

**THE NKF-KDOQI (2002) CKD
DEFINITION AND
CLASSIFICATION SYSTEM:
*Limitations and Problems***

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A Contrarians Lament

***“A critic is a man who
leaves no turn
unstoned”***

George Bernard Shaw

New York Times

November 5, 1950

KDOQI-CKD (2002):

Original Intent

- ***Define*** chronic kidney disease (CKD) and to classify its stages, irrespective of underlying disease
 - ***Evaluate*** laboratory measurements for the assessment of kidney disease
 - ***Associate*** the level of kidney function with complications of CKD
 - ***Stratify*** the risk of loss of kidney function (ESRD) and development of cardiovascular disease (CVD) and other complications of CKD
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Original Intent:

**Classification system was to
be applied (*unmodified*) to
both population analysis
and to individual patient
management**

Chronic Kidney Disease (CKD): *Classification-(NKF-K/DOQI-2002)*

<u>Stage</u>	<u>Kidney Damage</u>	<u>eGFR*</u> (ml/min/1.73m ²)
1	+	≥90
2	+	60-89
3	NA	30-59
4	NA	15-29
5	NA	<15 (or dialysis)

(*calculated from serum creatinine level by the abbreviated MDRD equation; NA= not applicable: findings must persist for ≥3 months)

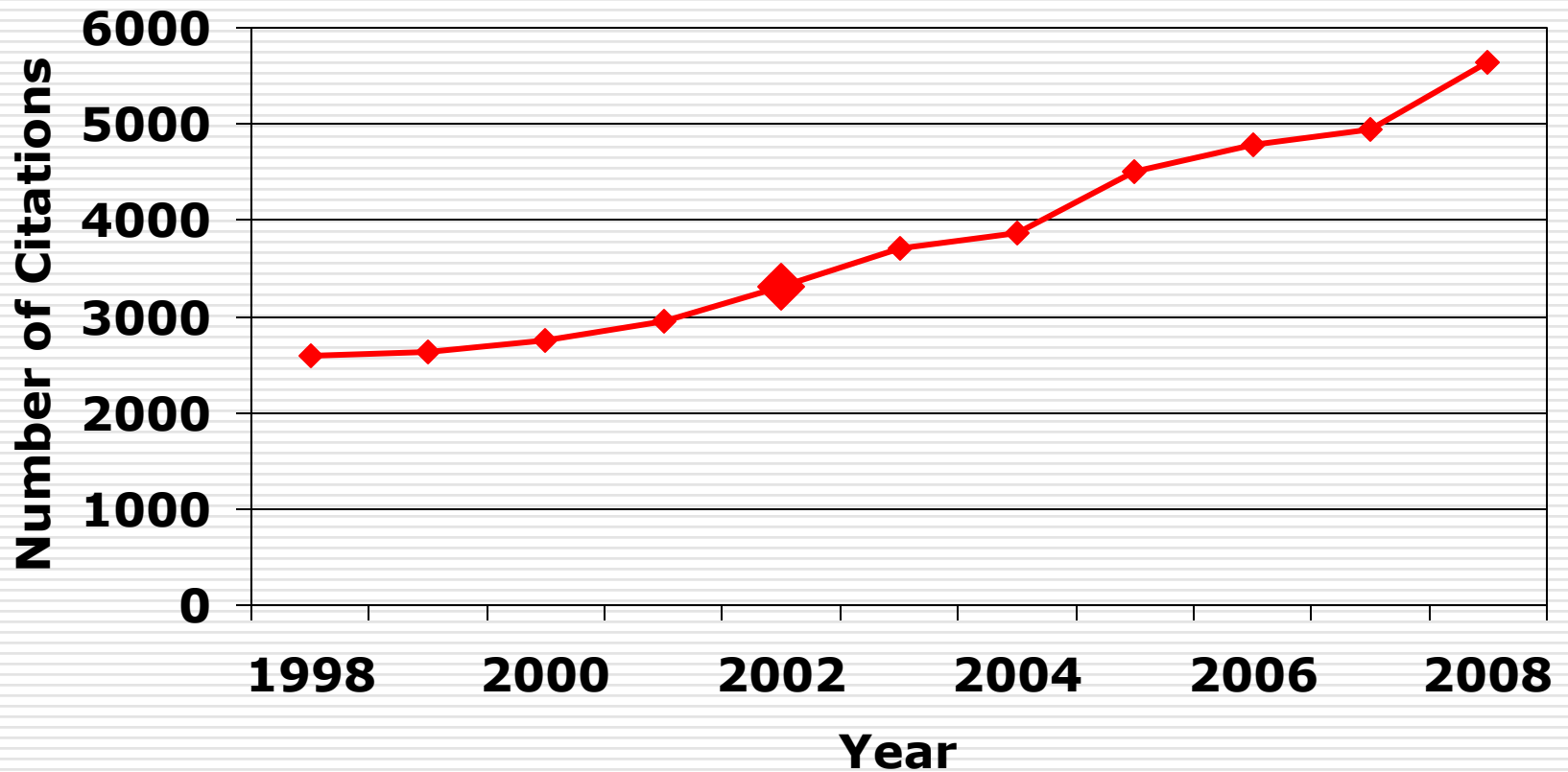
The KDOQI-CKD Classification System

Benefits

(Real and Perceived)

- ❑ *Brought order to the chaos* of nosology of CKD
 - ❑ *Increased awareness* of the “public health” problem of CKD in the general population and in general physicians
 - ❑ *Galvanized research* (clinical, basic, epidemiological) on the issue of CKD
 - ❑ *Stimulated interest in early detection* (population and targeted screening) of CKD
 - ❑ *Minimized* untimely start of dialysis
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Chronic Kidney Disease: *Citations in PubMed: 1998-2008*



The KDOQI-CKD Classification System

Limitations and Problems

(Real and Perceived)

- ❑ Described as a **staging** system, it is really a **grading** system based on **arbitrary** bands of eGFR values
 - ❑ Asserts that **normal** GFR is $>90\text{ml/min/1.73m}^2$ and an GFR $<60\text{ml/min/1.73m}^2$ is **pathological** across all adult ages, genders and ancestral groups
 - ❑ Ignores **age- and gender-**related changes in GFR
 - ❑ Linked to an **imprecise** measurement of GFR- the 4 variable eGFR (MDRD)
 - ❑ Allows the “diagnosis” of CKD based on eGFR **alone**
 - ❑ Conflates **isolated “microalbuminuria”** (in absence fo diabetes or corroborating evidence of “kidney damage”) with “kidney disease”
 - ❑ Links **“complications”** of “CKD” (e.g.CVD)to levels of eGFR, without reference to albuminuria
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KDOQI-CKD (2002) Classification-

Consequences of its Pitfalls

- ❑ ***Overestimated*** the global societal burden of CKD (Stages 1-4)
 - ❑ Generated many ***unnecessary*** referrals from FP/GP to Nephrology (false-positive diagnosis of CKD)- leading to anxiety/expense
 - ❑ Promoted ***screening*** for CKD (***de facto and overt***) using eGFR
 - ❑ Promoted eGFR-defined CKD as a ***surrogate*** for CVD and ESRD risk- without consideration of role of albuminuria
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CKD Prevalence-USA:

NHANES (KDOQI-Based:1999-2004)

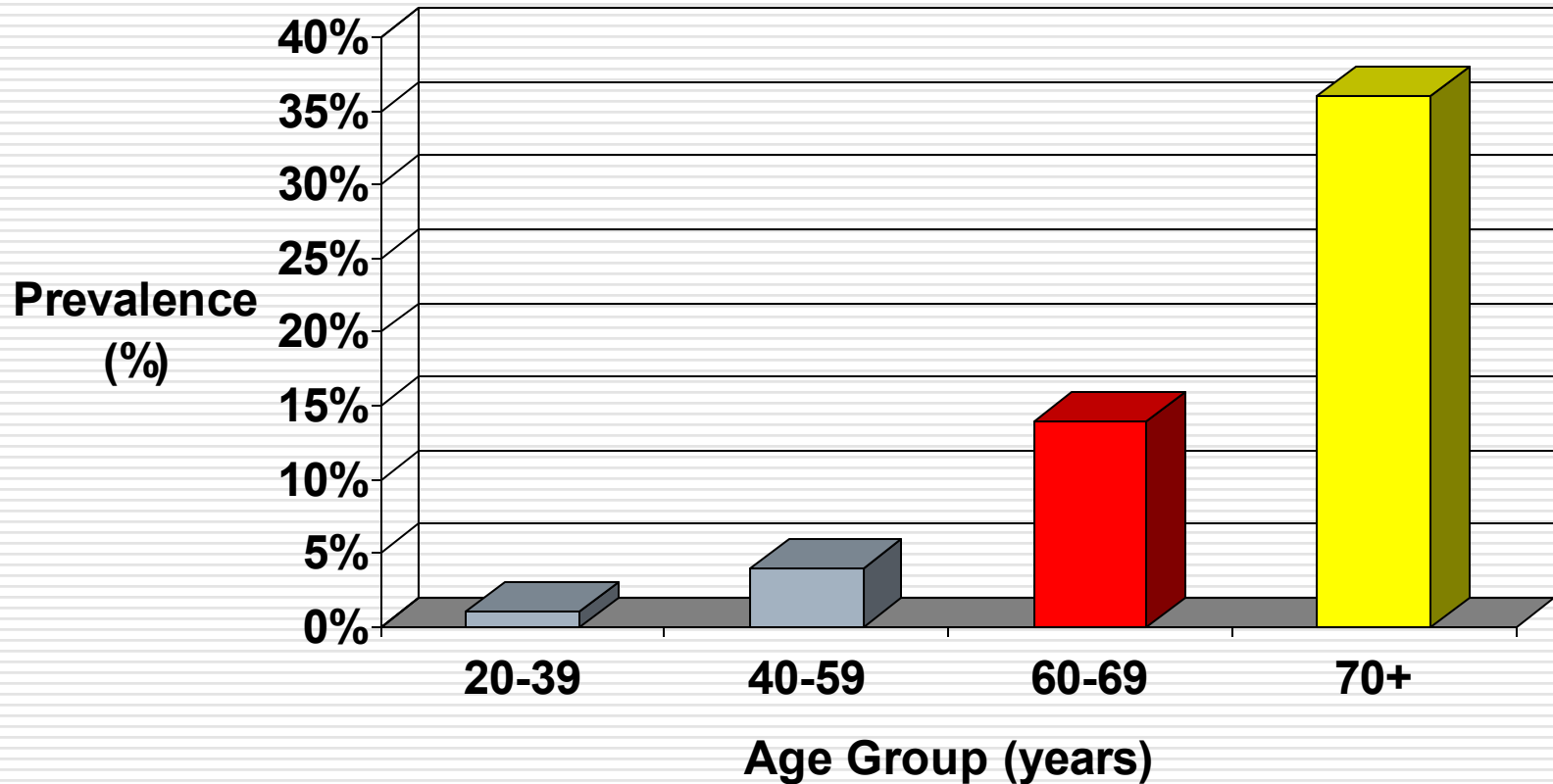
(Coresh et al JAMA, 2007)

Stage	Prevalence (%)	Prevalence (x 10 ⁶)
1	1.78	3.6
2	3.24	6.5
3	7.69	15.5
4	0.35	0.7
<i>Total 1-4</i>	<i>13.07</i>	<i>26.3</i>

***(One in every 7.6 persons over
age 20-- 60% with Stage 3
CKD)***

CKD-NHANES

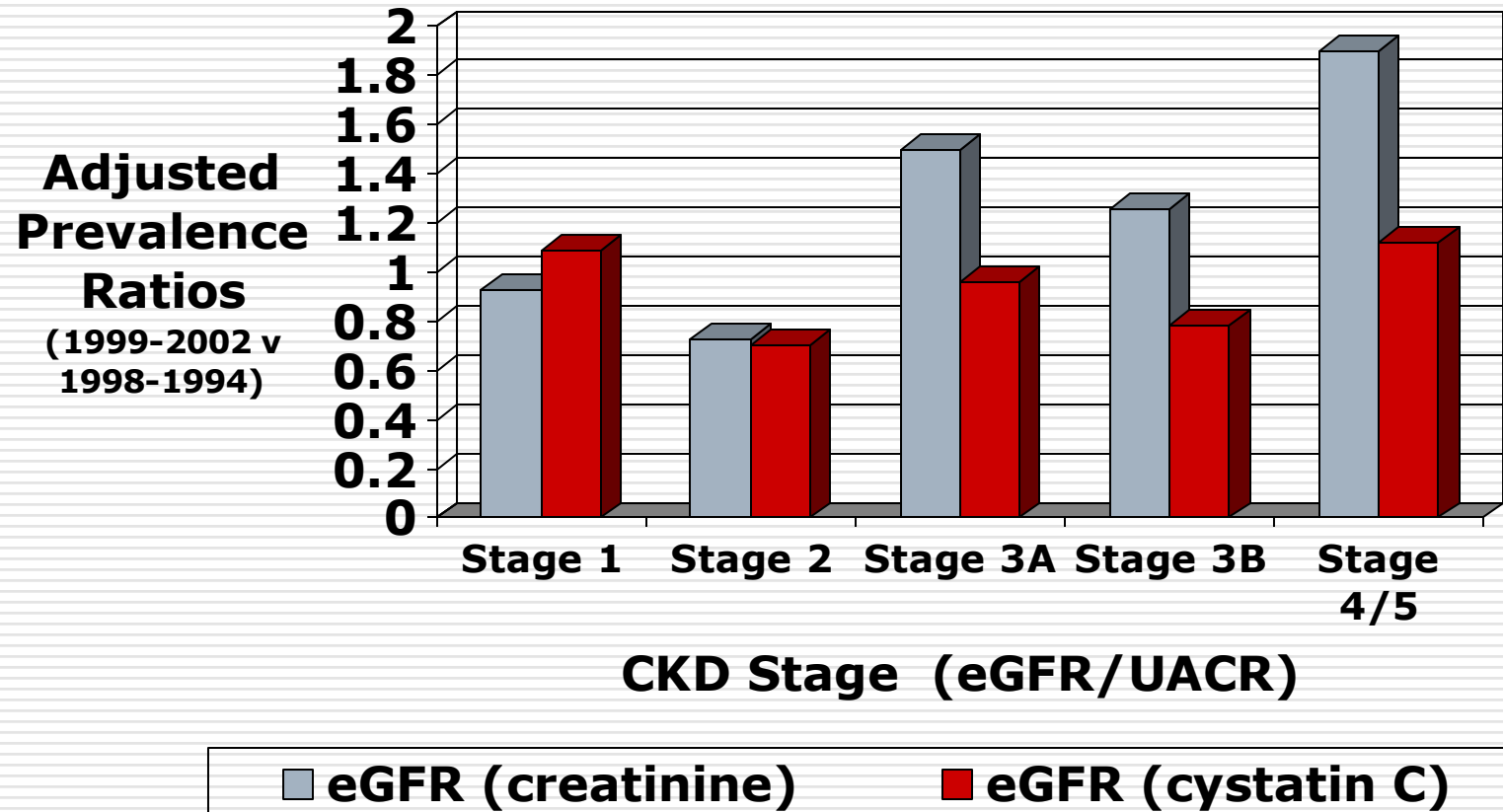
Prevalence of CKD (KDOQI) Stage 3 by Age (1999-2004)



CKD Prevalence Trends:

eGFR (creatinine) v eGFR (cystatin C)

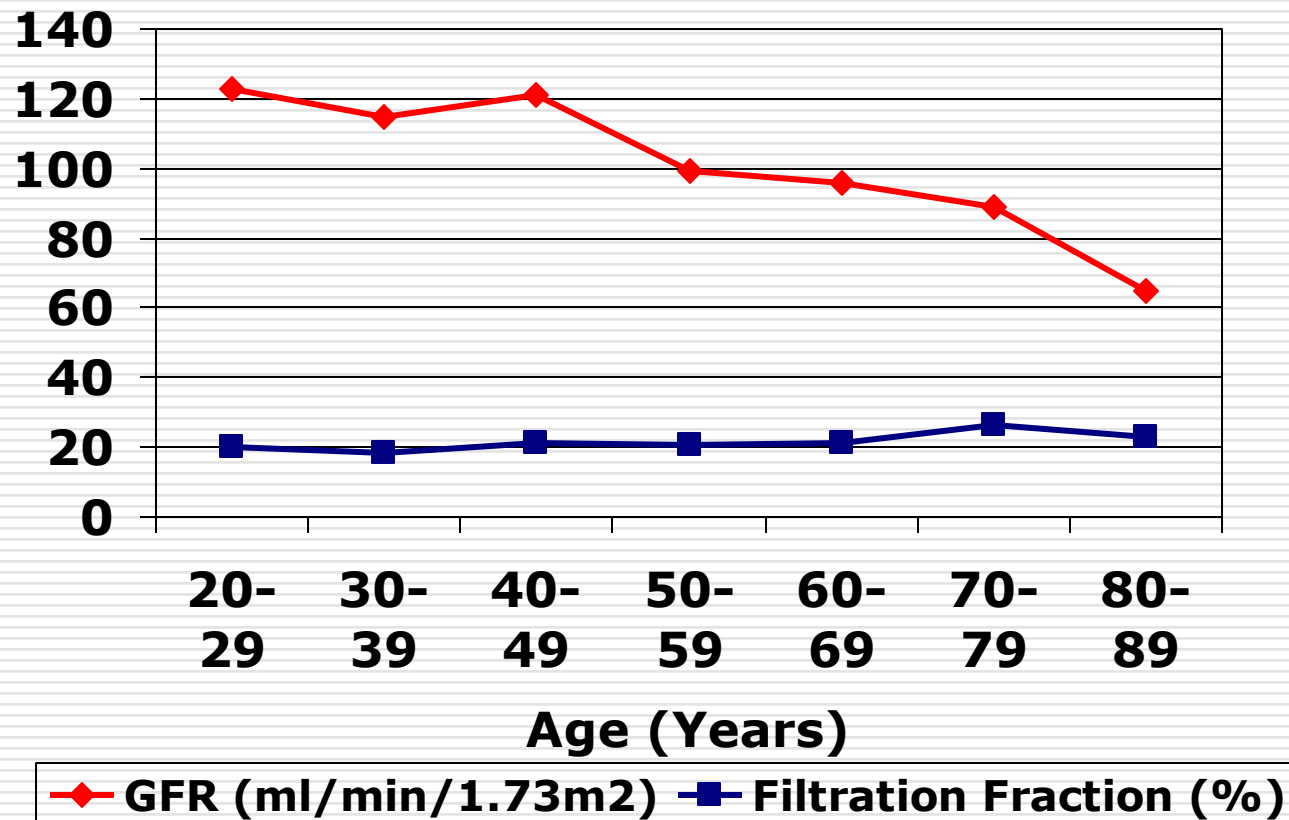
(1988-1994 vs 1999-2002 NHANES;
Foley R, et al CJASN 4:965, 2009)



Aging and GFR

Glomerular Filtration Rate (Cin) and Filtration Fraction (Cin/RPF) in Ageing

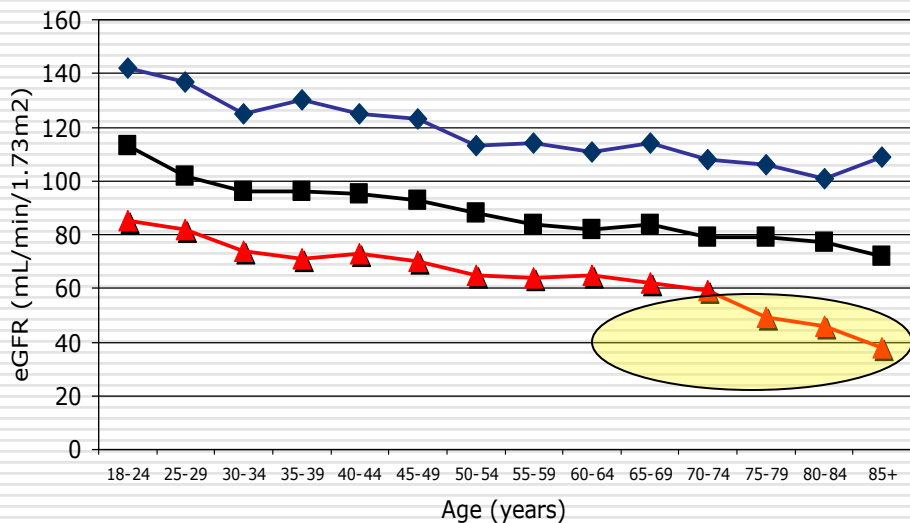
(Davies and Shock, J Clin Invest 29:496, 1950)



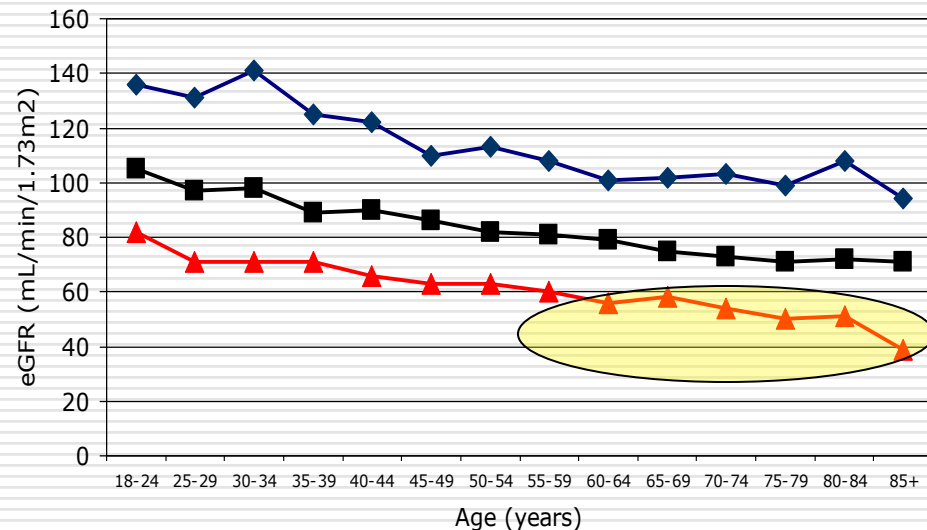
CKD:

eGFR in "Healthy" Caucasians by Gender

Males



Females

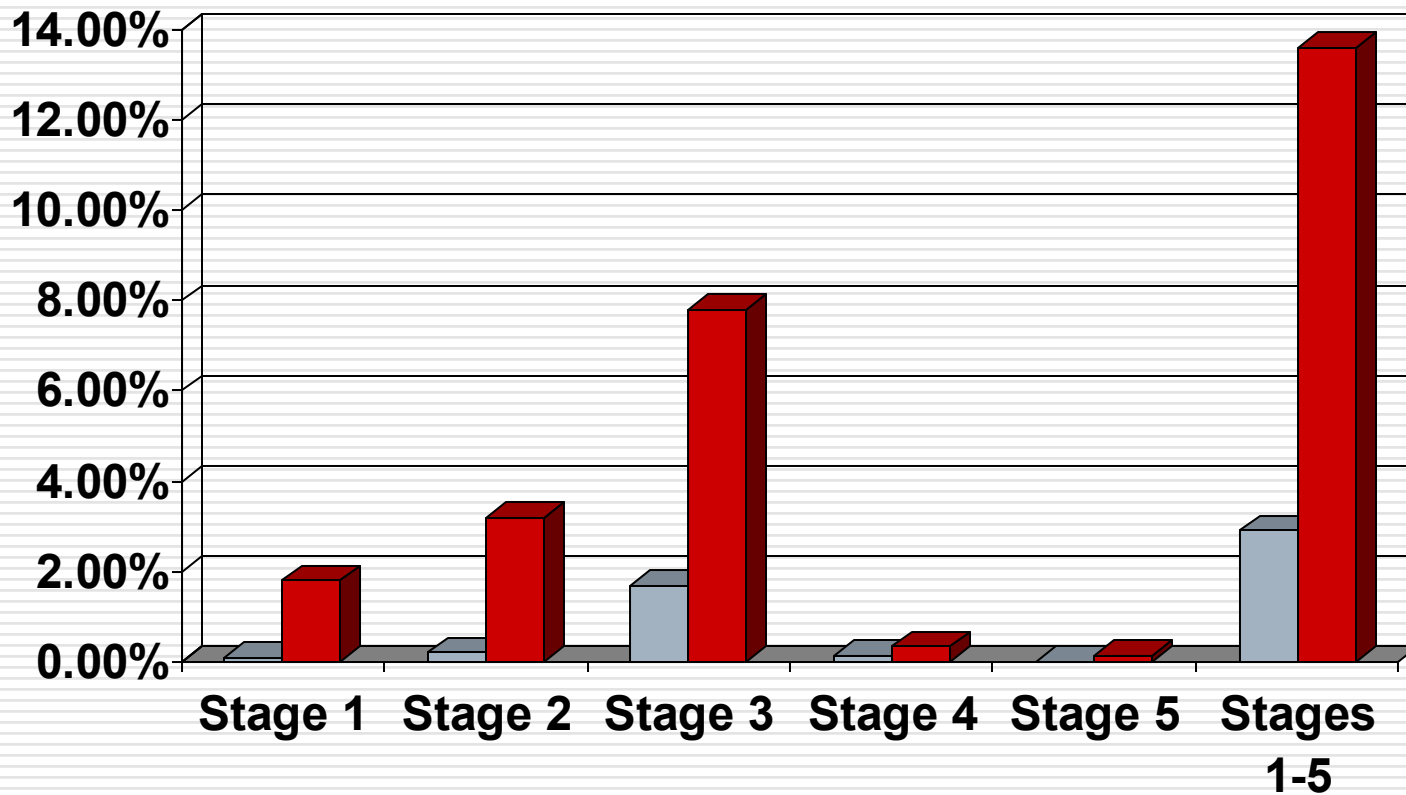


- ◆◆◆ 95th Percentile
- ◆■ 50th Percentile
- ▲◆▲ 5th Percentile

(Wetzels, J et al; Nijmegen Biomedical Study, 2008)

CKD Prevalence: *Kaiser-Permanente Age/ Microalbuminuria-Adjusted* and *Standard* KDOQI Criteria

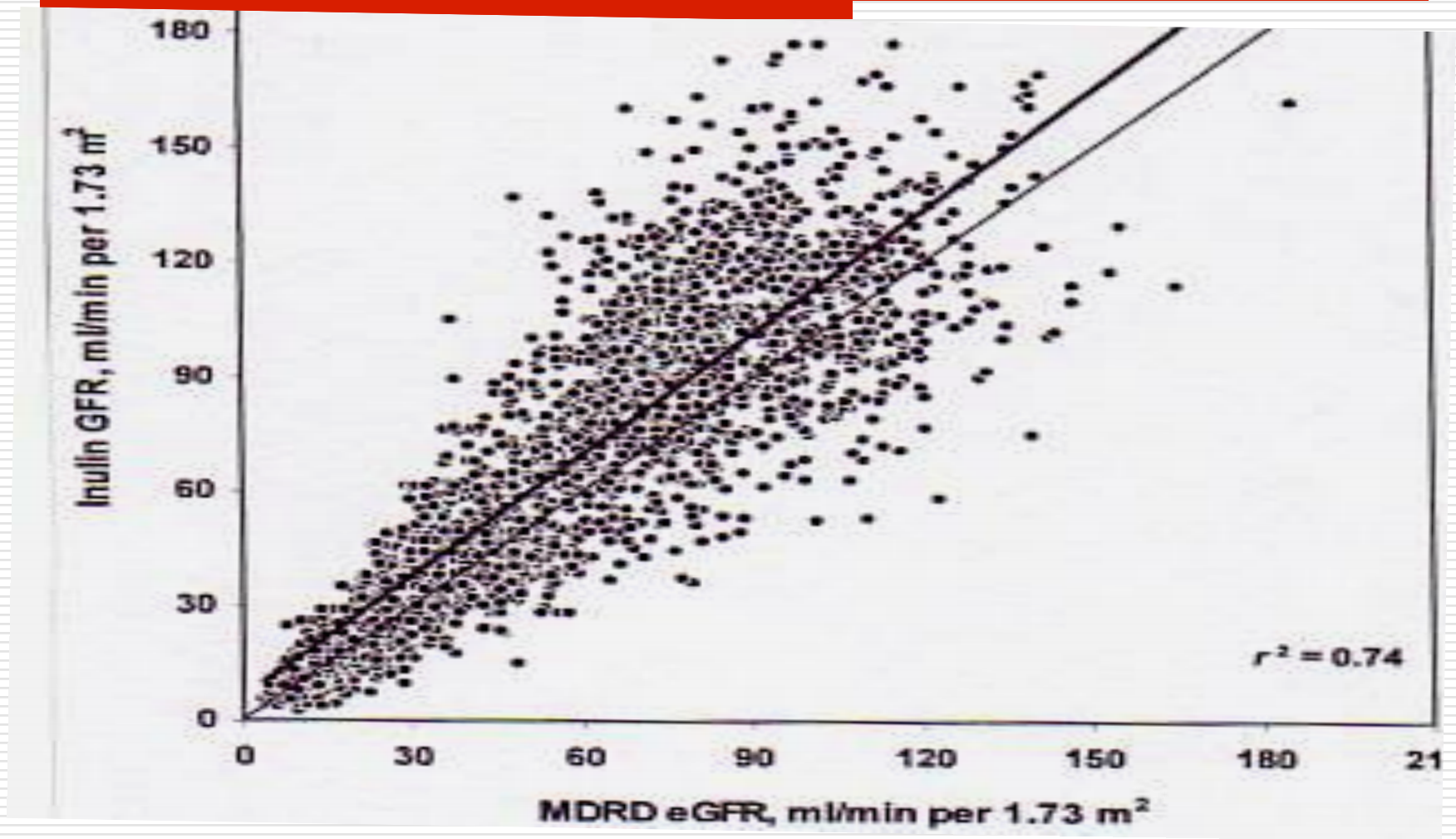
(Rutkowski, et al AJKD, 2009; Coresh, et al JAMA, 2008)



eGFR (MDRD): ***Precision and Bias***

eGFR (MDRD) vs mGFR (Cin)

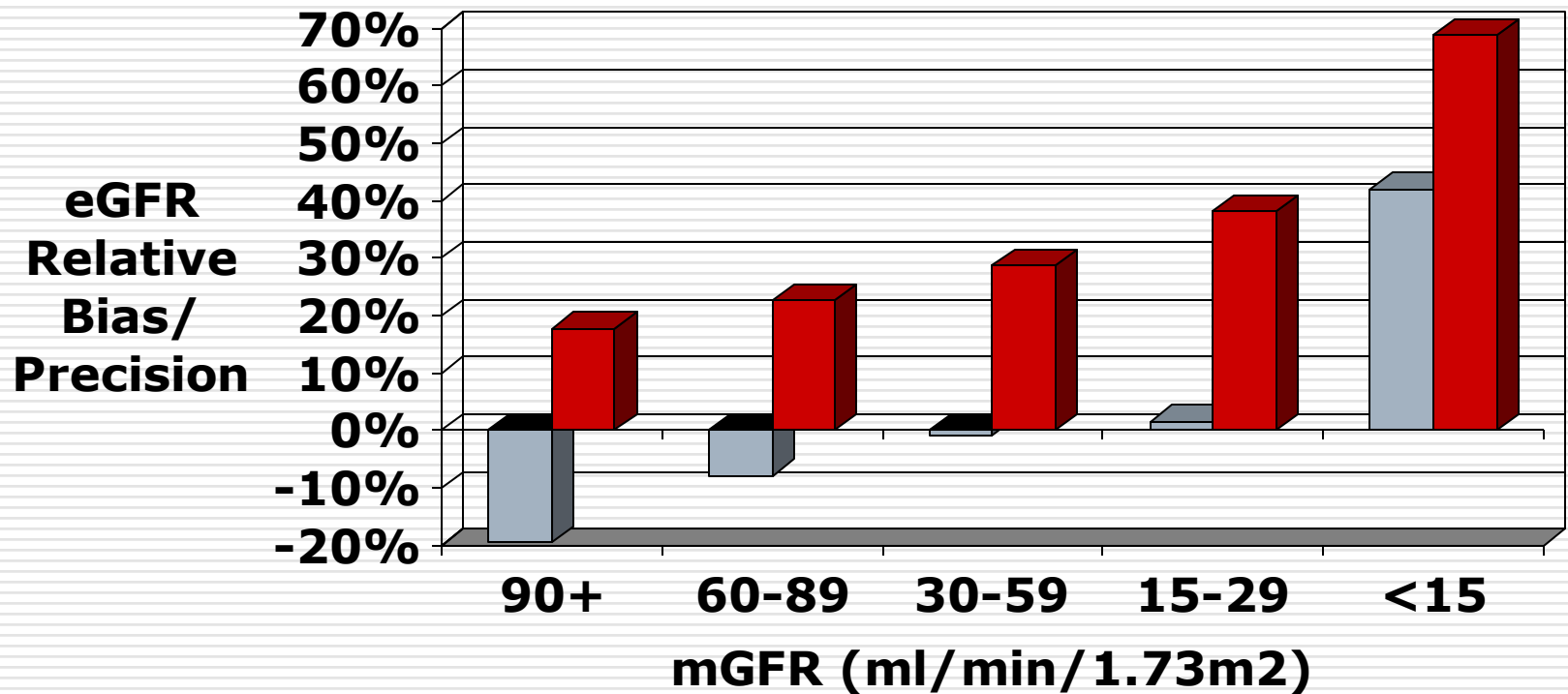
(Botev, et al, CJASN, 2009)



Precision and Bias:

eGFR (MDRD) vs mGFR (Cin)

(Botev R, et al CJASN 4:899-906, 2009)



■ Bias (% mean difference) ■ Precision (% one SD of mean)

Concordance of CKD Stage According to mGFR (C_{edta}) and eGFR (MDRD)

(Froissart, et al. JASN, 2005)

(2095 subjects; 1995 with CKD/162 normal donors)

mGFR	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5
>90	67%	32%	0.6%	0	0
60-89	16%	64%	21%	0.2%	0
30-59	0.5%	12%	78%	10%	0
15-29	0	0	17%	79%	4.2%
<15	0	0	3.1%	32%	65%

eGFR and Diagnosis of CKD: *An Illustration*

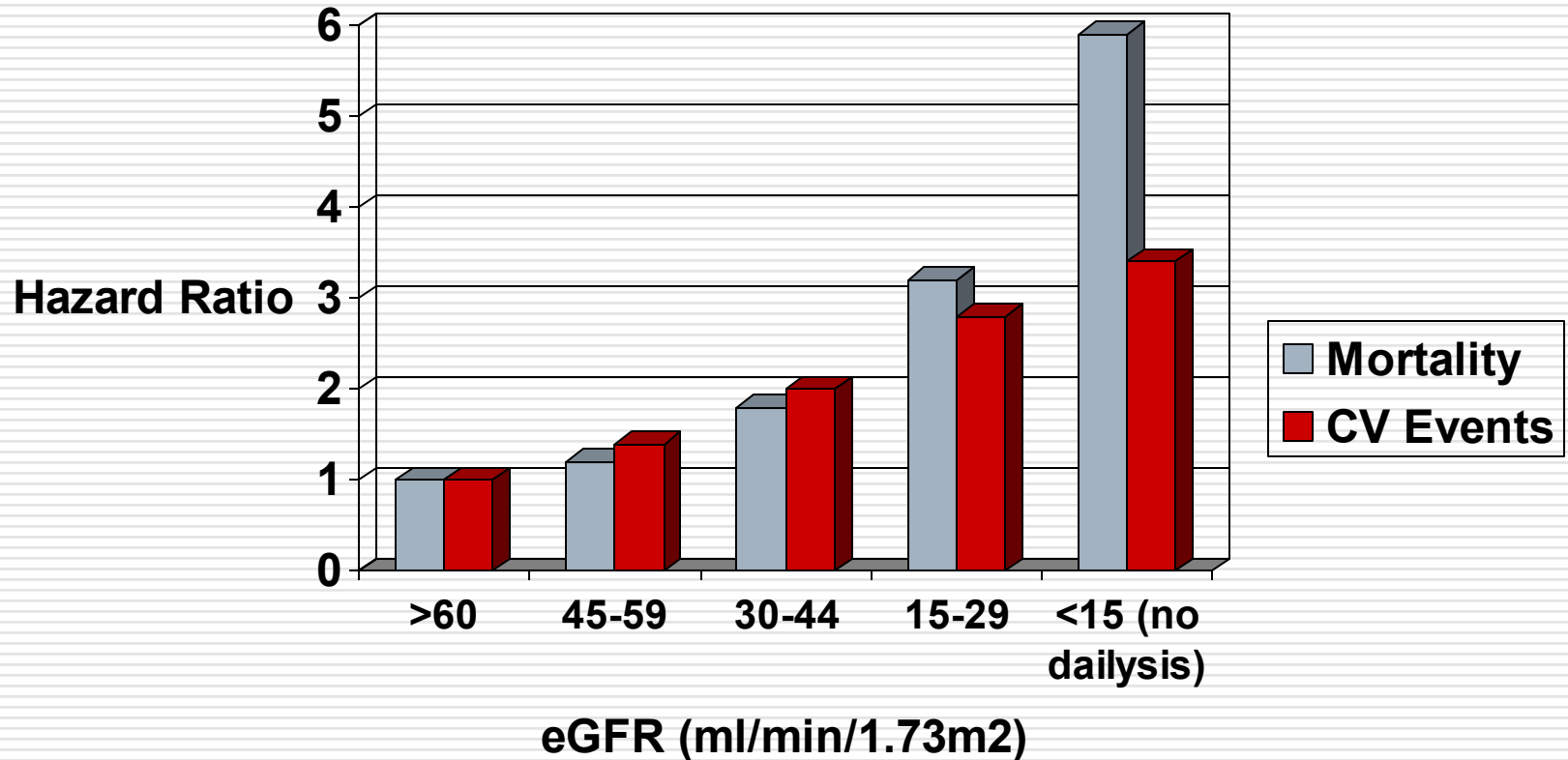
- A 25 year old man with an eGFR of **55** ml/min/1.73m² is 45% below the median for his age and -25 ml/min/1.73m² *below* the 5th percentile for age and gender
- A 75 year old man with an eGFR of **55**ml/min/1.73m² is 30% below the median for his age and +5 ml/min/1.73m² *above* the 5th percentile for age and gender
- ***WHICH ONE HAS SIGNIFICANT CKD?***

CKD and Complications: ***Cardiovascular Disease*** ***(CVD)***

CKD-CVD:

Adjusted HR for All-Cause Mortality and CV Events

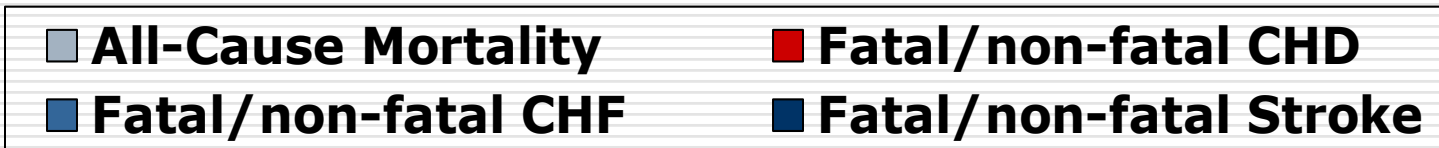
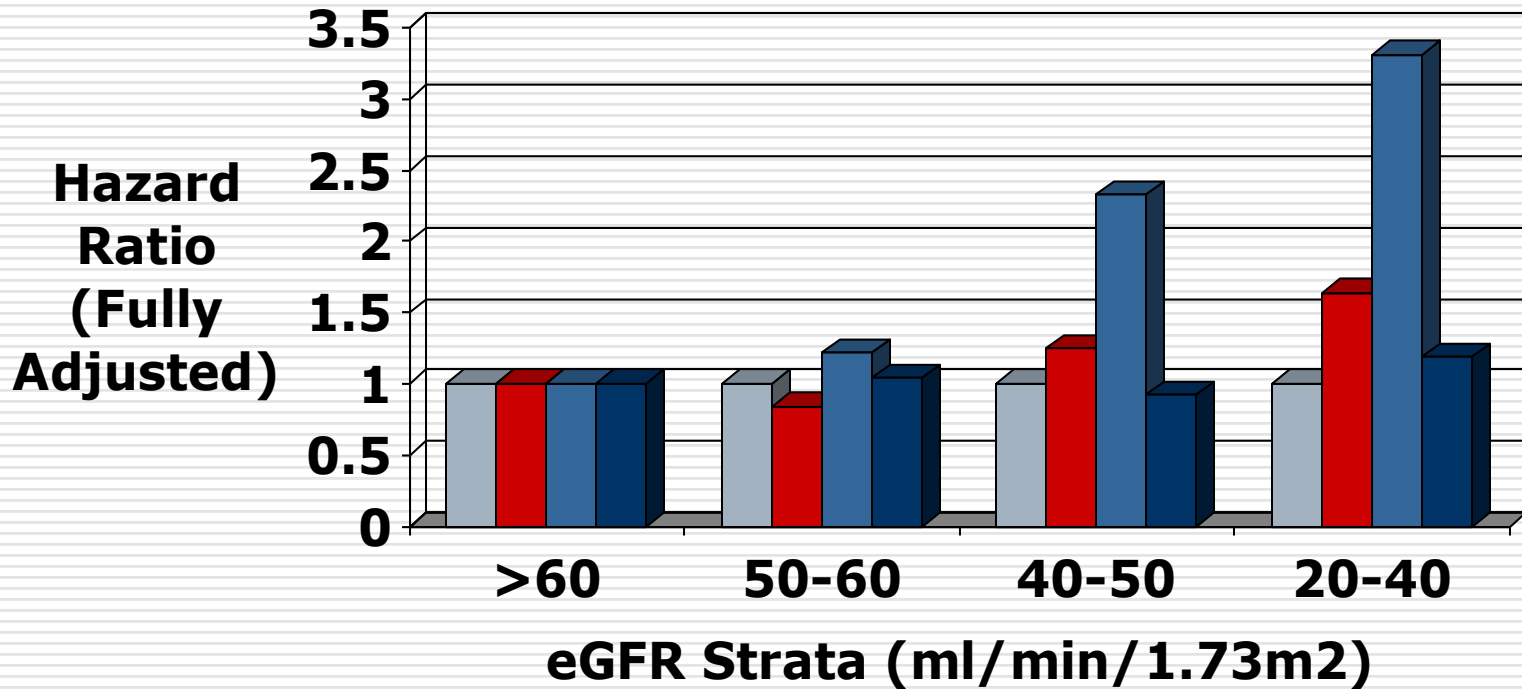
(Go et al, NEJM)



eGFR and Mortality Risk in the Elderly: *Over 70 years of age*

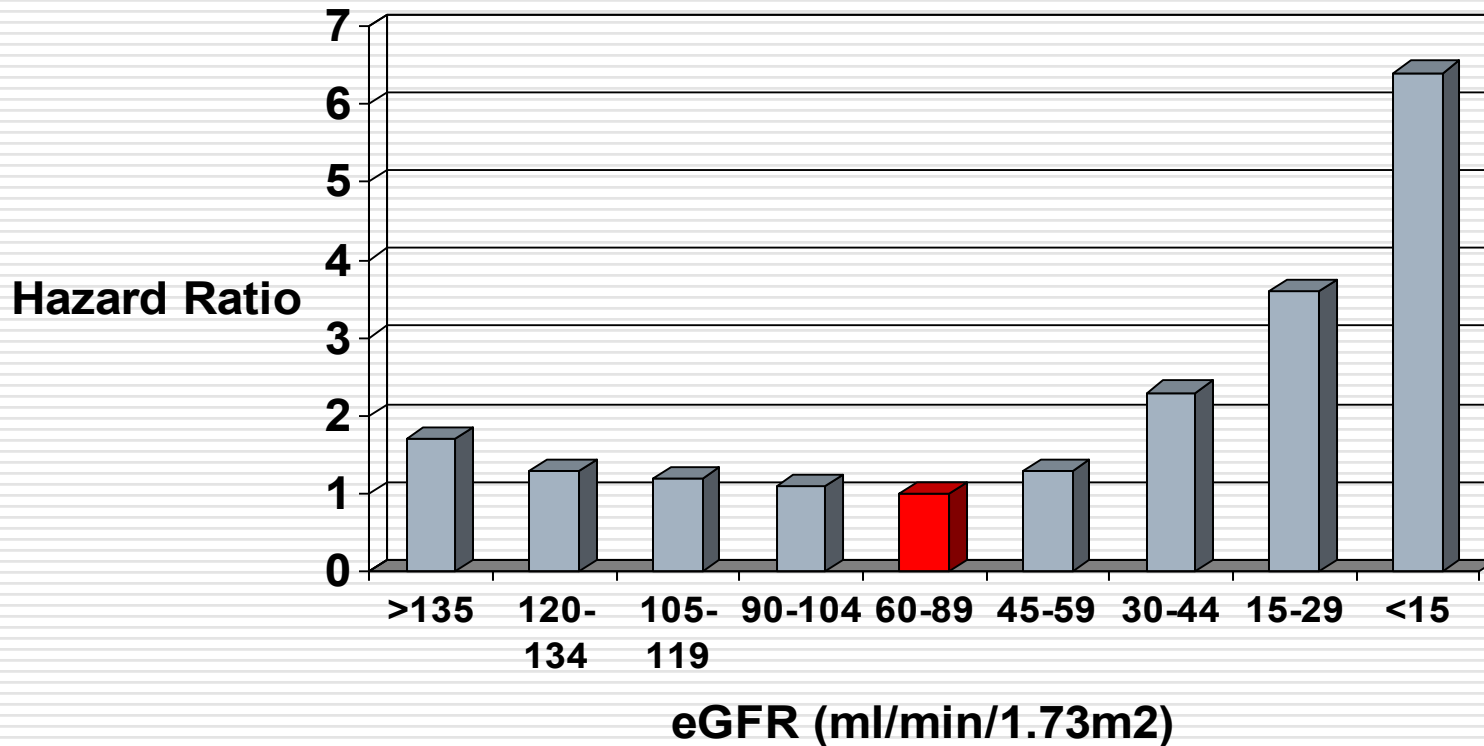
(PROSPER; n=5804)

(Ford I, et al PLoS Med 6:76, 2009)



All-Cause Mortality and eGFR

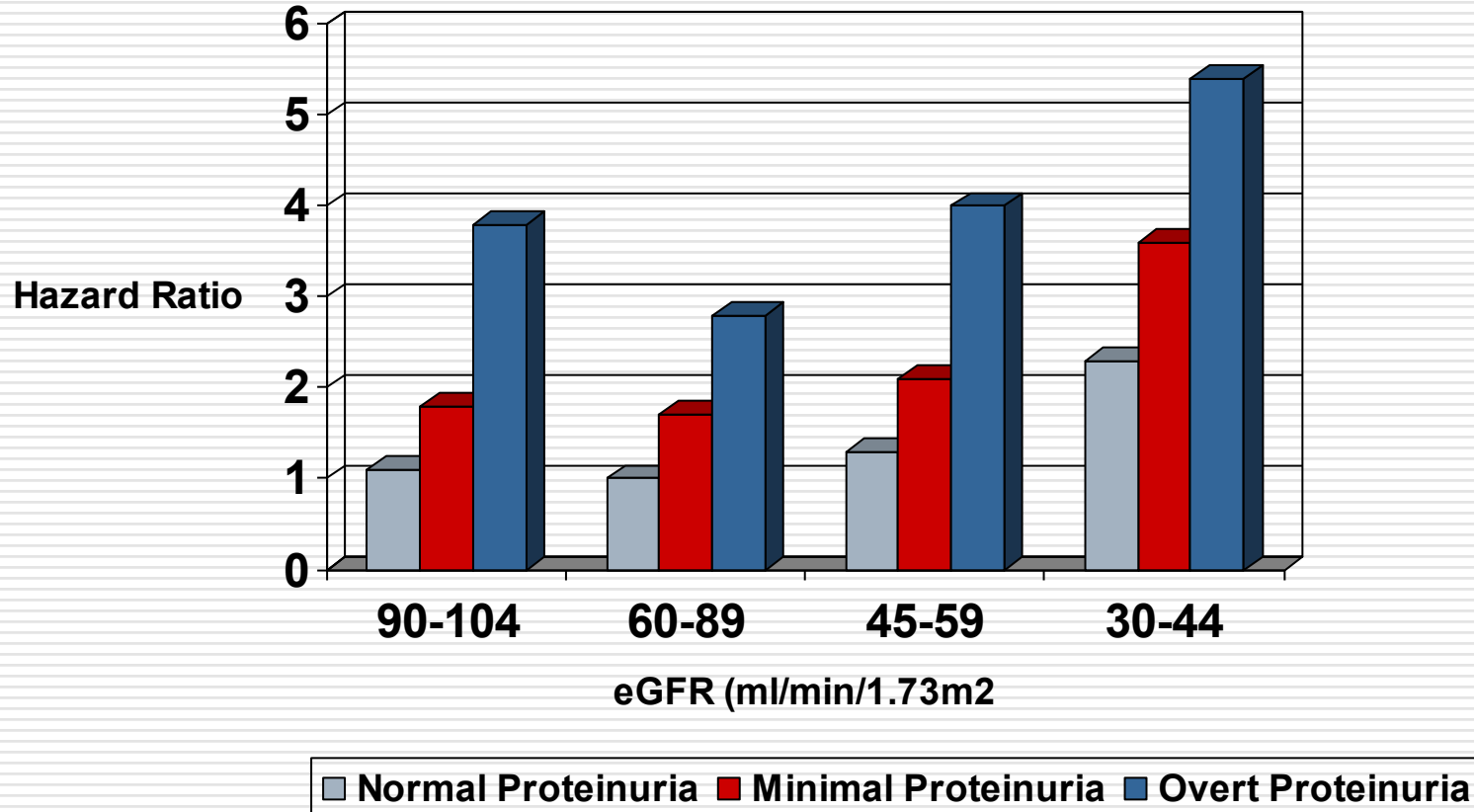
Taiwan Health Management Institution Study
(462,293 Adults-No abnormal proteinuria)
(Wen, CP et al. The Lancet 371:2173, 2008)



All-Cause Mortality and Proteinuria

(At same eGFR strata)

*Taiwan Health Management Institution Study;
Lancet 2008*

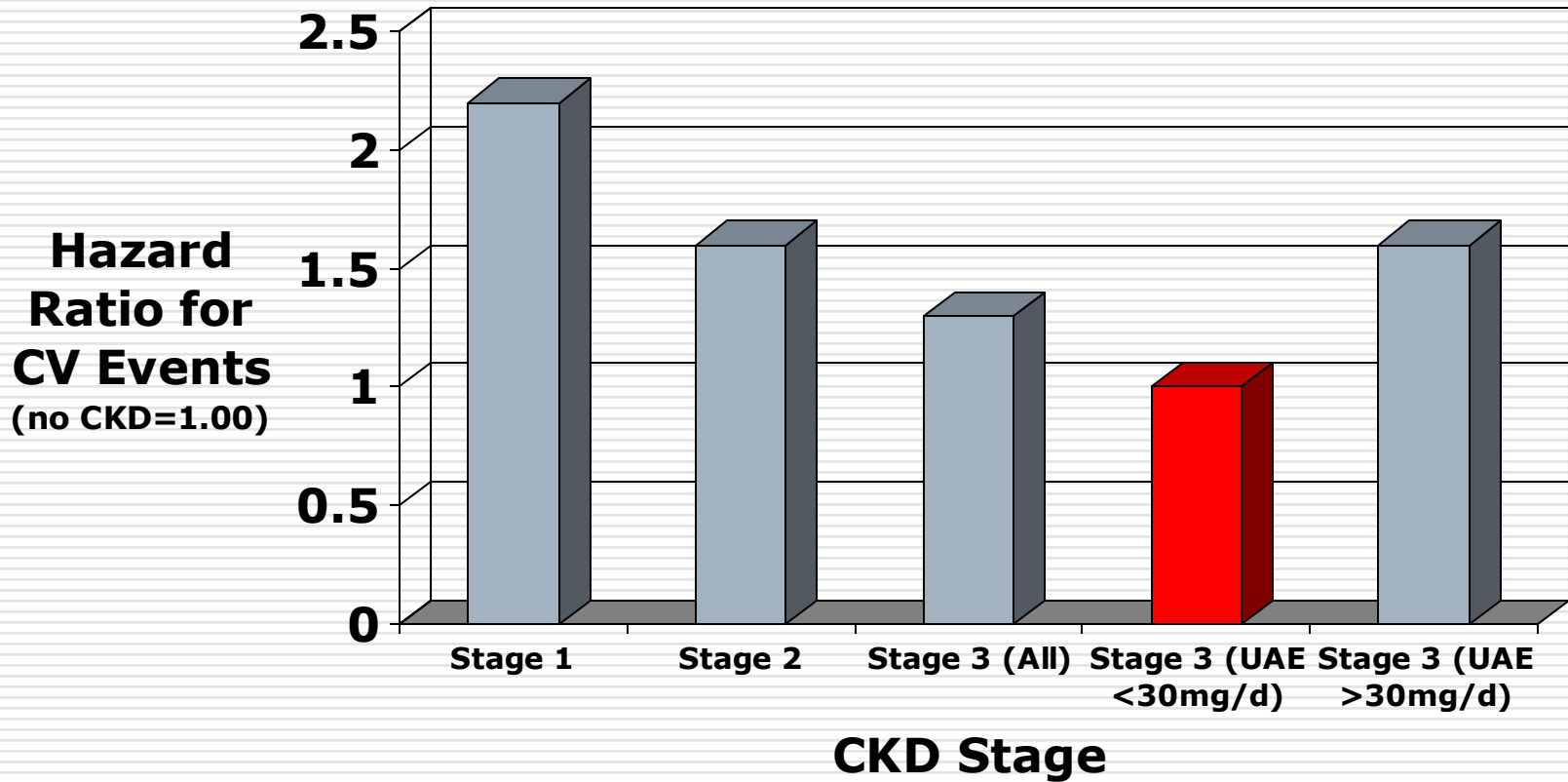


CKD Stage 3

Risk of Cardiovascular Disease

(Brantsma AH, et al and PREVEND. NDT, 2008)

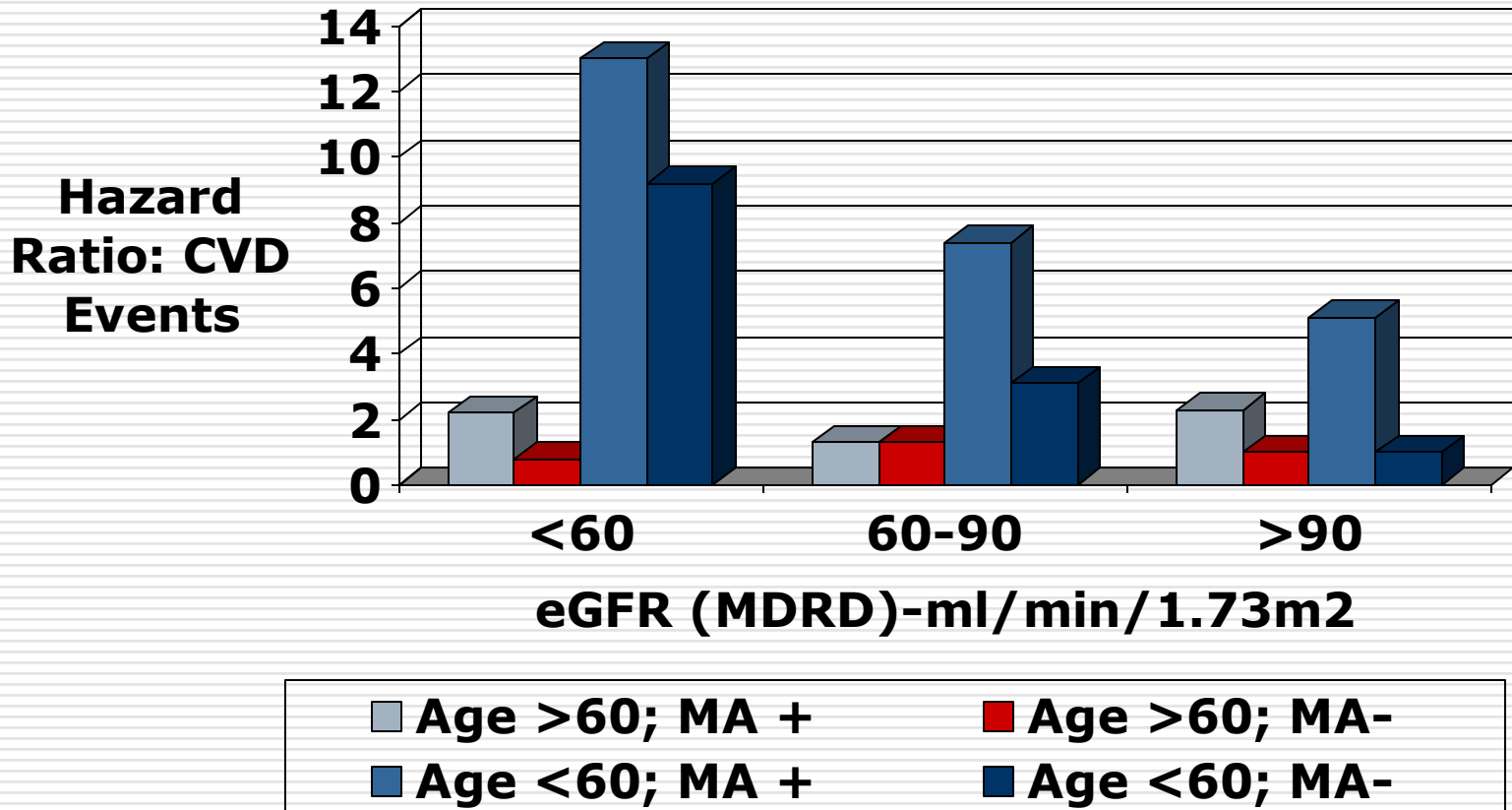
(n=8495- 1590 with CKD)



CVD events and CKD:

PREVEND Study

(van der Velde M, et al. ASN, 2008)

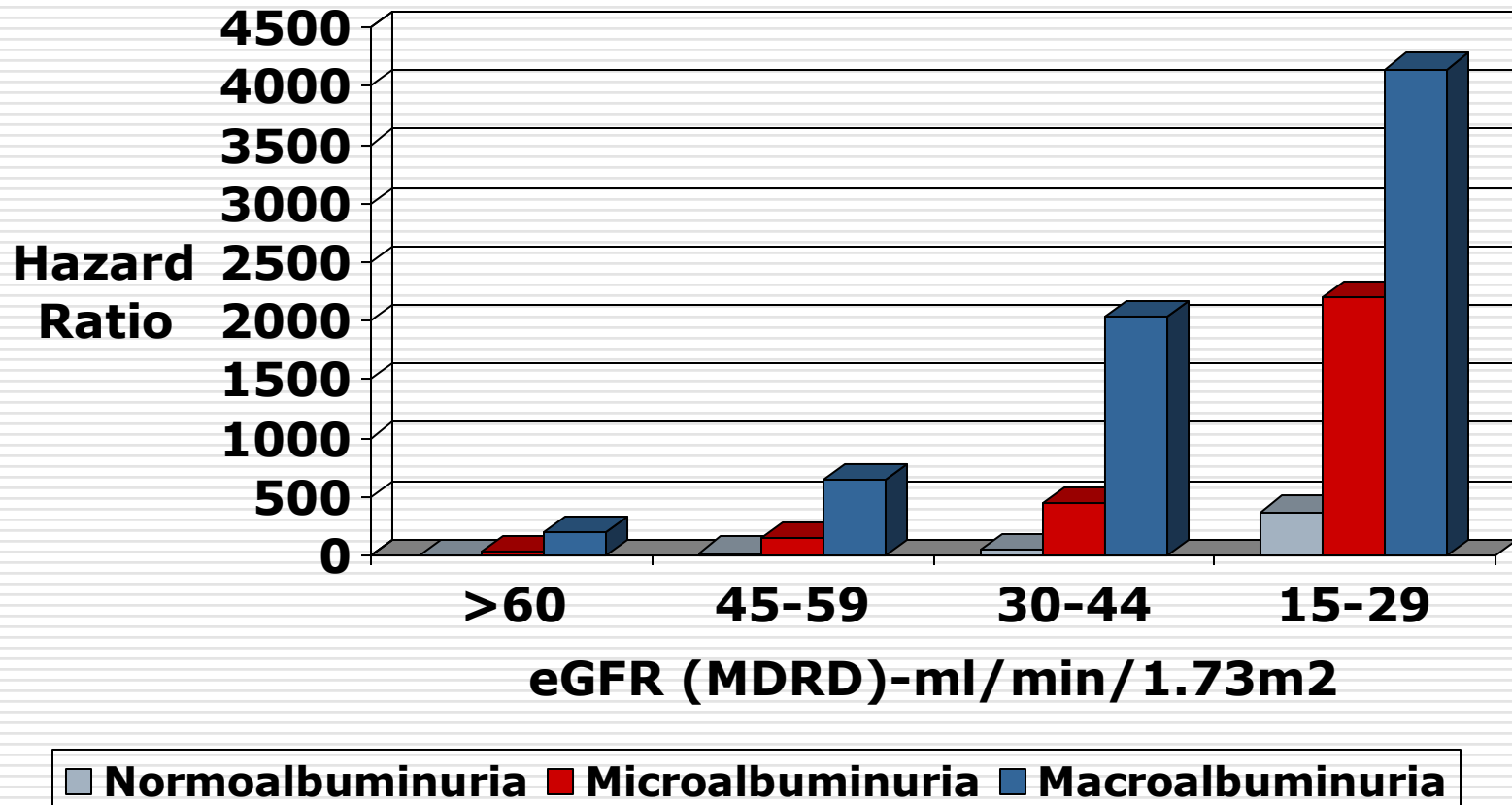


CKD and Complications: ***Progression to ESRD***

The HUNT-II Study-

Adjusted 10 year risk of ESRD according to eGFR and Albuminuria

(Hallan S, et al JASN 20:1069-1077, 2009)



The Problems with CKD Classification: *Conclusions-2009*

- eGFR (1999) and KDOQI-CKD (2002) interacts to greatly *overestimate* the societal burden of CKD- Stages 1-4
- The “Diagnosis” of CKD by *arbitrary* eGFR thresholds (not adjusted for age and gender) leads to a significant *error* rate (false positive Stage 3 CKD)
- Risk of Complications of CKD, based on eGFR alone are *overemphasized-* neglects the multiplier effect of albuminuria
- Conflation of isolated “microalbuminuria” (without abnormal eGFR or diabetes) as a “kidney disease” lacks a firm *rationale*
- Screening for CKD based on eGFR alone cannot be *justified* as cost-effective for prevention of ESRD or CVD

What is “CKD”?

- Is it a ***Diagnosis***?--- For a population or an individual?
 - Is it a ***Post-diagnostic*** step to ***grade*** the severity and determine the risks of progression or complications ?
 - Is it a ***non-specific means of categorizing patients*** with generic manifestations of specific kidney diseases?
 - ***Or all three?***
-

“It ought to be remembered that there is nothing more difficult to take in hand, more perilous to conduct or more uncertain in its success than to take the lead in the introduction of a new order of things”

Niccolo Machiavelli- The Prince, 1513

THANK YOU !!!
