"LA NEFROLOGIA IN ETA' GERIATRICA"

Funzione renale ed età e stima della GFR

Martino Marangella

S.C. Nefrologia e Dialisi

A.O. Ordine Mauriziano di Torino

Piano della presentazione

- **Variazioni della funzione renale con l'età: dati di popolazione, dati longitudinali**
- Modalità e attendibilità di misura della funzione renale nell'anziano
- Incidenza di CKD nell'anziano
- La nefrosclerosi senile ed il ruolo delle comorbilità
- Implicazioni cliniche della perdita di funzione

Impact of age on glomerular filtration estimates

Nephrol Dial Transplant (2009) 24: 97–103

Table 1. Characteristics of the study populations (mean ± SD)

Origin	Cohort A (outpatients with completed 24-h creatinine clearance)	Cohort B (ambulatory patients from non-hospital based clinic with normal serum creatinine)
Number	773	7551
Age	54.0 ± 16.4 years	55.8 ± 13.4 years
Range	18–90 years	18–102 years
Female	44.6%	52.8%
Body surface area	1.84 ± 0.22 m^2	NA
24-h urinary volume	2.06 ± 0.75 l	NA
24-h urinary creatinine	13.5 ± 4.3 mmol/l	NA
Serum creatinine	143 ± 93 μmol/l	75 ± 13.6 μmol/l
CCL	79.8 ± 42 ml/min/1.73 m^2	NA
CCL_c	67.2 ± 39.8 ml/min/1.73 m^2	

CCL: Cl Creat

CCL_c: Cl Creat corretta per secrezione tubulare

Impact of age on glomerular filtration estimates

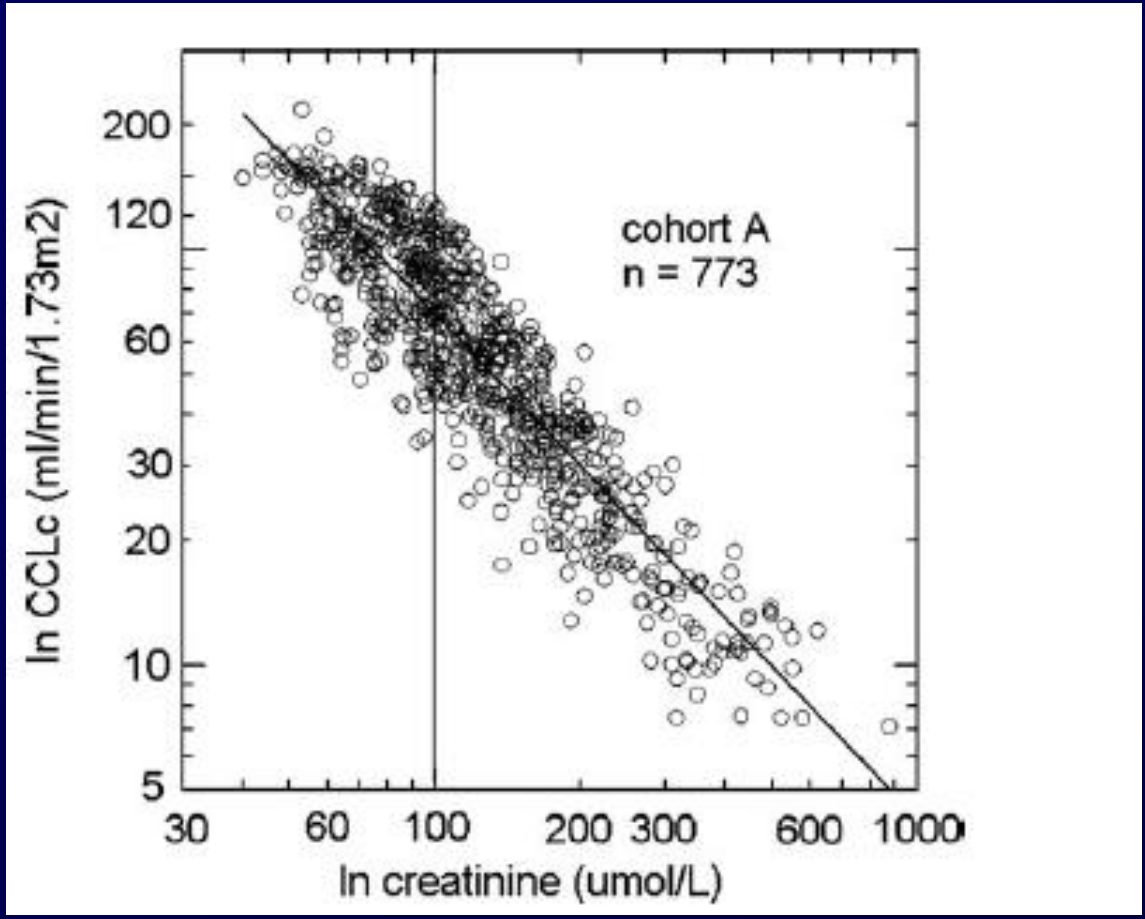
Nephrol Dial Transplant (2009) 24: 97–103

Table 2. Equations used for eGFR

MDRD exponential format	$eGFR = 186 \times (Cr/88.4)^{-1.154} \times age^{-0.203} \times 0.742$ (if female)
MDRD multiple linear format	$\ln(eGFR) = 10.398 - 1.154 \ln(Cr) - 0.203 \ln(age) - 0.298\, sex$
MAYO	$\ln(eGFR) = 1.911 + \frac{464}{Cr} - \frac{16520}{Cr^2} - 0.00686\, age - 0.205\, sex$
CHUQ (this study)	$\ln(eGFR) = 10 - 1.164 \ln(Cr) - 0.000084\, age^2 - 0.319\, sex$

Impact of age on glomerular filtration estimates

Nephrol Dial Transplant (2009) 24: 97–103



Impact of age on glomerular filtration estimates

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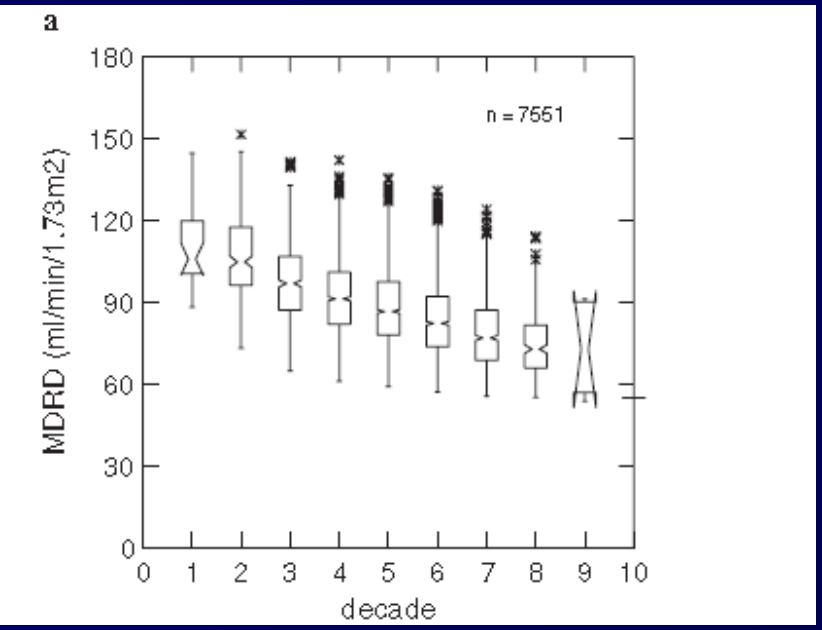
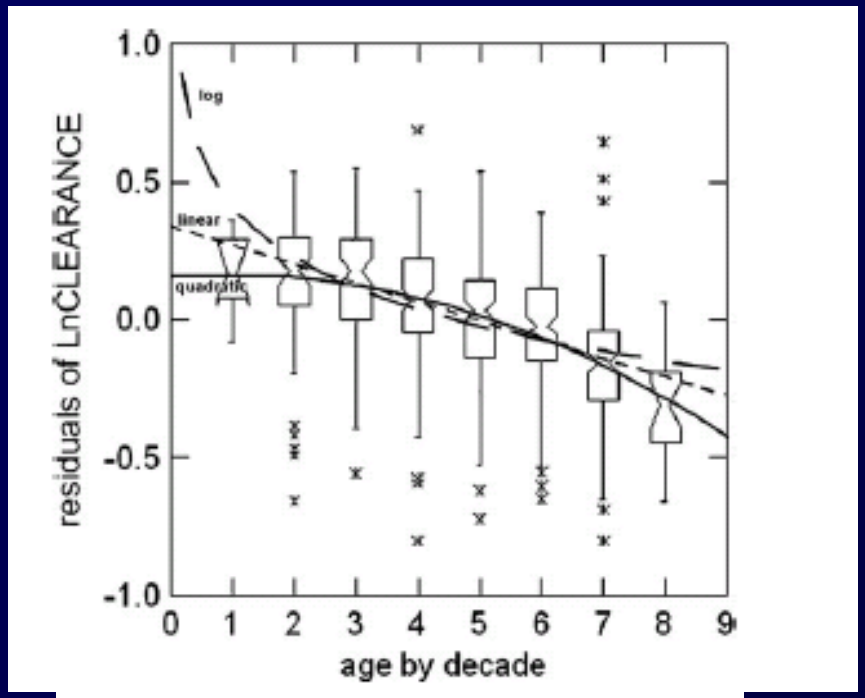
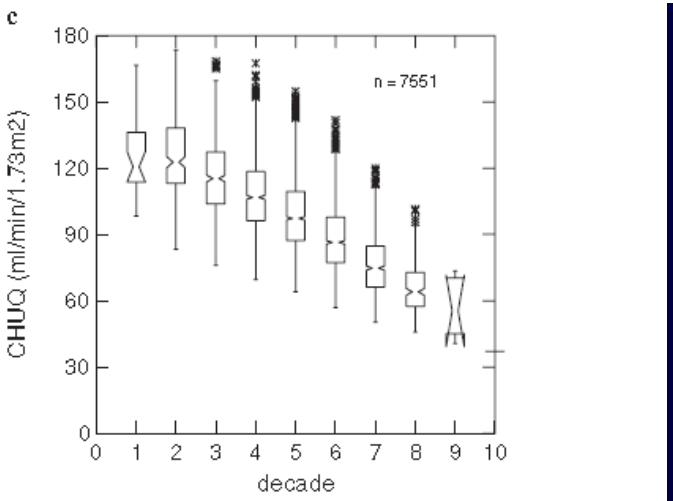


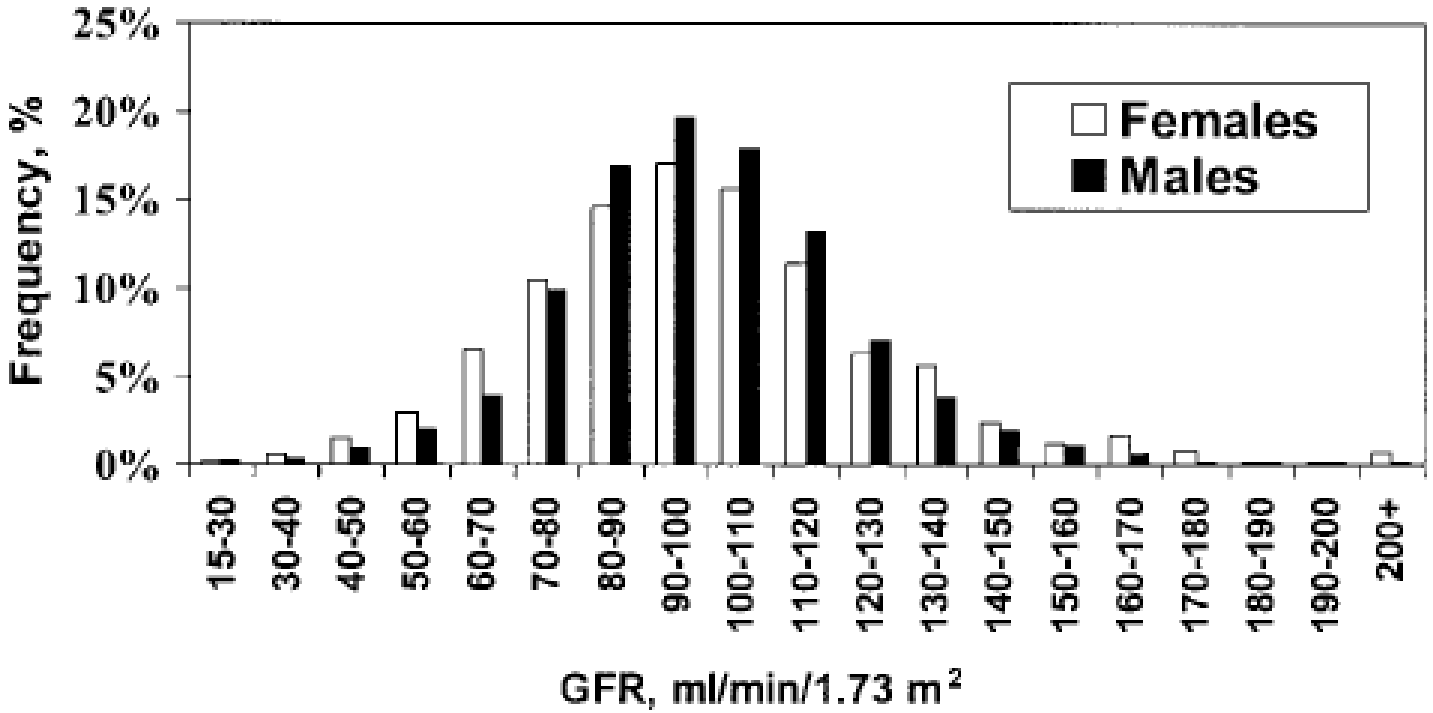


Mean decline : 5 mL/min/decade



Prevalence of Chronic Kidney Disease and Decreased Kidney Function in the Adult US Population: Third National Health and Nutrition Examination Survey

American Journal of Kidney Diseases, Vol 41, No 1 (January), 2003: pp 1-12



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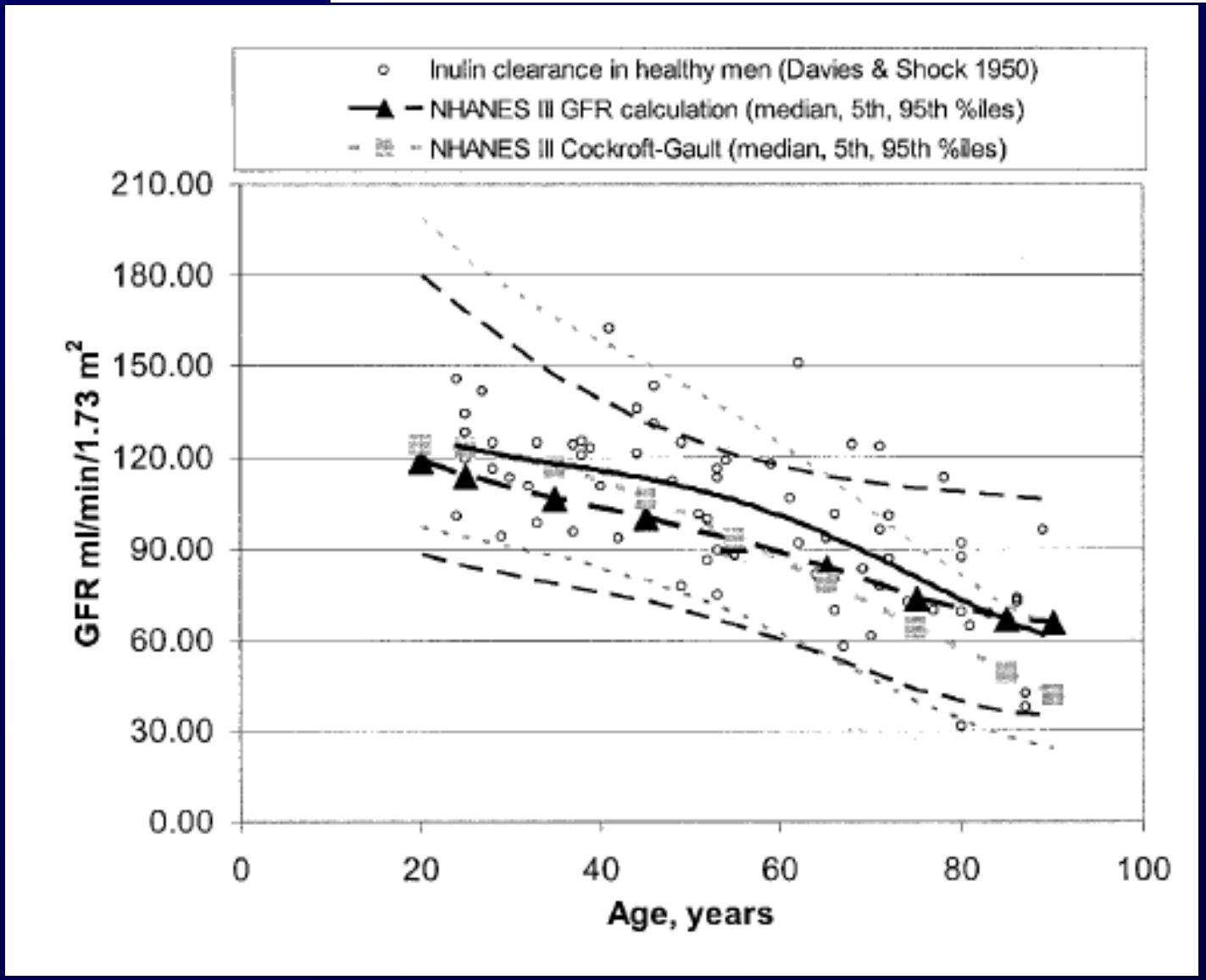
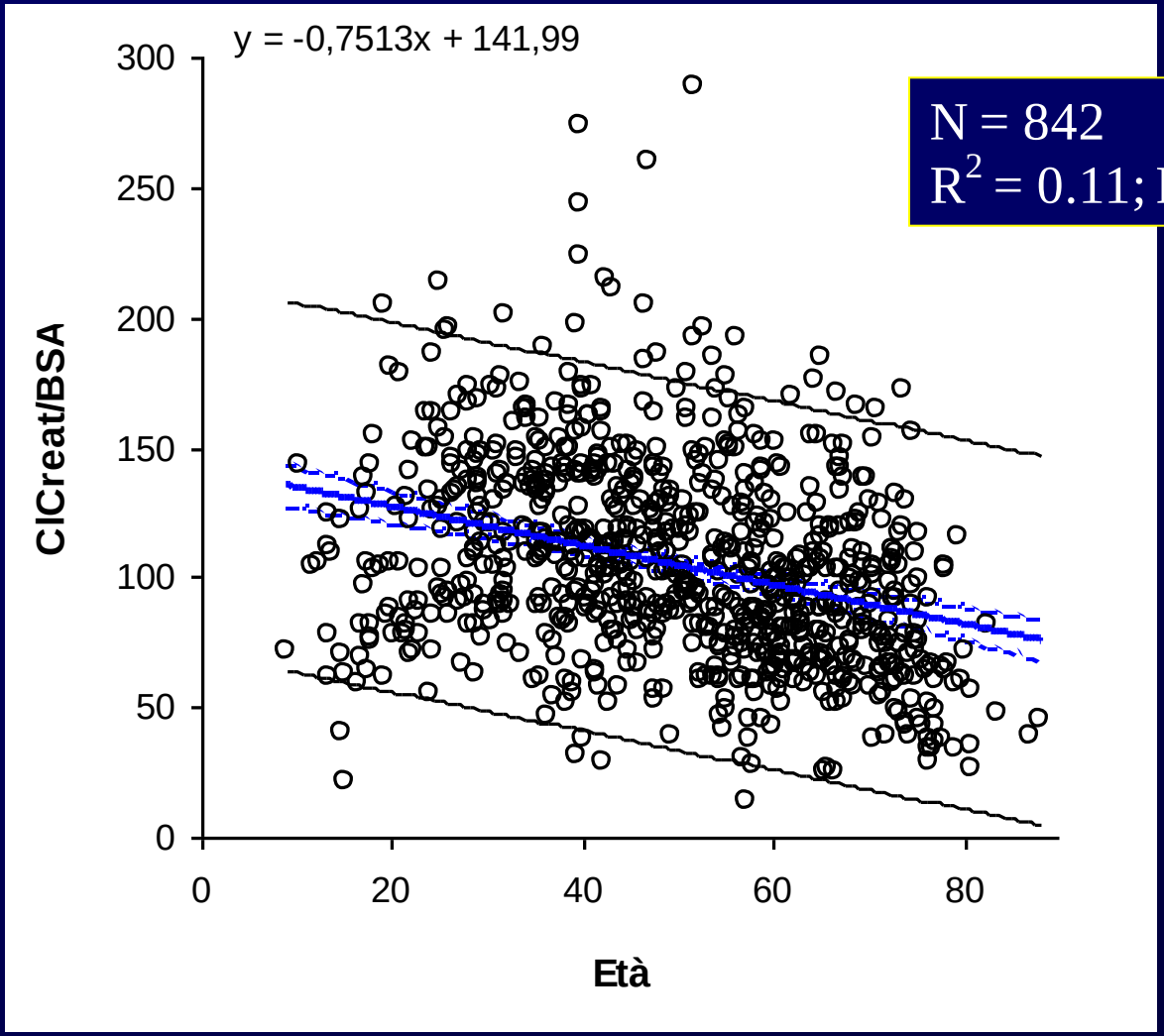
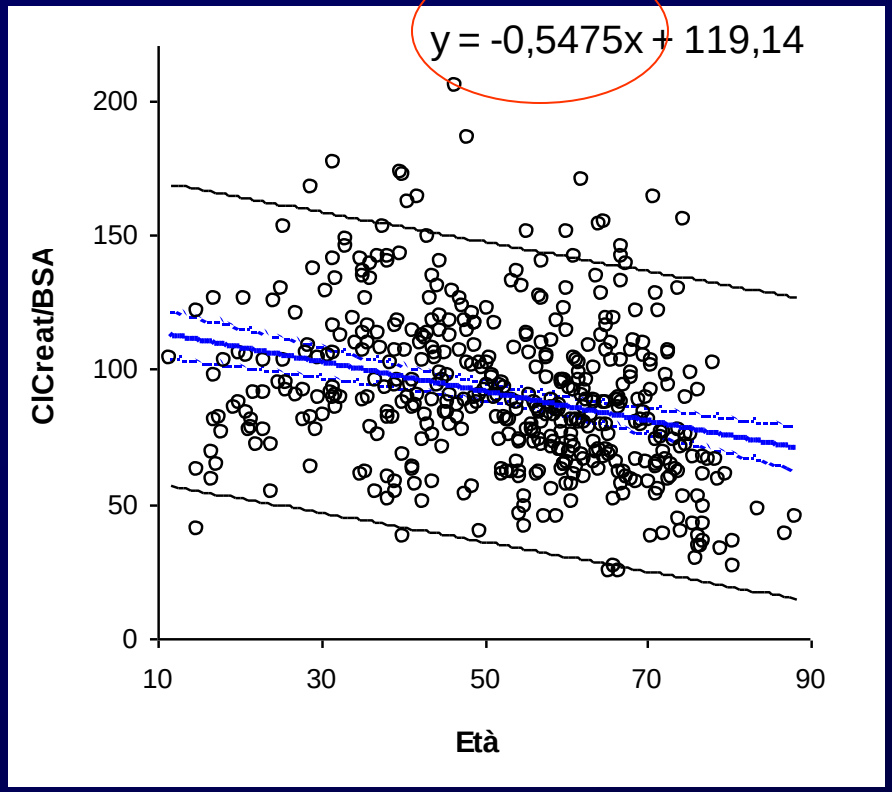


Casistica S.C. Nefrologia A.O. Mauriziano

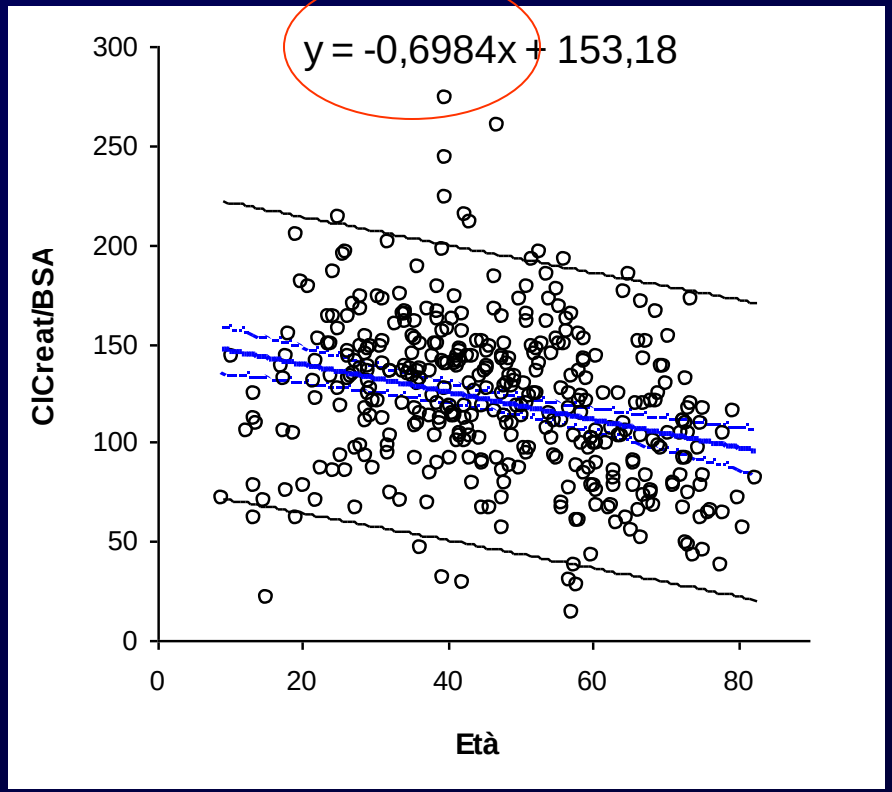


Casistica S.C. Nefrologia A.O. Mauriziano

Donne, N = 452
$R^2 = 0.10$; $P<0.0001$



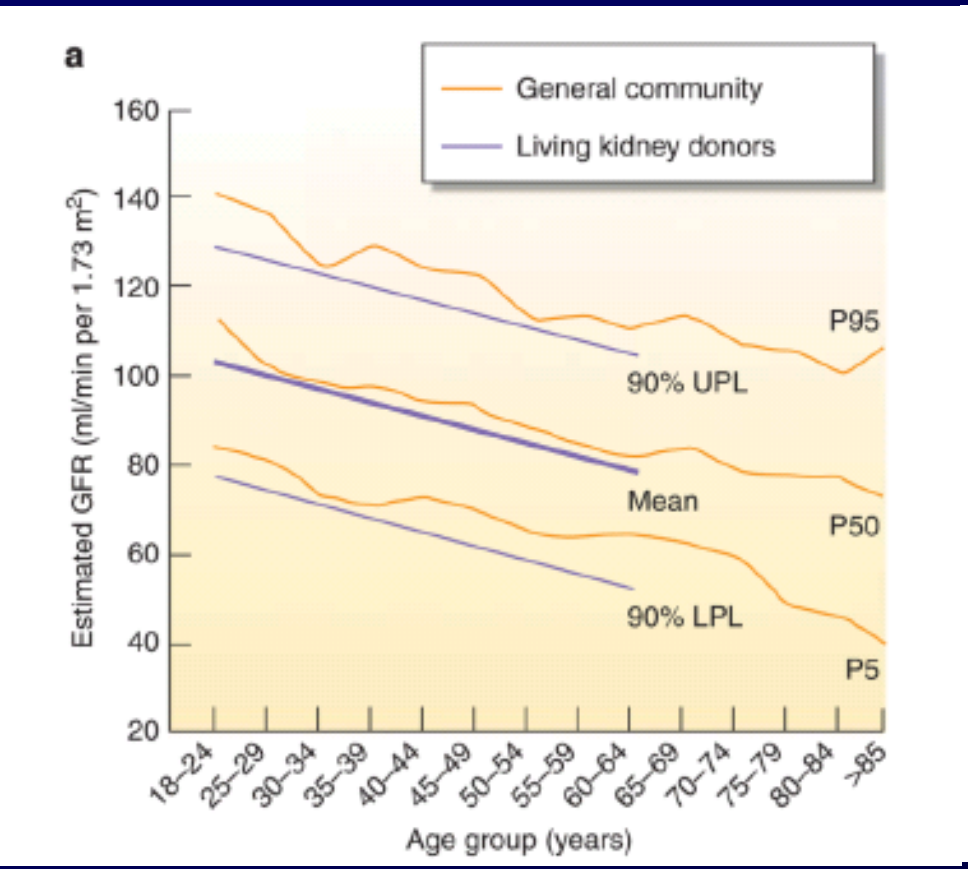
Maschi, N = 389
$R^2 = 0.10$; $P<0.0001$

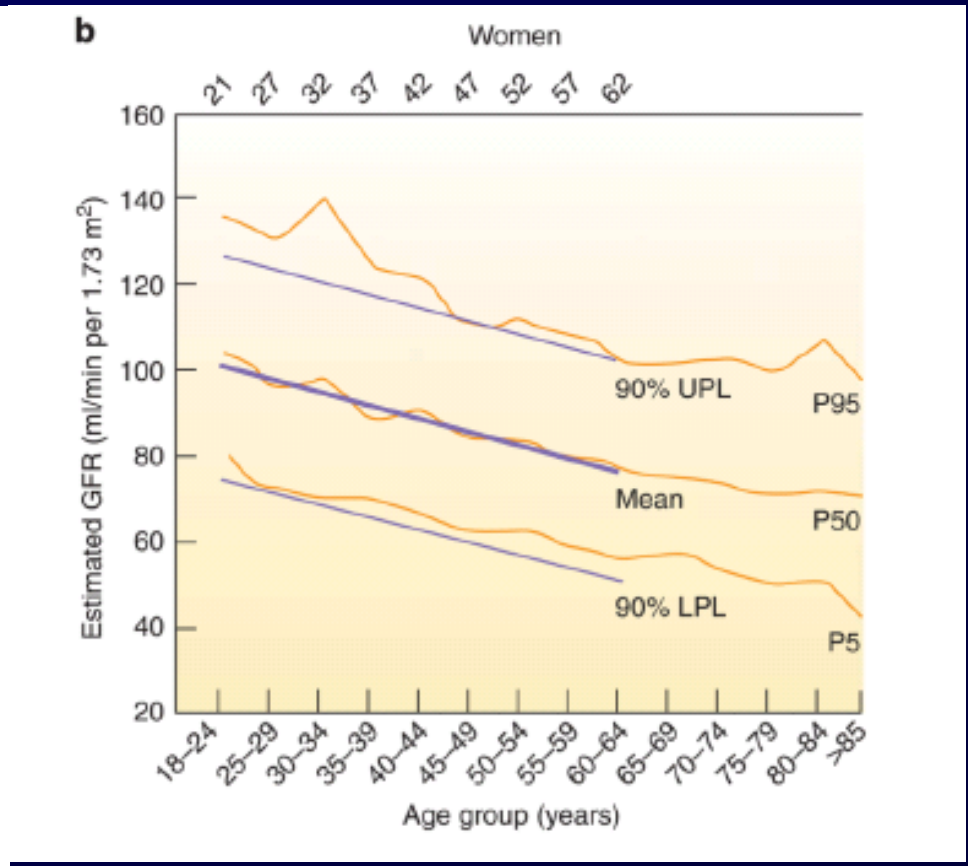


The implications of anatomical and functional changes of the aging kidney: with an emphasis on the glomeruli

Richard J. Glassock[1] and **Andrew D. Rule**[2]

Kidney Int. 2012 August ; 82(3): 270–277.





Longitudinal studies on the rate of decline in renal function with age

Lindeman RD, Tobin J, Shock NW. J Am Geriatr Soc. 1985

- Jn a group of 254 "normal" subjects, the mean decrease in creatinine clearance was 0.75 ml/min/year over a 23-year follow-up
- The slopes of the creatinine clearance vs. time fell into a normal distribution around this mean.
- One third of all subjects followed had no absolute decrease in renal function
- A small group of patients showed a statistically significant increase ($P < 0.05$) in creatinine clearance with age.

Piano della presentazione

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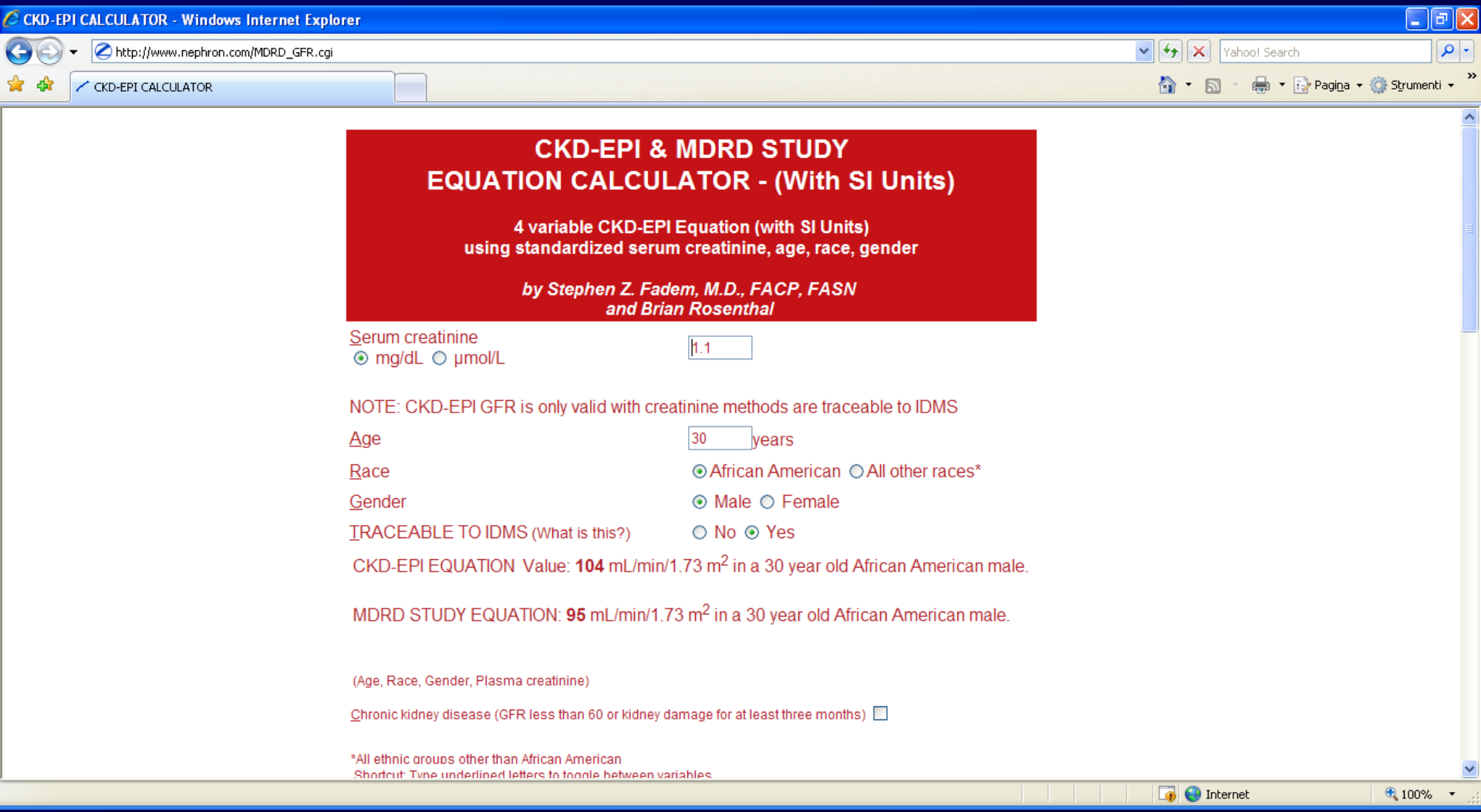
eGFR : Calcolo con la formula MDRD o CKD-EPI

uso di sCr standardizzata



Accuracy of the MDRD (Modification of Diet in Renal Disease) Study and CKD-EPI (CKD Epidemiology Collaboration) Equations for Estimation of GFR in the Elderly

Am J Kidney Dis. 2013;61(1):57-66

Setting & Participants: Participants (n = 394; median age, 80 [range, 74-97] years)

Index Test: GFR estimated using the MDRD Study, CKD-EPI$_{cr}$, CKD-EPI$_{cys}$ and CKD-EPI$_{cr\text{-}cys}$ equations.

Reference Test: GFR measured using an iohexol clearance method.

Accuracy

(percentage of estimates within 30% of measured GFR [P_{30}]) was 81%, 83%, 86%, and 86% for the MDRD Study, CKD-EPI$_{cr}$, CKD-EPI$_{cys}$, and CKD-EPI$_{cr\text{-}cys}$ equations, respectively. Accuracy of the MDRD Study equation was inferior ($P = 0.004$) to the CKD-EPI$_{cr}$ equation at GFR >60 mL/min/1.73 m^2.

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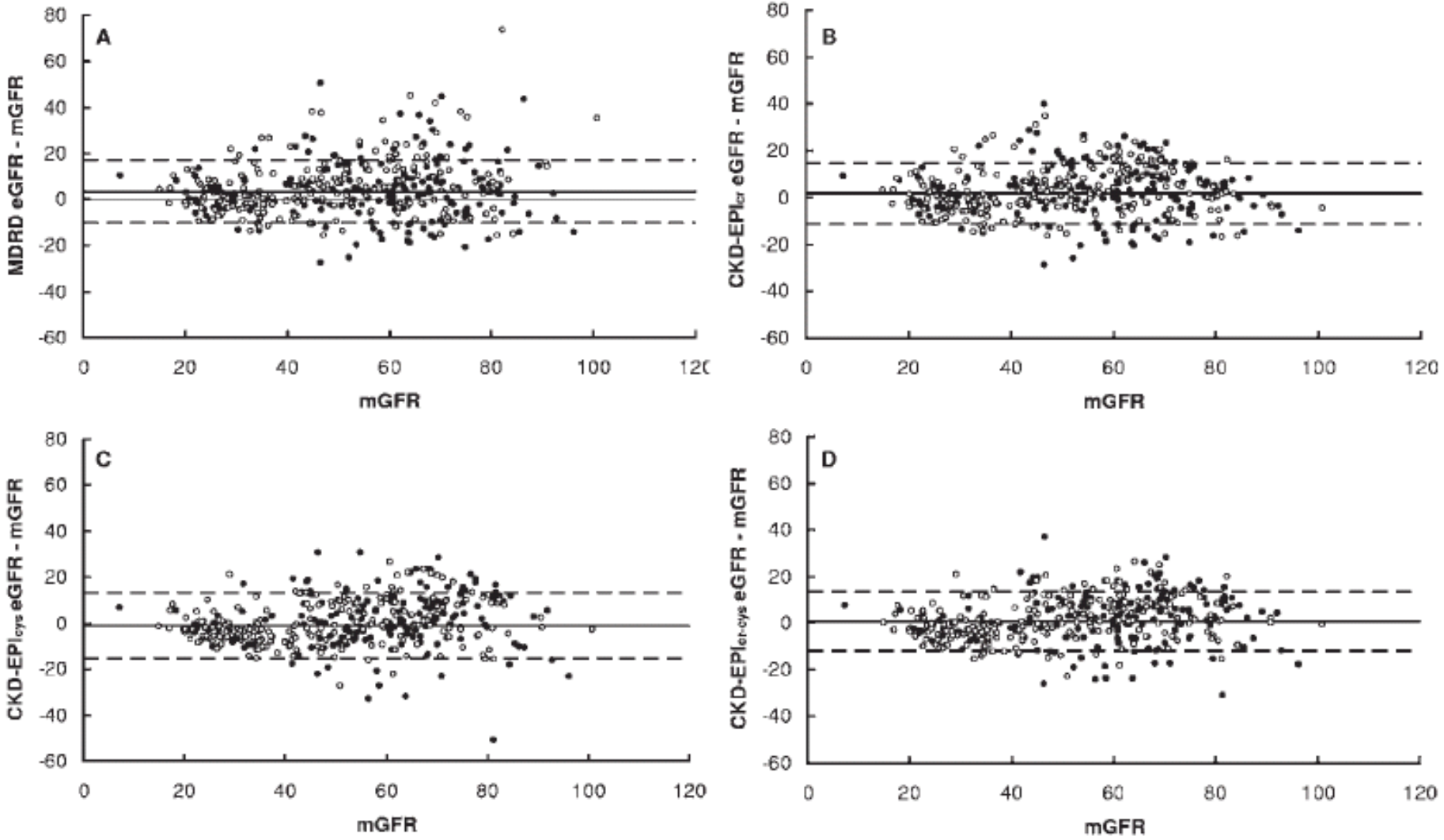


Accuracy of the MDRD (Modification of Diet in Renal Disease) Study and CKD-EPI (CKD Epidemiology Collaboration) Equations for Estimation of GFR in the Elderly

Am J Kidney Dis. 2013;61(1):57-66

CONCLUSIONI

1. CKD-EPI$_{Cr}$ più accurata rispetto ad MDRD, ma solo per eGFR > 60 mL/min/1.73 m^2
2. La misura di accuratezza (differenza di ±15% rispetto a Cl Iohexolo) variava fra 81-86%
3. La stima del filtrato glomerulare con eGFR dà risultati soddisfacenti anche nella popolazione anziana

How to assess renal function in the geriatric population

JNEPHROL 2010; 23 (S15): S46-S54

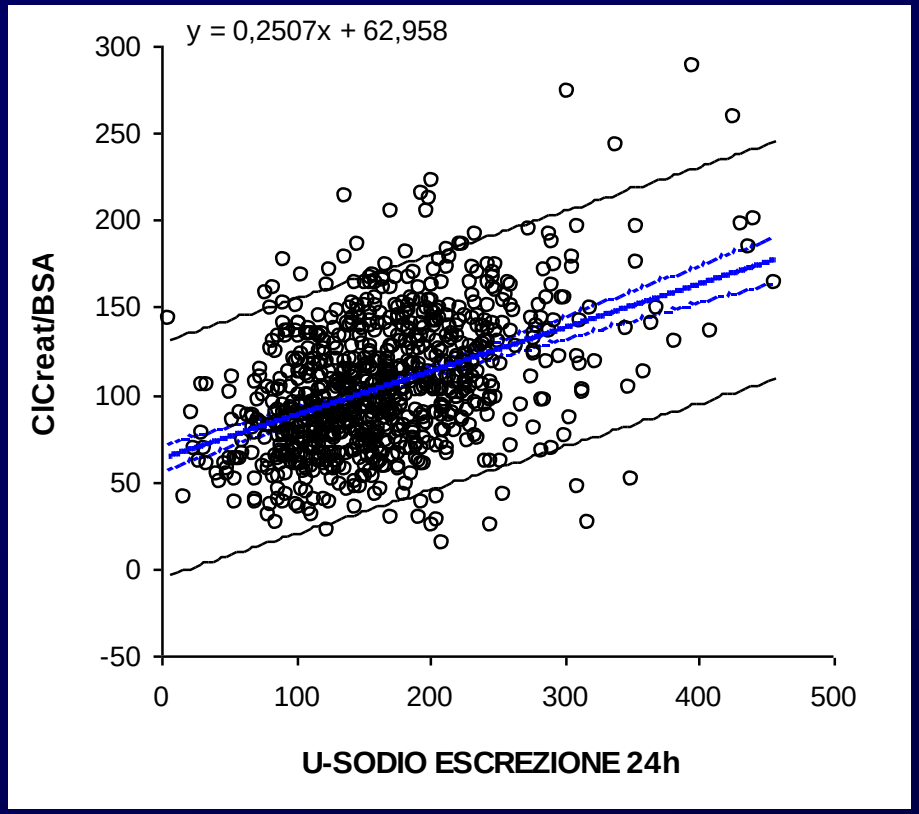
TABLE I
FACTORS AFFECTING RENAL FUNCTION WITH AGING

Physiological	Pathological
• Low protein diet • Vegetarian habit	• Atherosclerosis/glomerulosclerosis • Hypertension • Heart failure • Diabetes/glucose intolerance • Obesity • Smoking habit • Drugs • Inflammation markers • Hyperlipemia

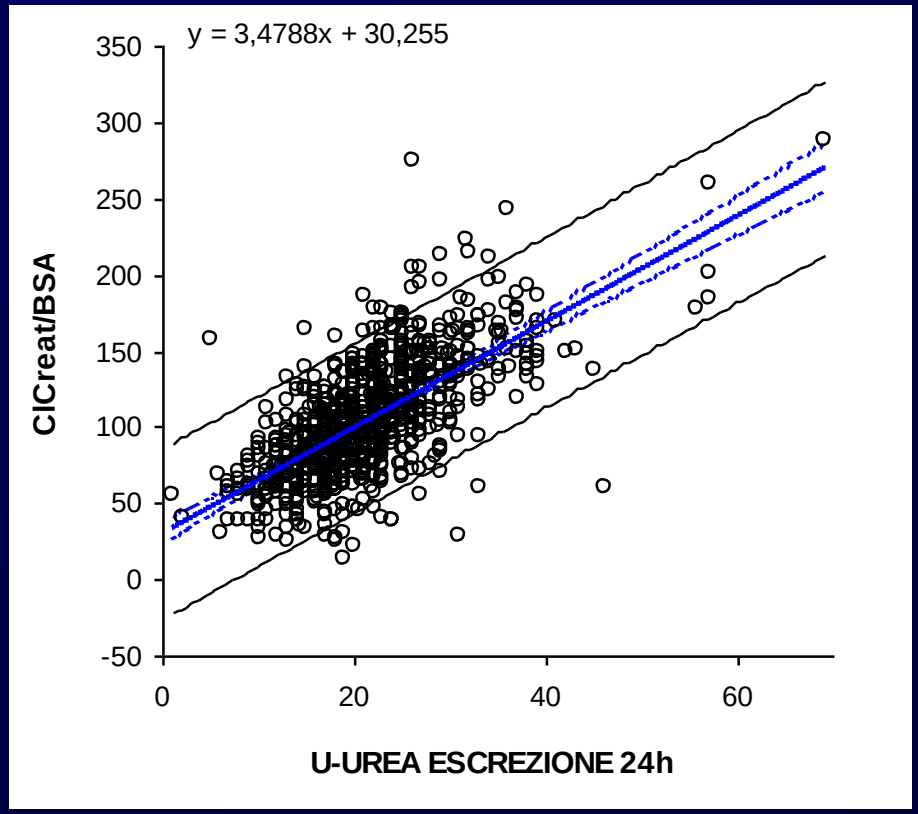
Casistica S.C. Nefrologia A.O. Mauriziano

N = 842

$R^2 = 0.19$; $P<0.0001$



$R^2 = 0.45$; $P<0.0001$



Piano della presentazione

- Variazioni della funzione renale con l'età: dati di popolazione, dati longitudinali
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Insufficienza renale cronica

Riduzione stabile ed irreversibile della funzione renale

- Stadio 1:
  - ✓ Danno renale con GFR normale (> 90 mL/min/1.73 m^2 bsa)
- Stadio 2:
  - ✓ Danno renale con lieve IR (GFR 60-90)
- Stadio 3
  - ✓ 3a: Moderata riduzione di funzione (GFR 60-45)
  - ✓ 3b: maggiore riduzione (GFR 45-30)
- Stadio 4:
  - ✓ Riduzione funzionale severa (GFR 15-30)
- Stadio 5:
  - ✓ IRC end-stage (GFR<15 mL/min/1.73 m^2bsa)

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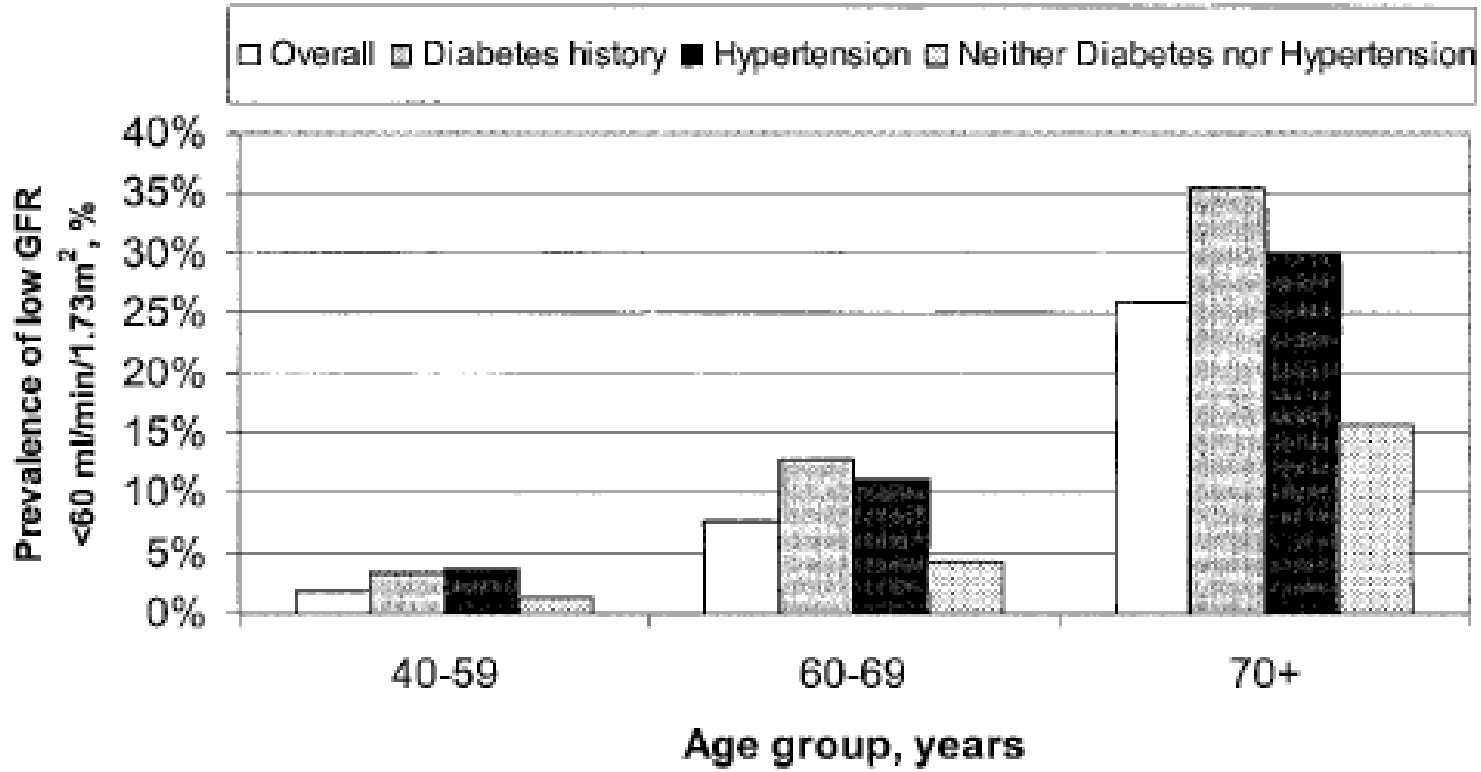
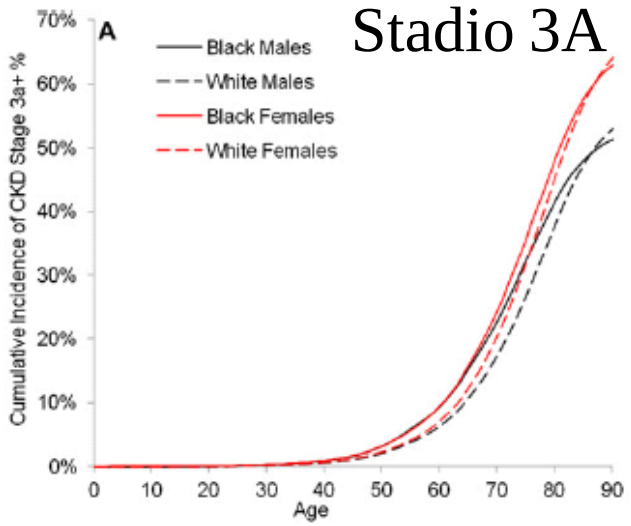


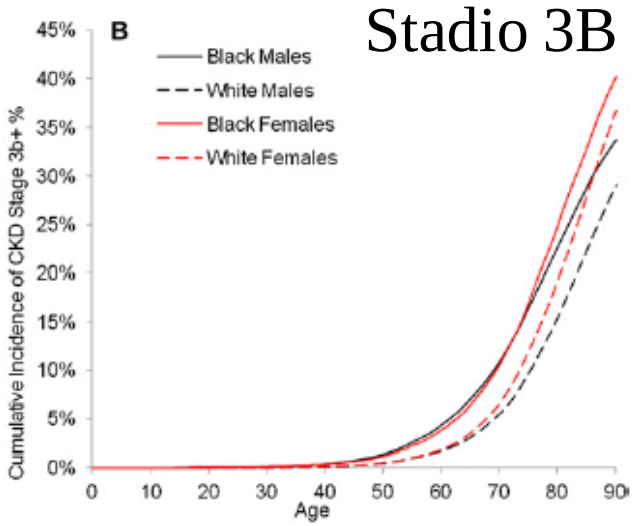
Lifetime Incidence of CKD Stages 3-5 in the United States

Morgan E. Grams, MD, MHS,[1,2] Eric K.H. Chow, MS,[3] Dorry L. Segev, MD, PhD,[2,3] and Josef Coresh, MD, PhD[1,2,4]

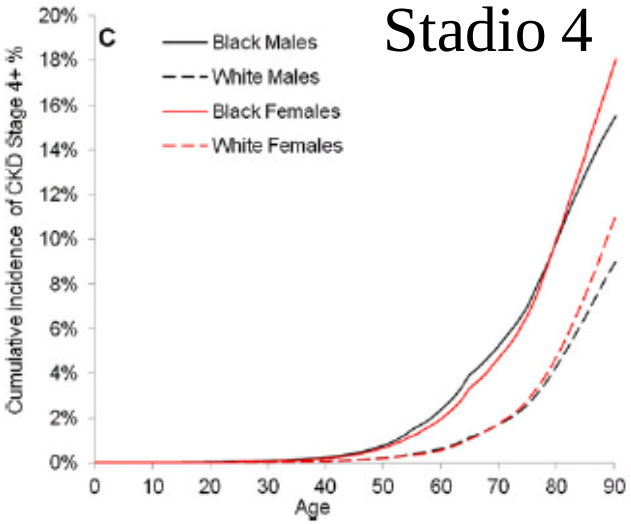
Am J Kidney Dis. 62(2):245-252. © 2013



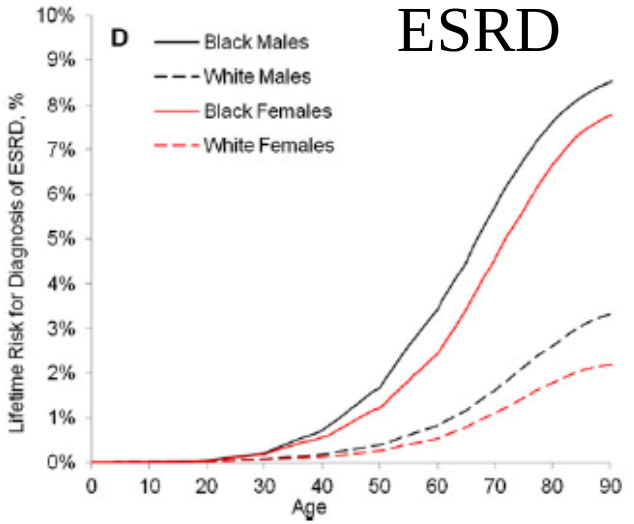
Stadio 3A



Stadio 3B



Stadio 4

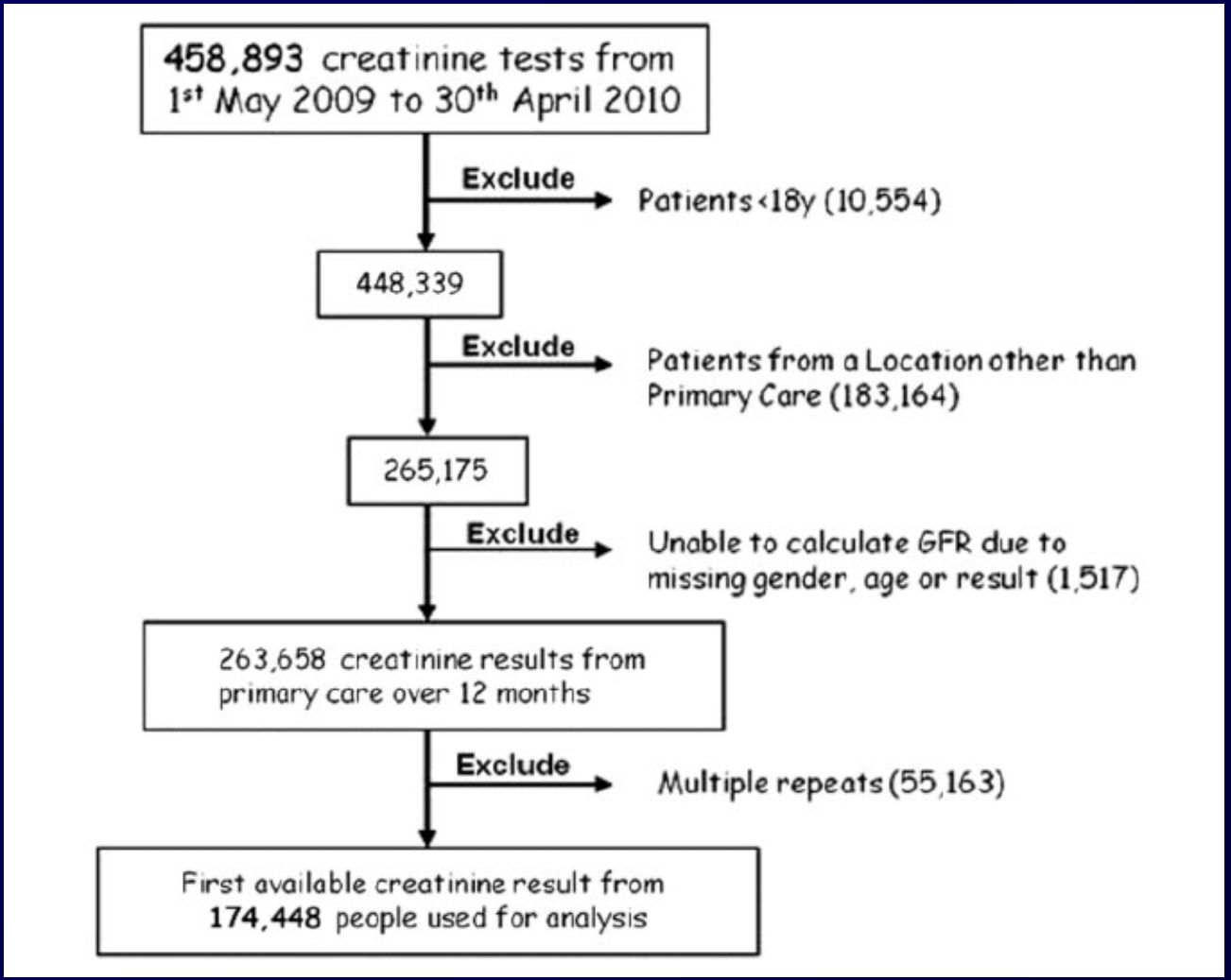


ESRD

Estimating glomerular filtration rate: comparison of the CKD-EPI and MDRD equations in a large UK cohort with particular emphasis on the effect of age

J.L. CARTER[1], P.E. STEVENS[2], J.E. IRVING[2] and E.J. LAMB[1]

Q J Med 2011; **104**:839–847



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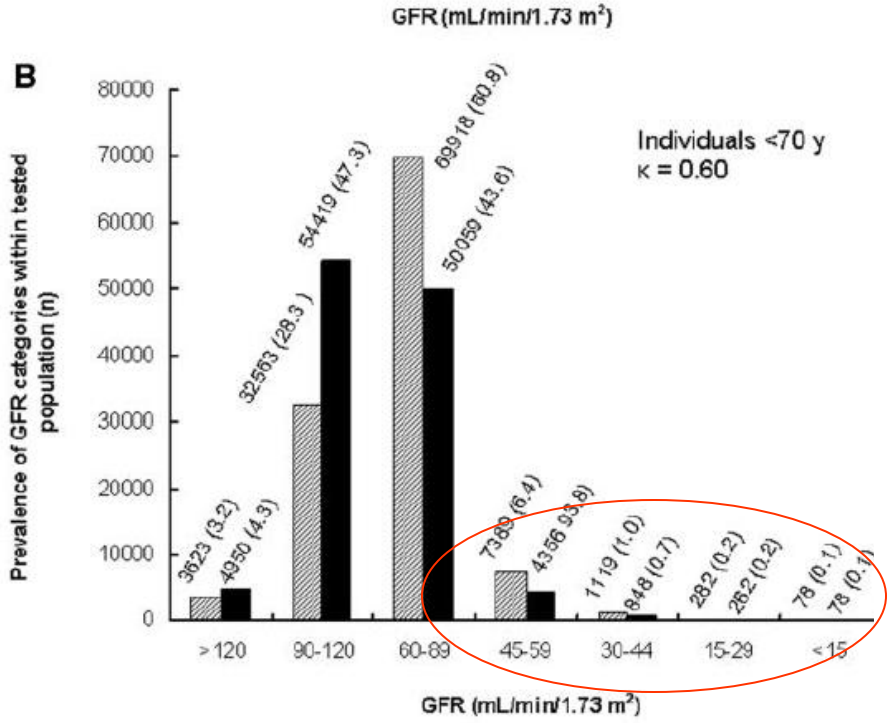
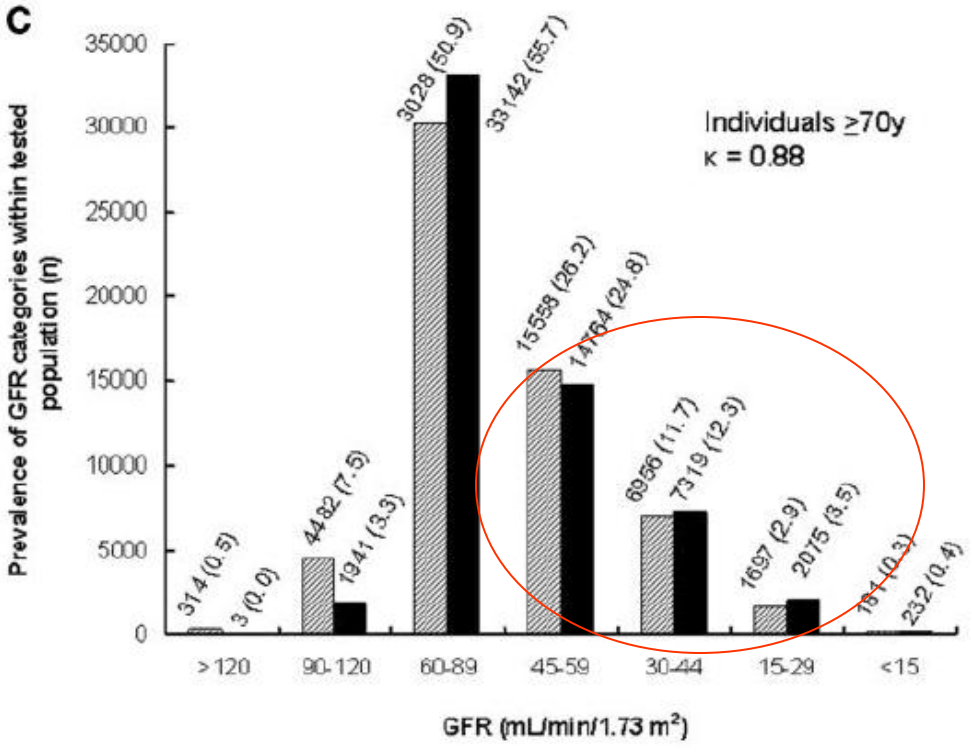


CKD-EPI

MDRD



Estimating glomerular filtration rate: comparison of the CKD-EPI and MDRD equations in a large UK cohort with particular emphasis on the effect of age

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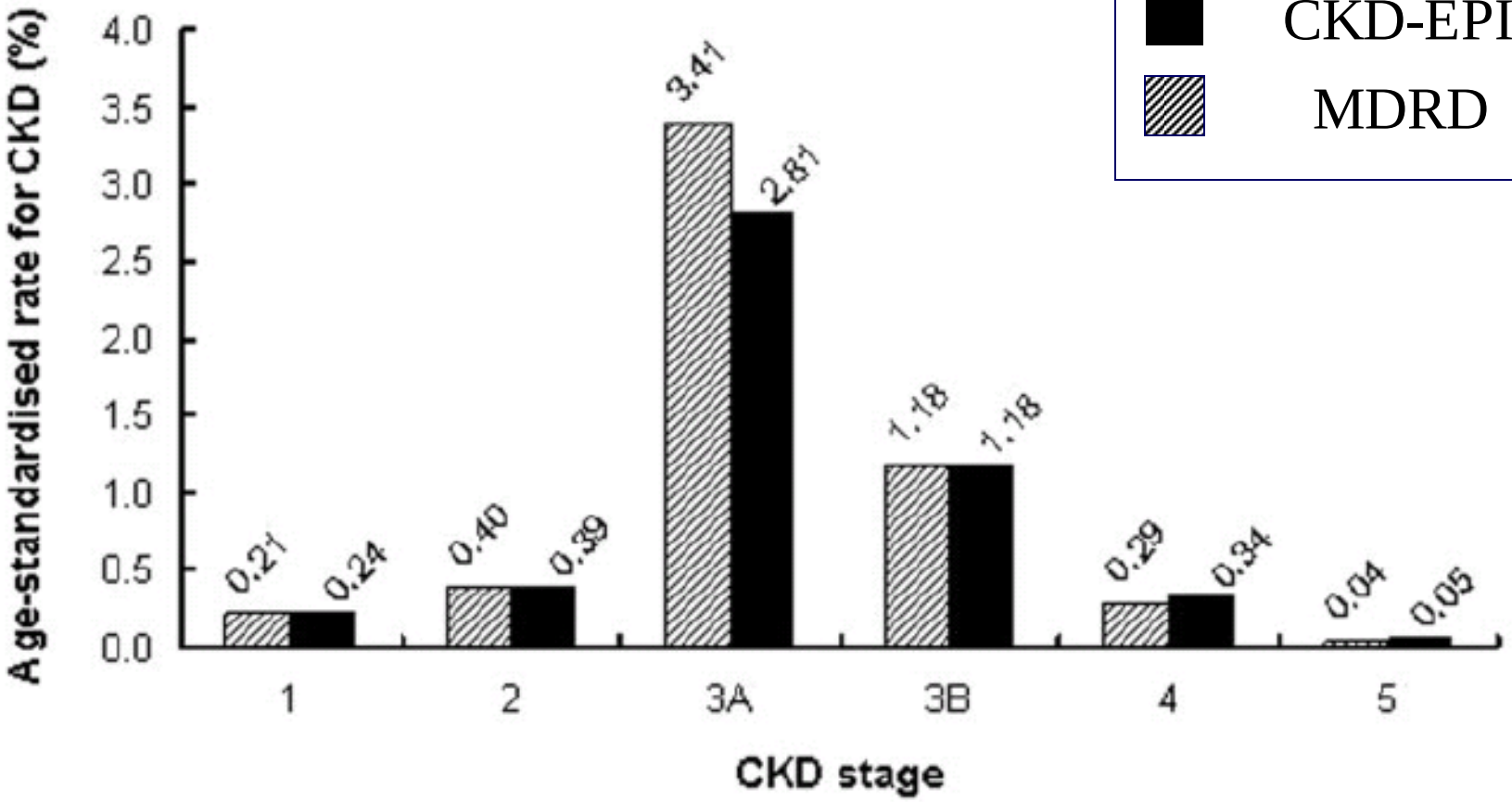

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Q J Med 2011; **104**:839–847

Mean CKD-EPI : 82 mL/min/1.73 m^2
Mean MDRD : 76 mL/min/1.73 m^2
P<0.0001

Mean bias = 5.0%
Range: 13% at age 18-29 vs –7.5% at age >90 yrs

<u>Conclusion</u>
CKD-EPI gives higher GFR and less CKD
At age >70 yrs little difference between methods
Among very elderly CKD-EPI gives higher CKD

Piano della presentazione

- Variazioni della funzione renale con l'età: dati di popolazione, dati longitudinali
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Aging and Physiological Changes of the Kidneys Including Changes in Glomerular Filtration Rate

Nephron Physiol 2011;119(suppl 1):p1–p5

Table 1. Senile hypofiltration: its mechanisms

Senile hypofiltration
Glomerulosclerosis
Mesangial expansion

Table 2. Senile renal vascular changes: its mechanisms

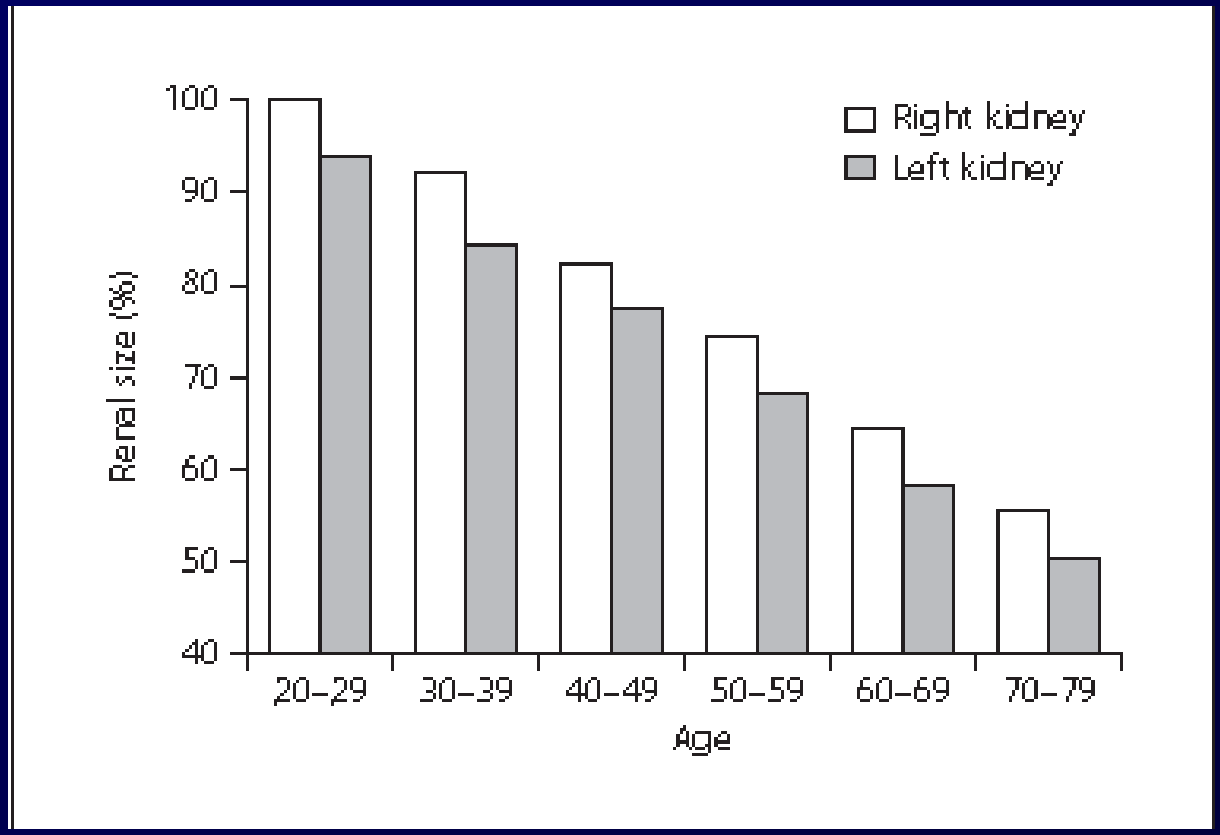
Renal vascular changes
Renal atherosclerosis
Vascular dysautonomy
Arteriole subendotelial hyalinosis
Aglomerular circulation

Table 3. Senile tubule-interstitial changes: its mechanisms

Tubule-interstitial changes
Tubular diverticuli
Tubular atrophy
Tubular fat degeneration
Reduced sodium reabsorption
Reduced potassium secretion
Interstitial fibrosis
Medulla hypotonicity

Senile Nephrosclerosis – Does It Explain the Decline in Glomerular Filtration Rate with Aging?

Nephron Physiol 2011;119(suppl 1):p6–p11



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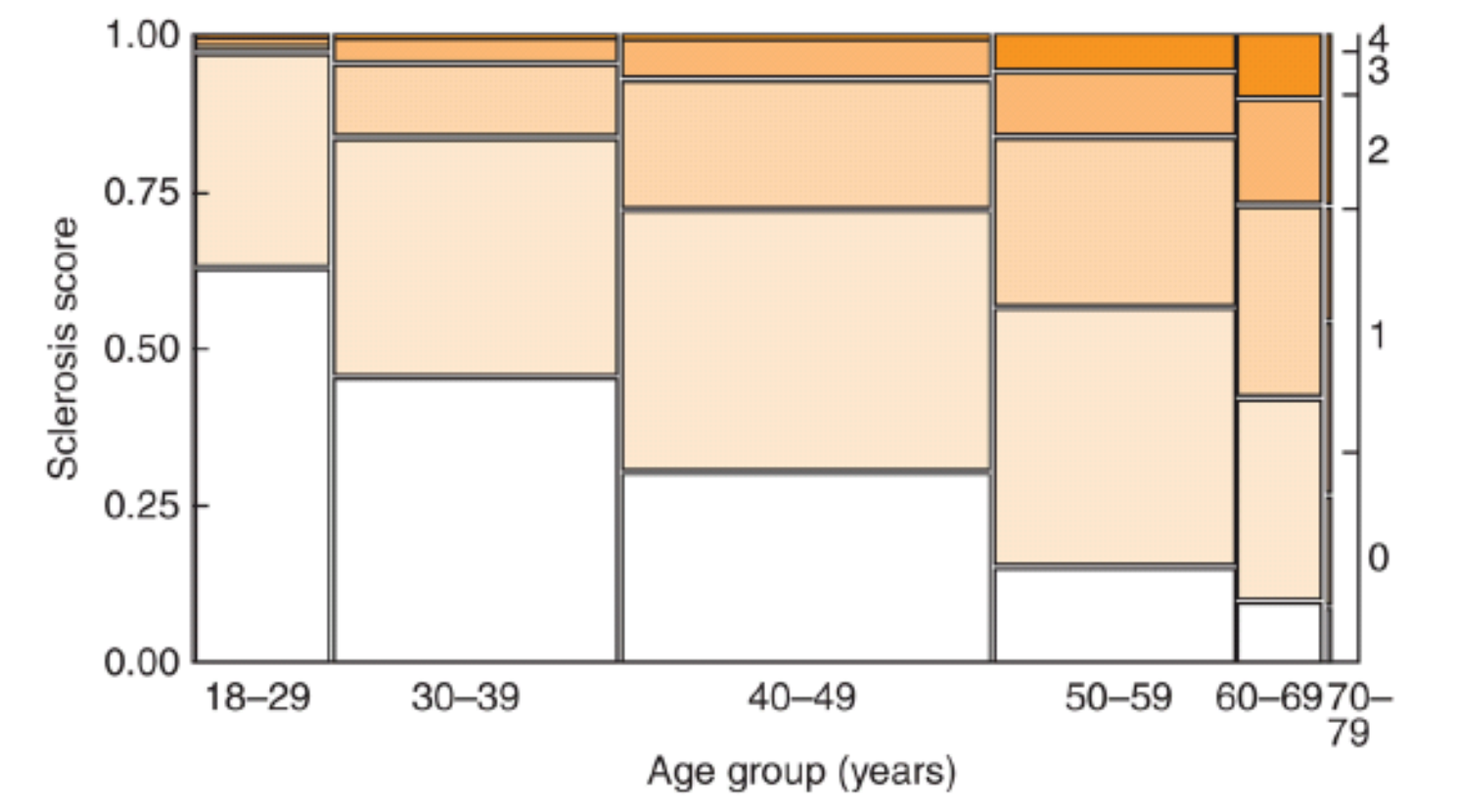


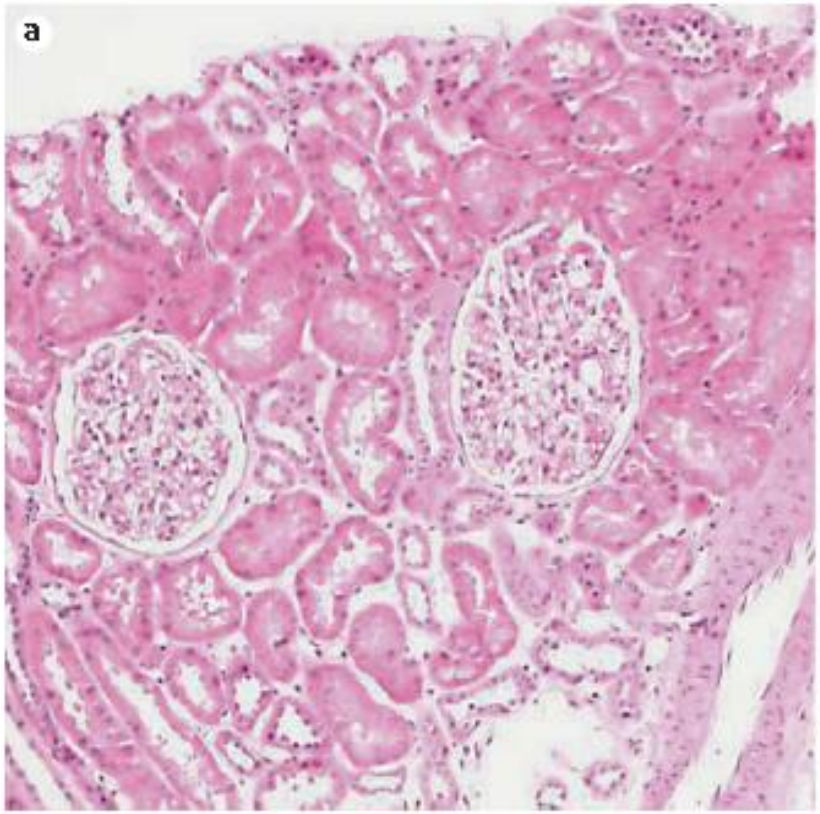
Legenda: 1. Glomerulosclerosi 2. Tubuloatrofia
3. Fibrosi interstiziale 4. Arteriolosclerosi

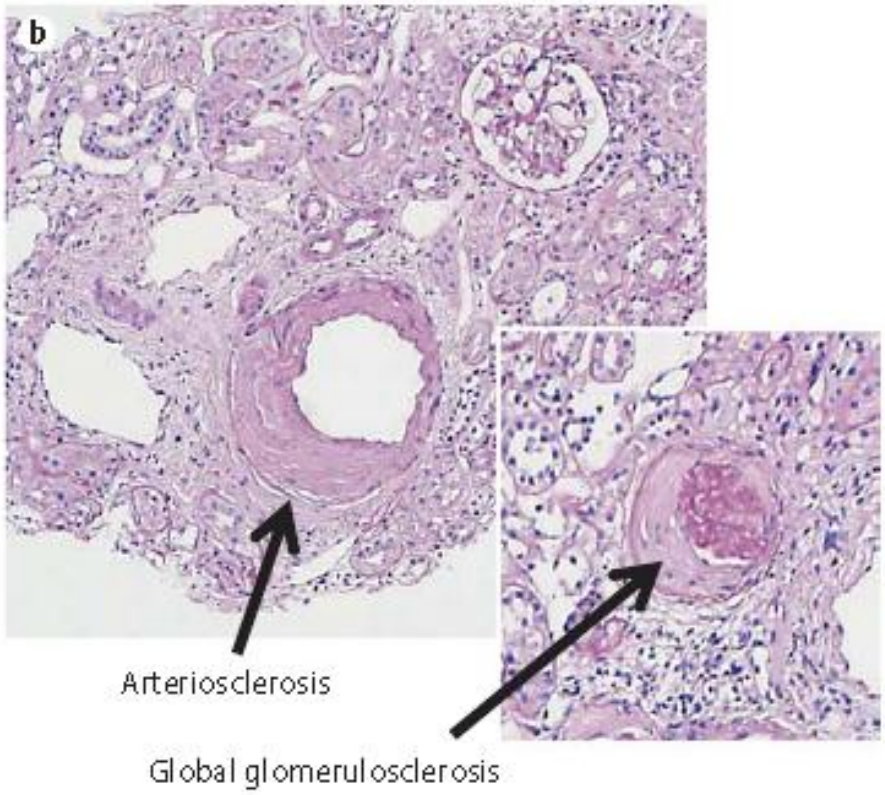
Senile Nephrosclerosis – Does It Explain the Decline in Glomerular Filtration Rate with Aging?

Nephron Physiol 2011;119(suppl 1):p6–p11

20-yr kidney donnor

70-yr kidney donnor





The implications of anatomical and functional changes of the aging kidney: with an emphasis on the glomeruli

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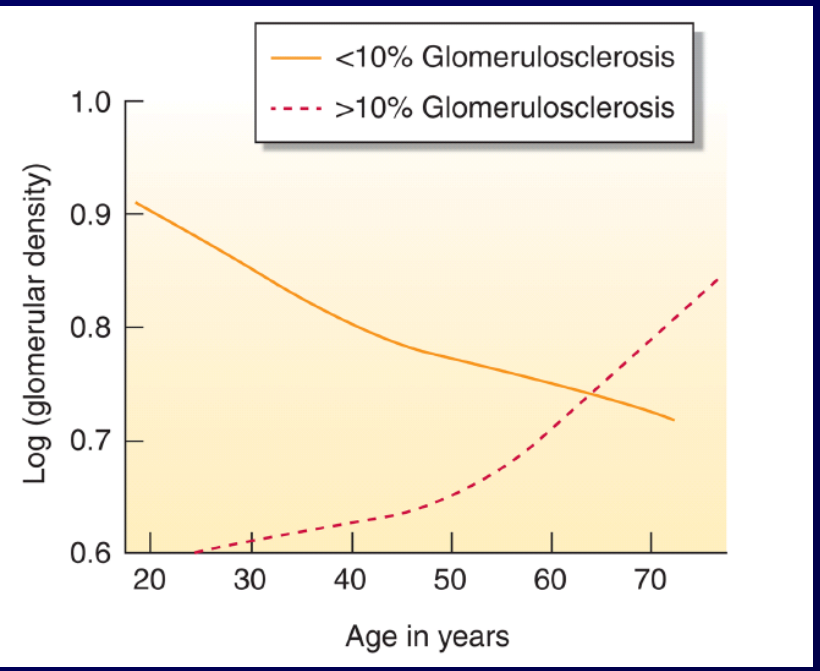


- ✓Con l'età aumenta la nefrosclerosi globale
- ✓Nonostante la perdita di nefroni il volume dei reni non si riduce, se non nei molto anziani
- ✓Aumenta il volume dei nefroni residui
- ✓Si riduce la densità nefronica

The association between age and nephrosclerosis on renal biopsy among healthy adults

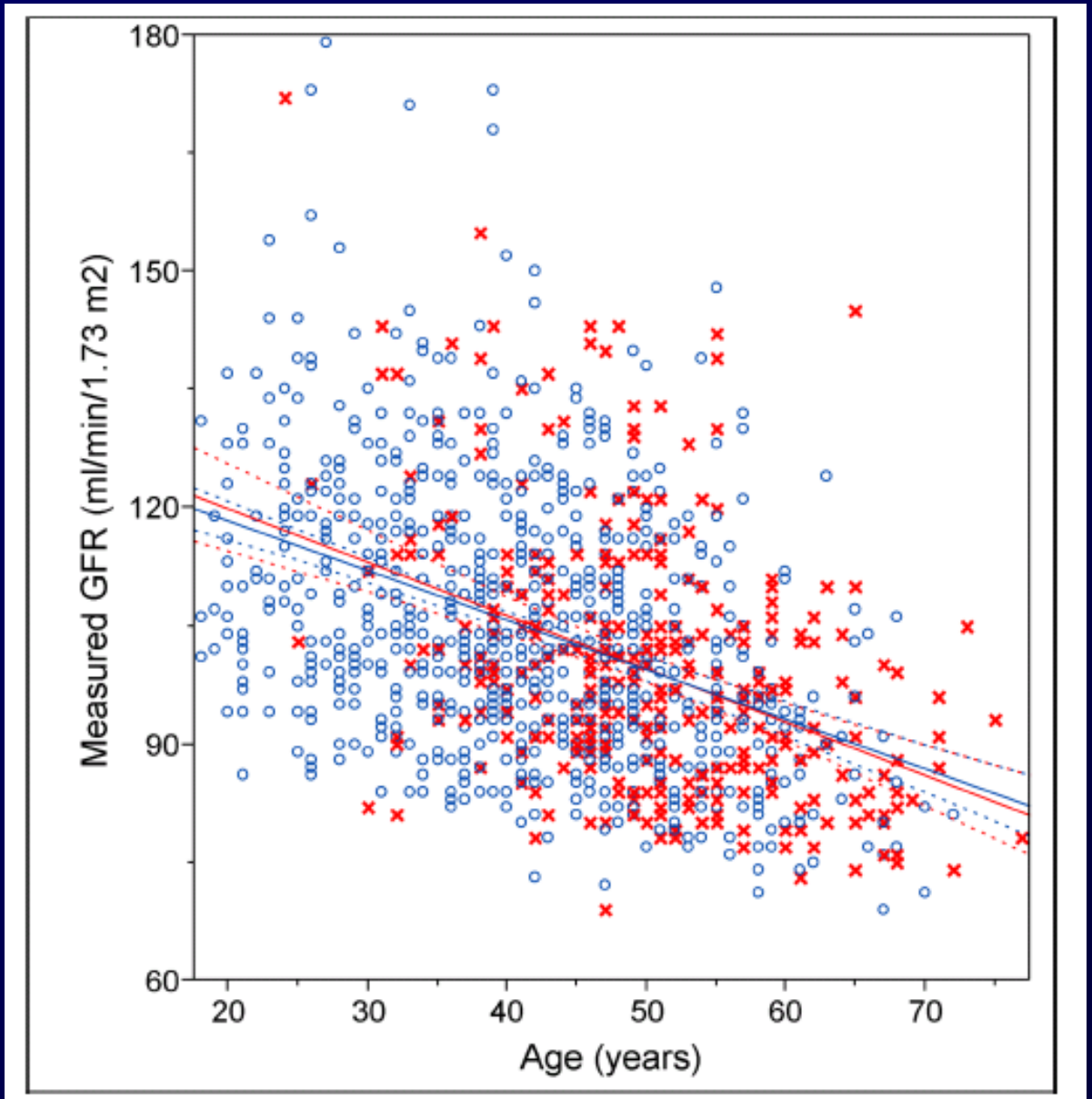
Ann Intern Med. 2010 May 4; 152(9): 561–567.

Prevalence of nephrosclerosis by age group among 1203 living kidney donors at the Mayo Clinic

Age group	Crude prevalence % (95% CI)	Crude prevalence after excluding persons on therapy for hypertension % (95% CI)
18-29 y	2.7% (1.1% to 6.7%)	2.7% (1.1% to 6.7%)
30-39 y	16% (12% to 20%)	15% (12% to 20%)
40-49 y	28% (24% to 32%)	26% (22% to 31%)
50-59 y	44% (38% to 50%)	42% (36% to 49%)
60-69 y	58% (47% to 67%)	55% (44% to 66%)
70-77 y	73% (43% to 90%)	75% (41% to 93%)
Overall	28% (25% to 30%)	26% (24% to 29%)

The association between age and nephrosclerosis on renal biopsy among healthy adults

Ann Intern Med. 2010 May 4; 152(9): 561–567.



Senile Nephrosclerosis – Does It Explain the Decline in Glomerular Filtration Rate with Aging?

Nephron Physiol 2011;119(suppl 1):p6–p11

However, the argument that the age-related decline in GFR can be fully explained by the development of nephrosclerosis in a subset of older adults is not supported by existing data.

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Piano della presentazione

- Variazioni della funzione renale con l'età: dati di popolazione, dati longitudinali
- Modalità e attendibilità di misura della funzione renale nell'anziano
- Incidenza di CKD nell'anziano
- La nefrosclerosi senile ed il ruolo delle comorbilità
- **Implicazioni cliniche della perdita di funzione**

How to assess renal function in the geriatric population

JNEPHROL 2010; 23 (S15): S46-S54

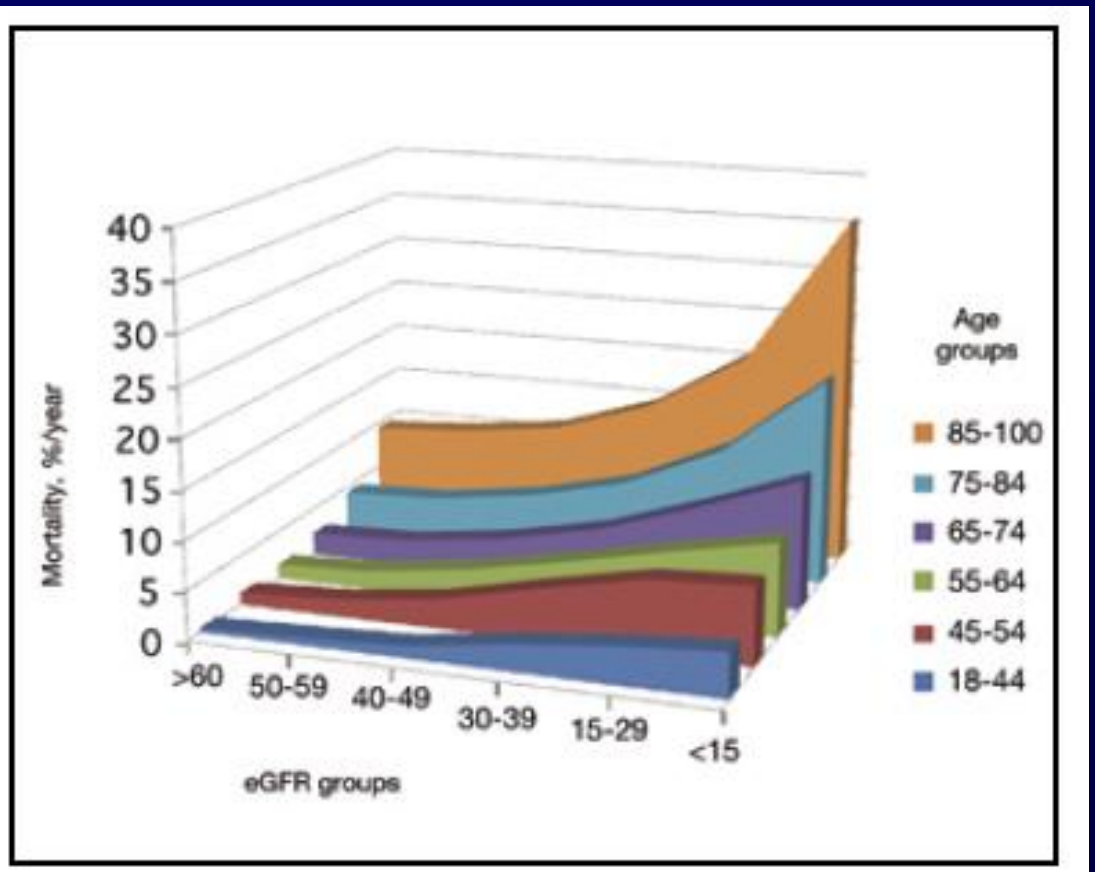
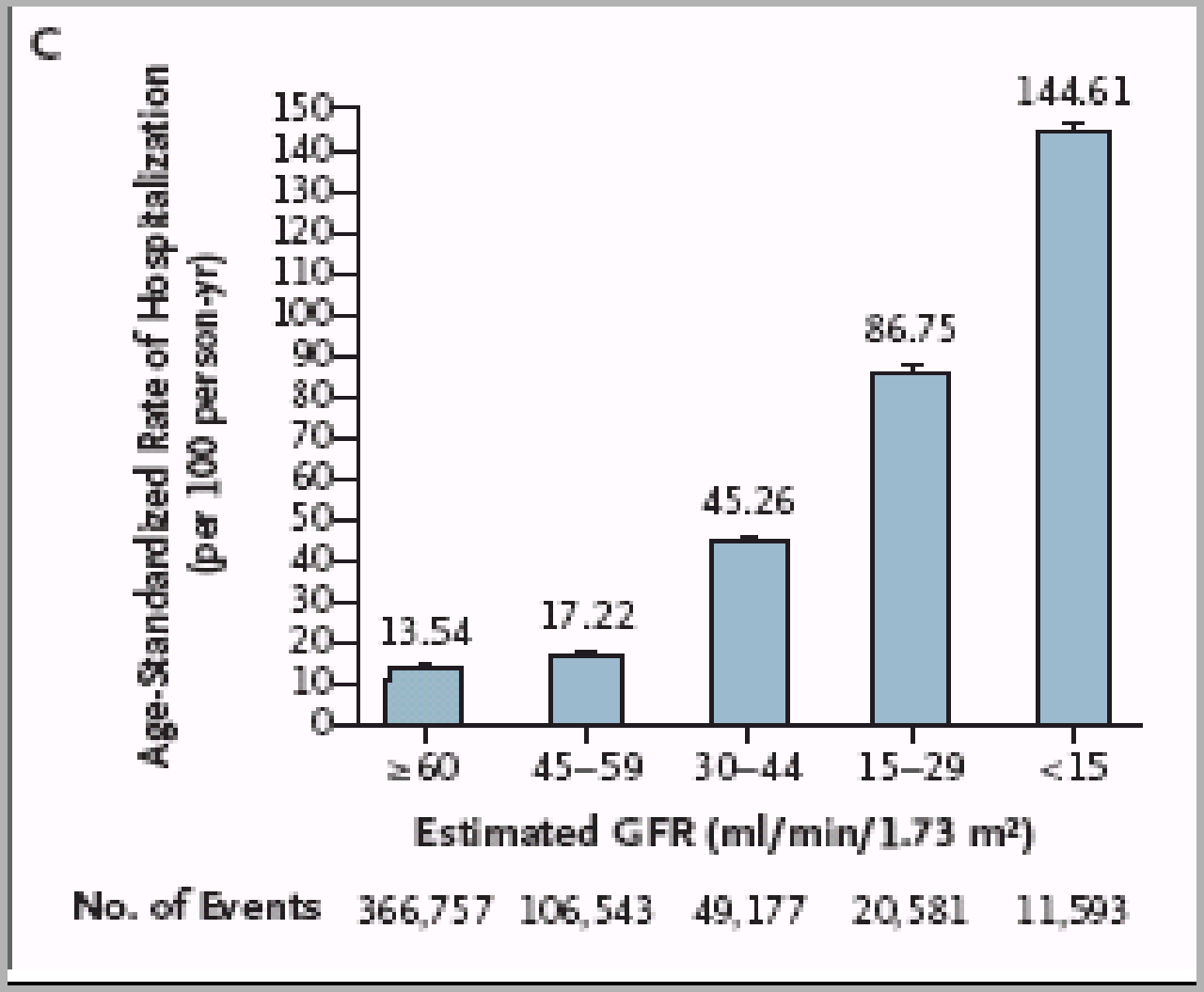
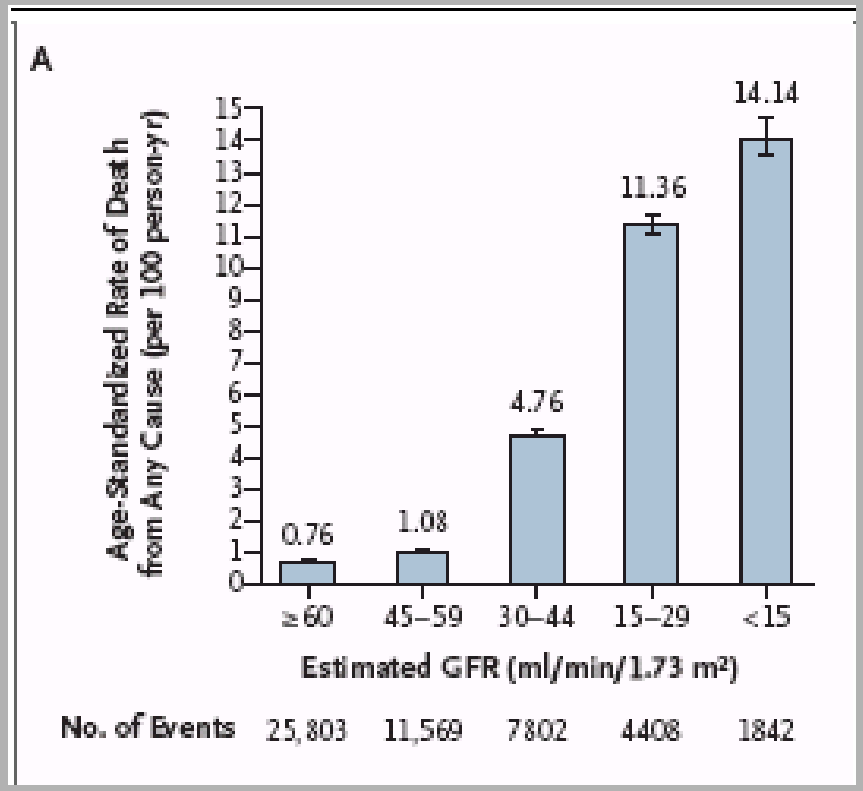


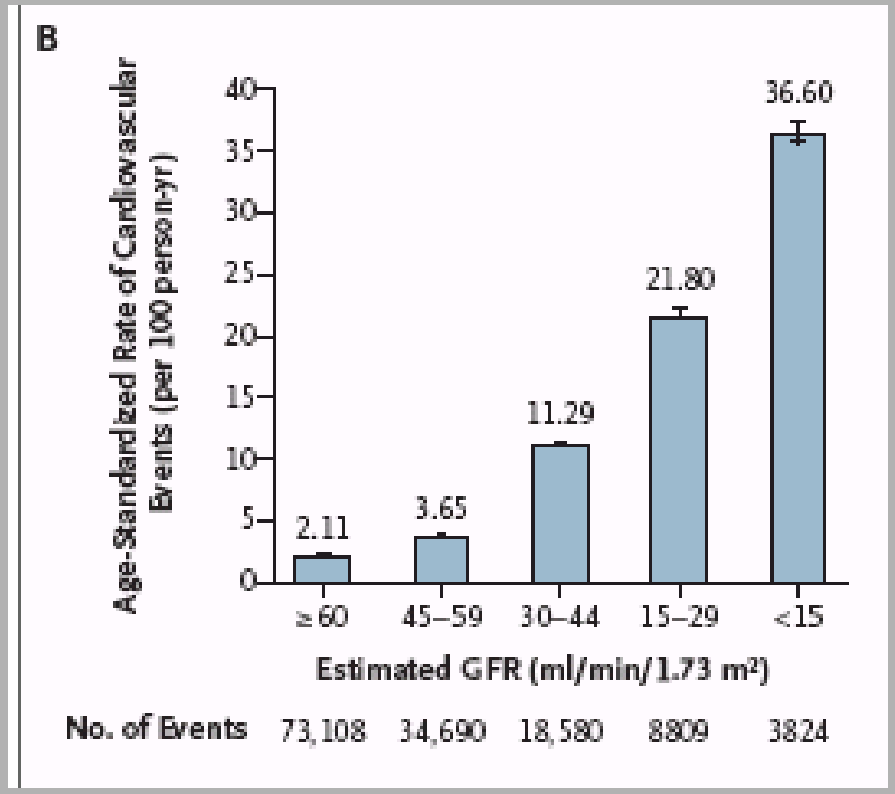
Fig. 3 - Mortality rate by age and estimated glomerular filtration rate (eGFR, in ml/min per 1.73 m²) (data from O'Hare et al (43)).

Il rischio di spedalizzazione in relazione con il grado di IRC



Il rischio relativo di morte in relazione con il grado di IRC





Frailty and Chronic Kidney Disease: The Third National Health and Nutrition Evaluation Survey

The American Journal of Medicine (2009) 122, 664-671

Table 3 Odds Ratios for Frailty: Multivariable Model

	OR of Frailty	95% CI
No CKD	1 (Reference)	—
CKD stage 1/2	2.21	1.49-3.28
CKD stage 3a	2.48	1.57-3.93
CKD stage 3b-5	5.88	3.40-10.16
Diabetes	1.68	1.16-2.45
COPD	2.20	1.20-4.03
Cancer	1.89	1.19-2.99
Arthritis	3.34	2.08-5.38

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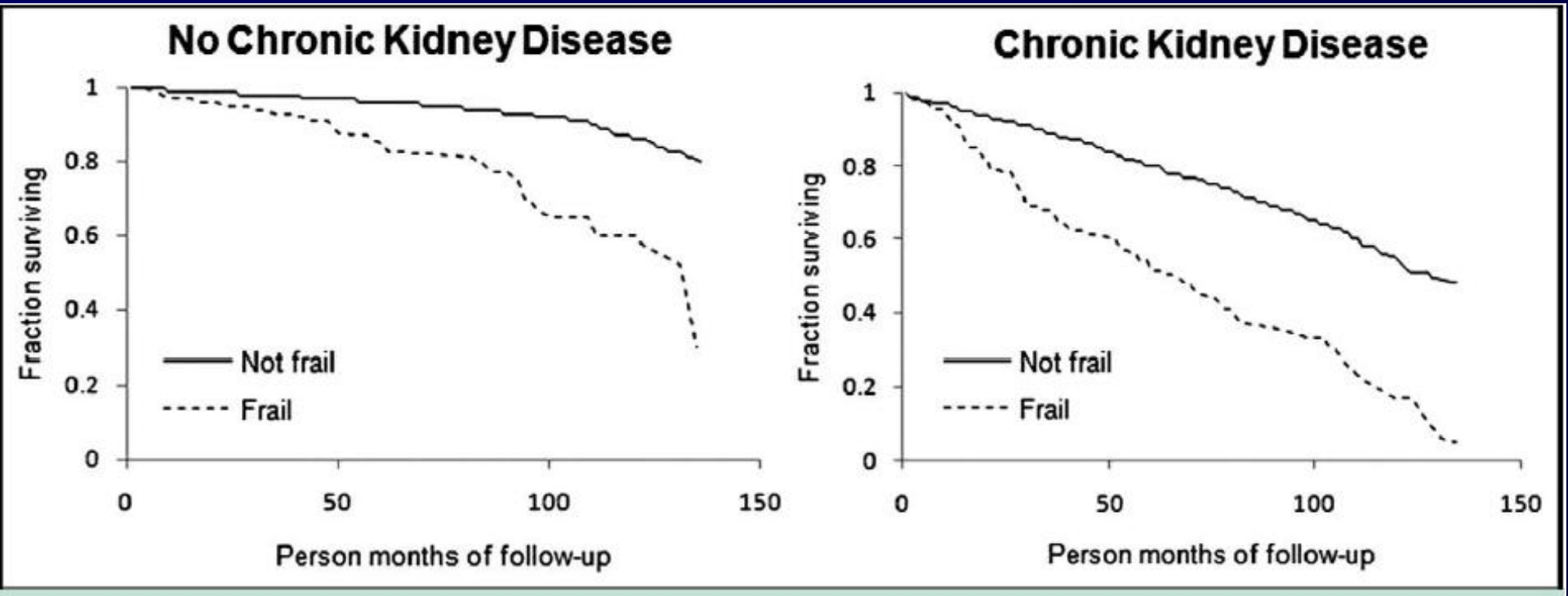

Figure 3 Frailty, chronic kidney disease, and survival.

CONCLUSIONI

- La funzione renale tende a peggiorare con l'età, anche se non in tutti i soggetti
- Il peggioramento è maggiore in presenza di comorbilità (DM, HT, SM)
- Le formule basate su Cr standardizzata sono abbastanza affidabili anche nell'anziano
- La Nefrosclerosi giustifica solo in parte la riduzione di funzione renale
- L'impatto della IR su fragilità e mortalità dell'anziano è statisticamente significativo