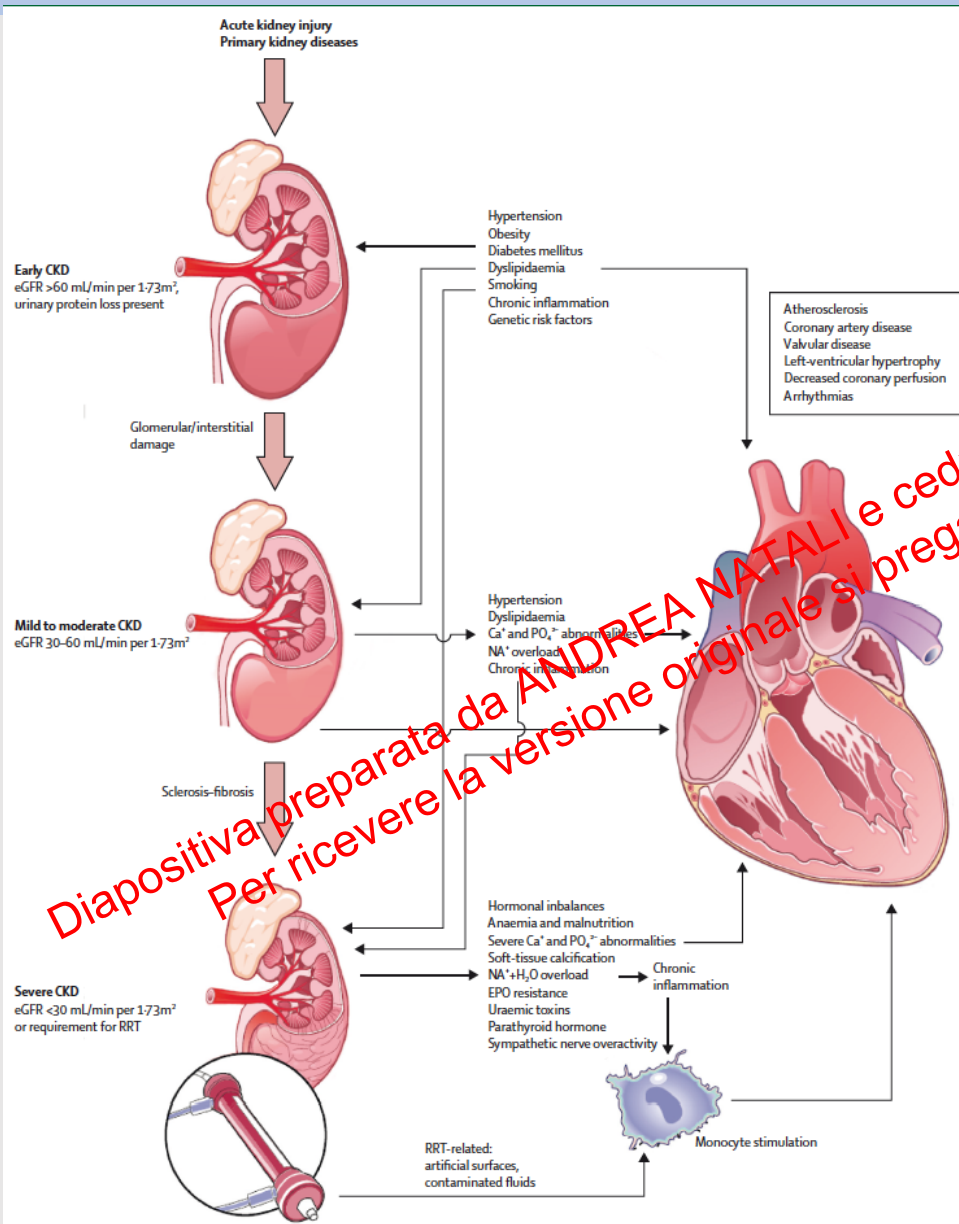
Sintesi



Outline

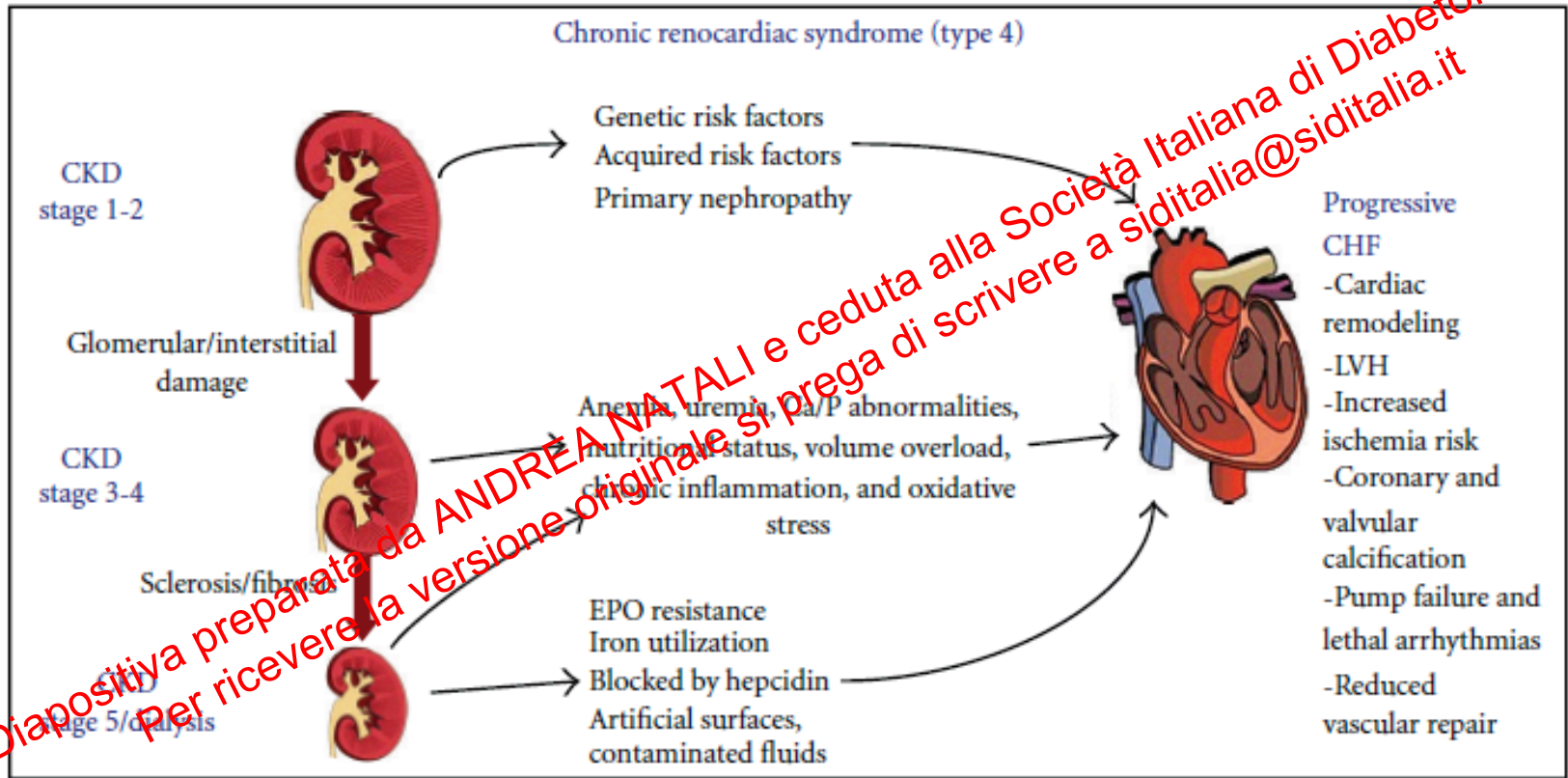


CKD = HF



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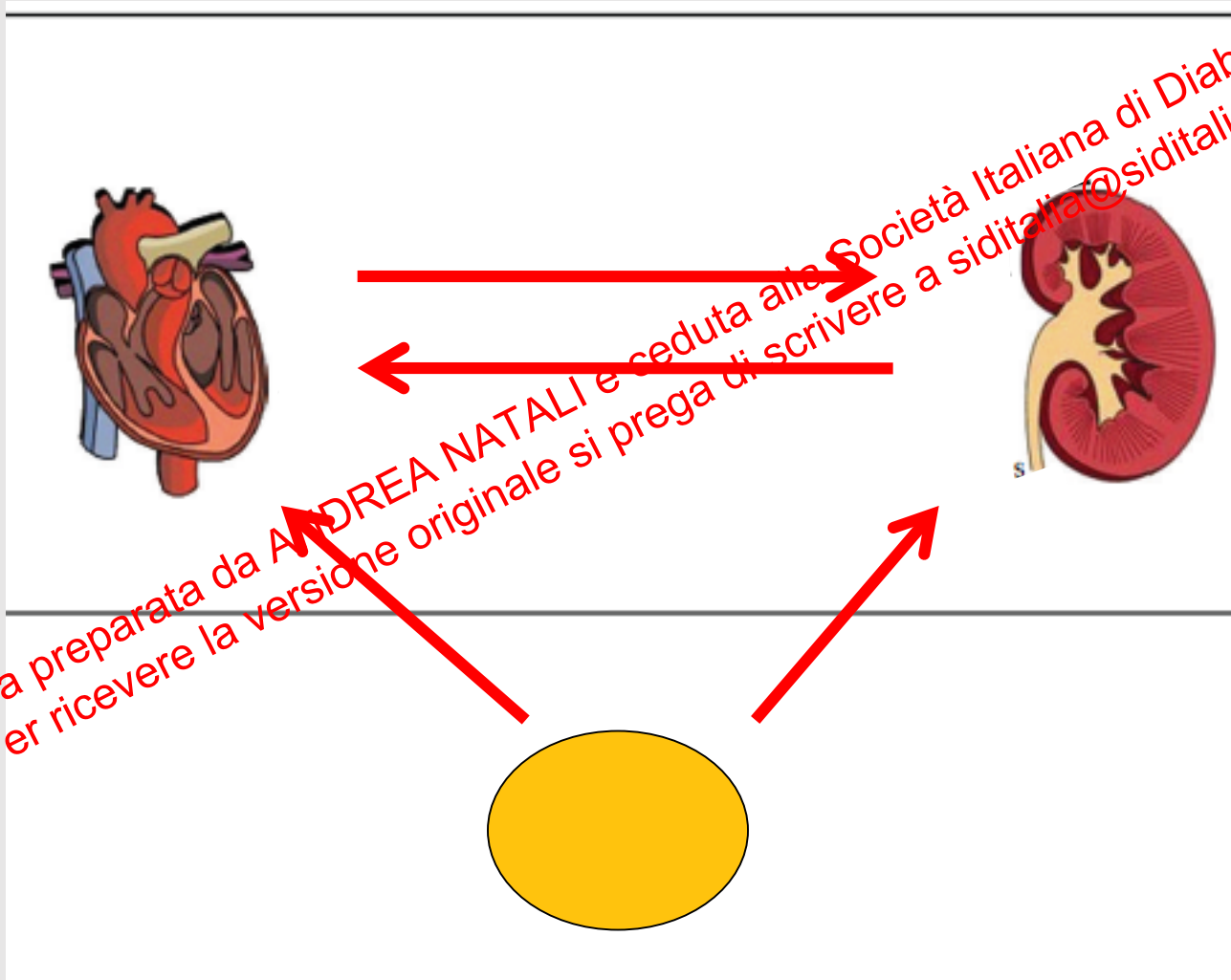
CKD = HF



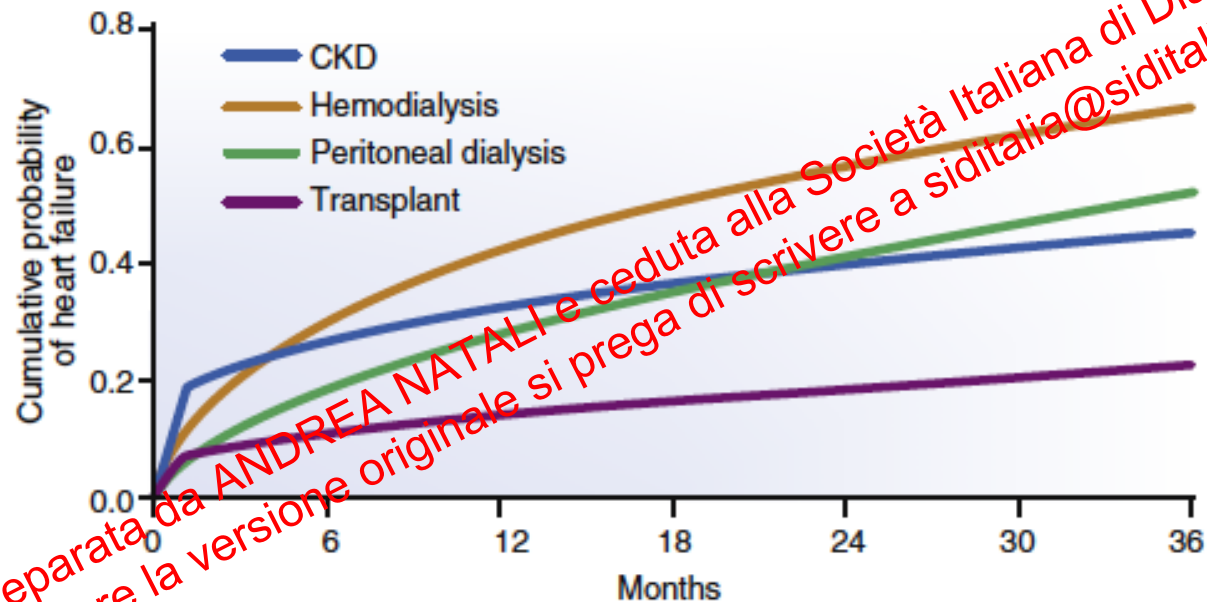
CVD risk factors in CKD

TRADIZIONALI	CORRELATI A IRC
Età avanzata Sesso maschile Ipertensione Ipertrofia ventricolare sinistra Dislipidemia Diabete mellito Fumo Inattività fisica Menopausa Storia familiare di CVD	Sovraccarico volume liquido extracellulare (ECFV) Anemia Alterato metabolismo Ca/P Infiammazione/Malnutrizione Stress ossidativo Iperomocisteinemia Fattori trombogenici Proteinuria

Rivediamo le linee guida



HF

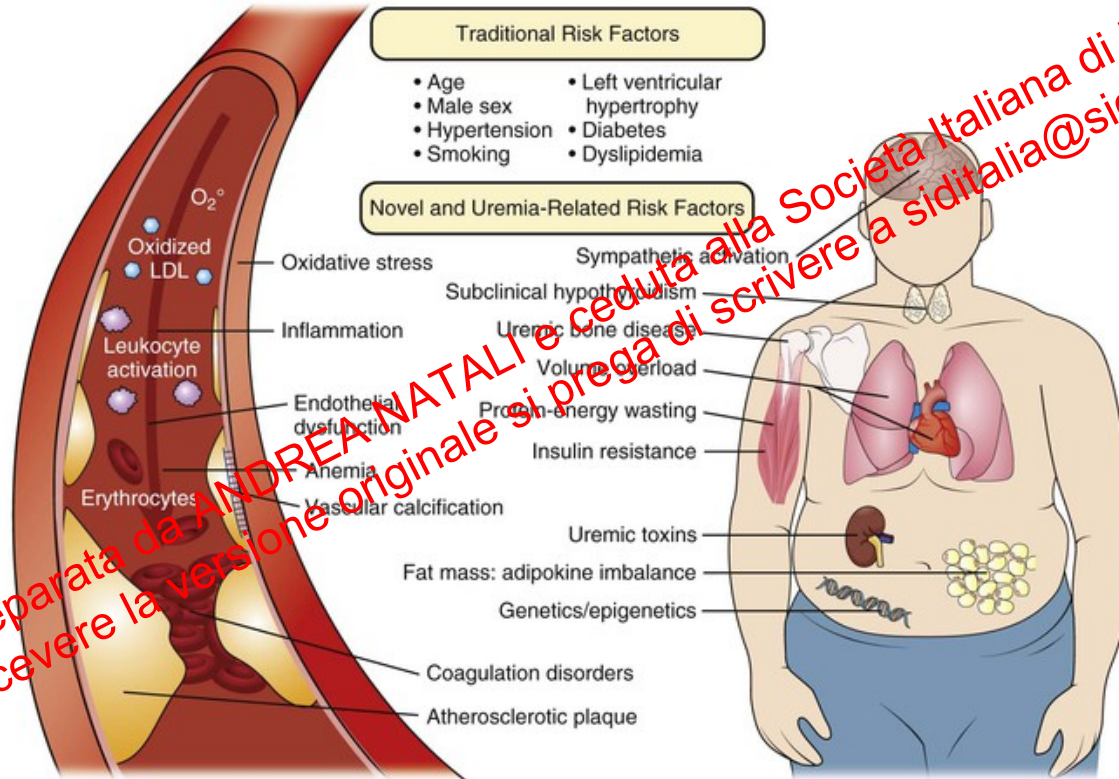


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CKD: Incident general Medicare CKD patients, age 66 & older, 2001–2003 combined
ESKD: Incident ESKD patients, age 20 & older
Patients with CHF at baseline excluded. Probabilities unadjusted

Rivediamo le linee guida

Risk Factors for Cardiovascular Disease in Chronic Kidney Disease



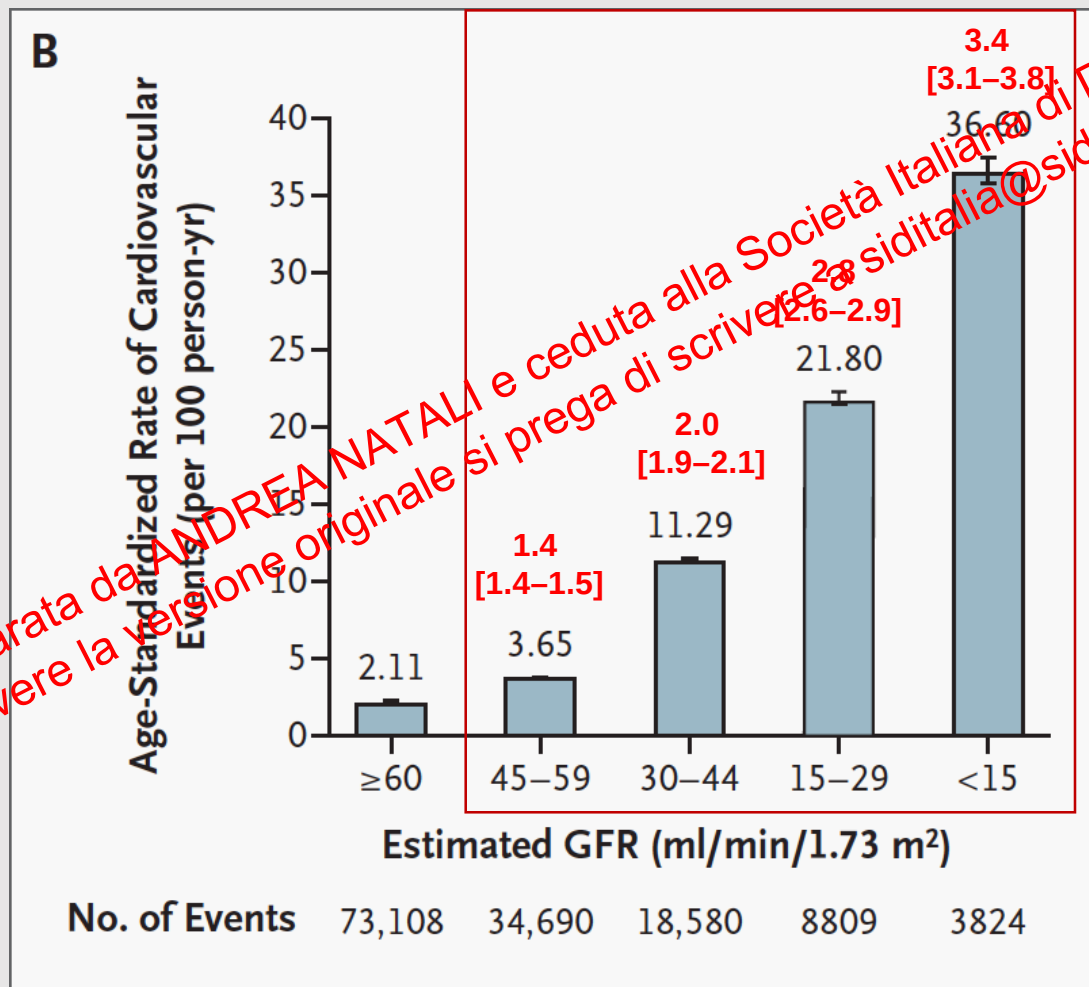
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Curva dose-risposta

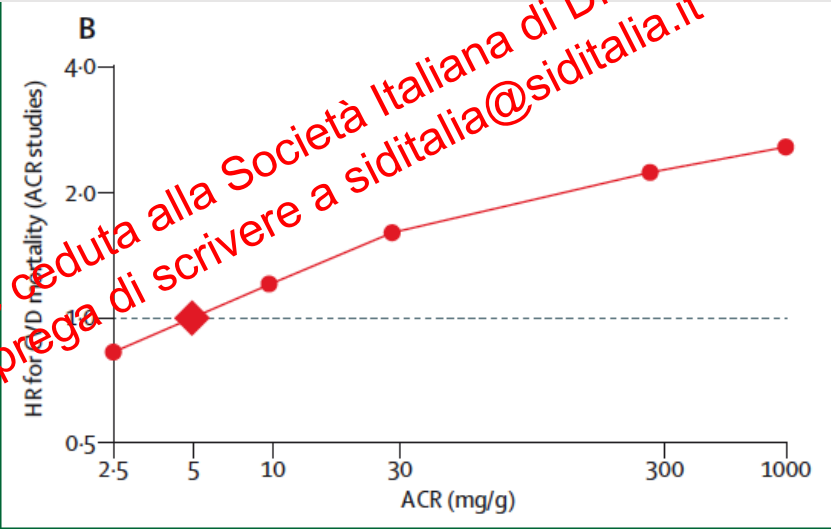
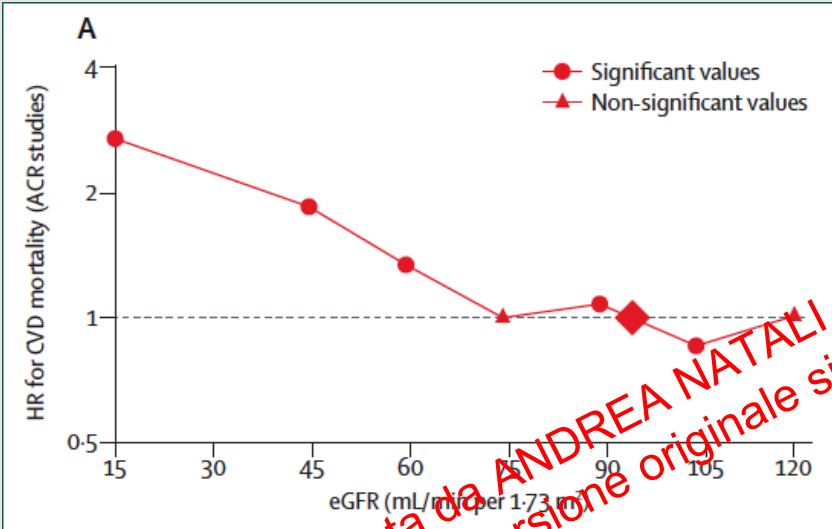
Kaiser Permanente - 1,120,295 adults, follow-up 2.84 years, age 52 yrs, 55% women



Chronic kidney disease and cardiovascular risk: epidemiology, mechanisms, and prevention

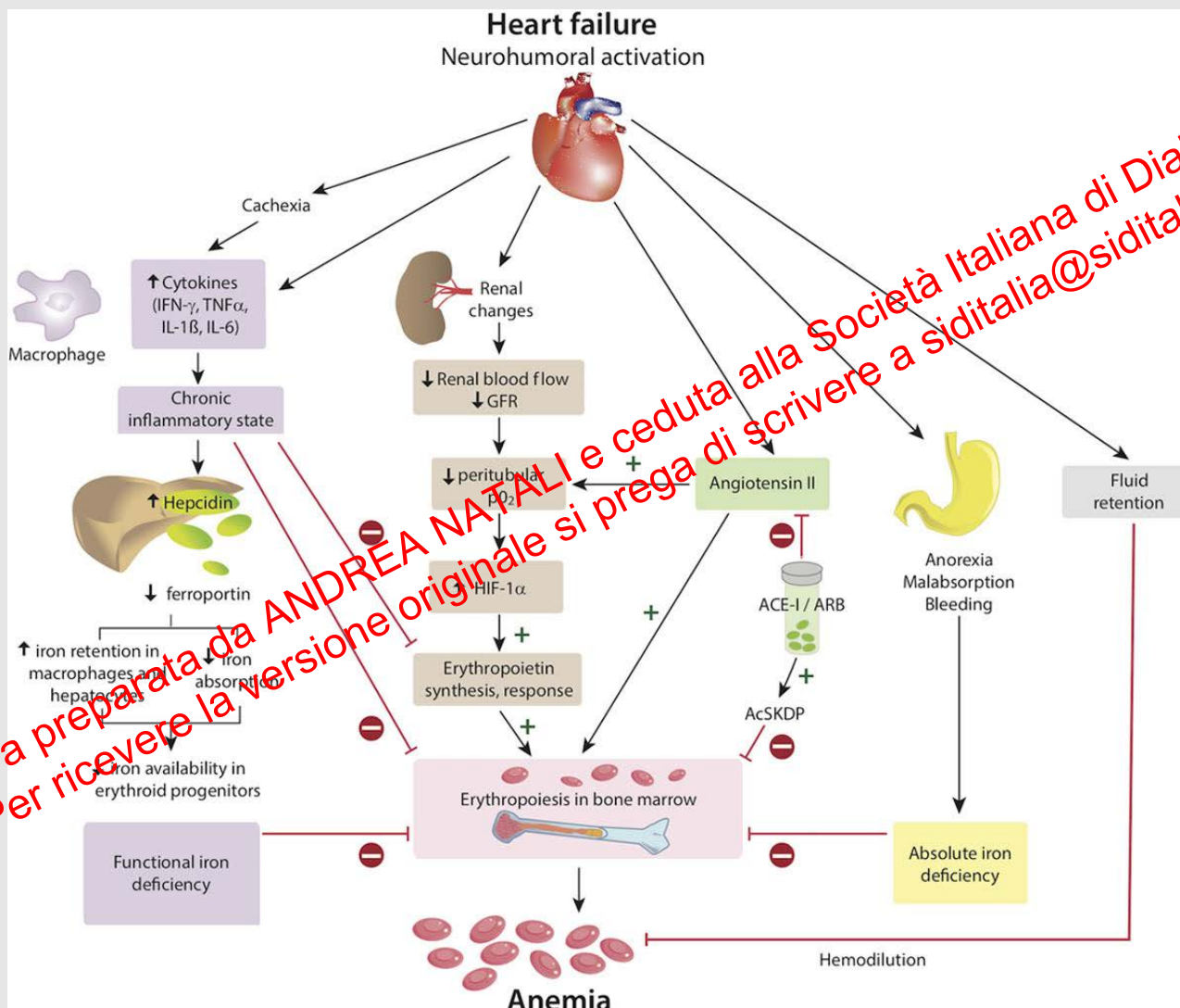
Ron T Gansevoort, Ricardo Correa-Rotter, Brenda R Hemmelgarn, Tazeen H Jafar, Hiddo J Lambers Heerspink, Johannes F Mann, Kunihiro Matsushita, Chi Pang Wen

1.4 million individuals were assessed in meta-analyses



After adjustment for traditional cardiovascular risk factors and albuminuria or eGFR

Anemia e prognosi in HF



Diapositiva preparata da ANDREA NATALI e ceduta alla Società Italiana di Diabetologia.
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Outline

Diapositiva preparata da ANDREA NATALI e ceduta alla Società Italiana di Diabetologia.
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Chronic and acute diseases/drugs

