

Enfermedades Ligadas al Envejecimiento de la Sociedad Actual.  
Importancia de la Investigación Traslacional.

# **Estudio de la progresión del daño vascular en la Enfermedad Renal Crónica. Proyecto Nefrona.**

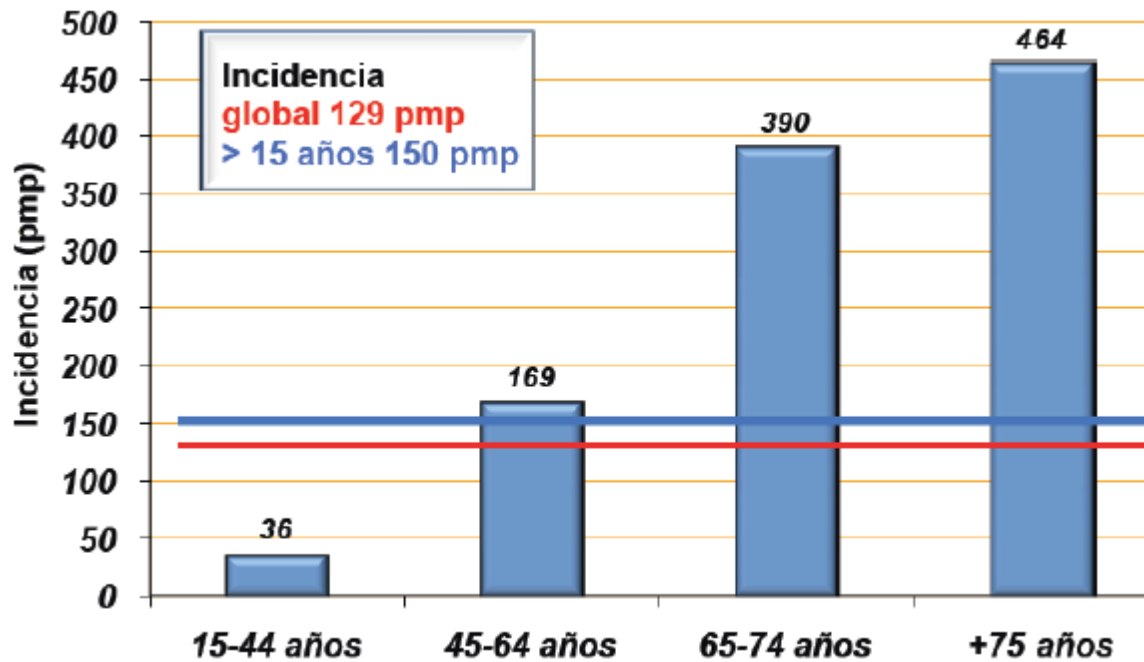
Jose Manuel Valdivielso

Institut de Recerca Biomedica de  
Lleida (IRBLleida)

# ERC. Enfermedad renal crónica

La ERC se define como la disminución de la función renal, expresada por un Filtrado Glomerular (FG)  $< 60$  ml/min o como la presencia de daño renal de forma persistente durante al menos 3 meses.

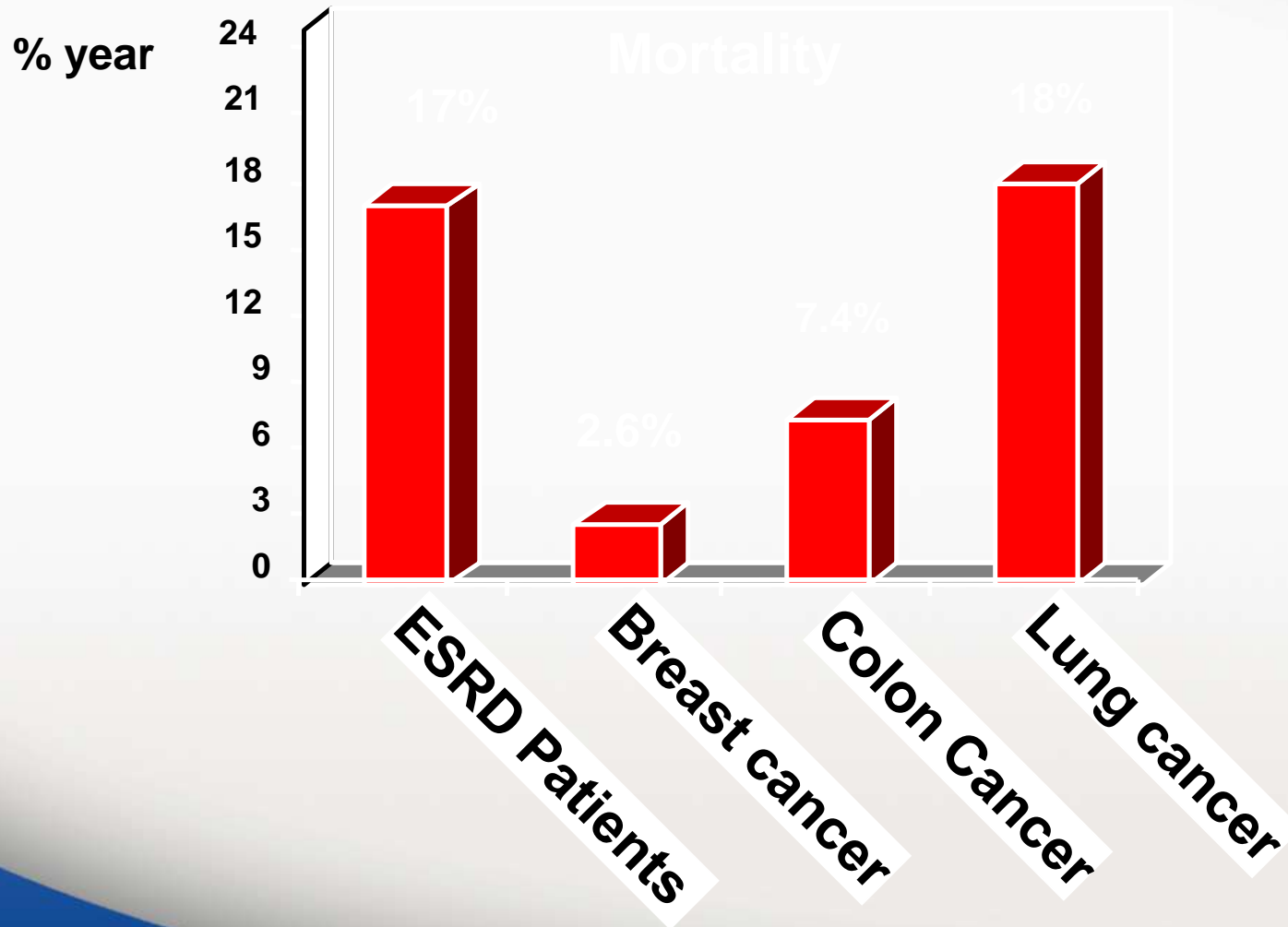
# ERC en España



Fuente: Web de la SEN Informe de Diálisis y Trasplante 2009



# Mortality/year in the US



SEER Cancer Statistics Review 1975-2000  
National Cancer Institute  
USRDS 2003



# Life-expectancy in USA-population (2002) Compared With Dialysis Patients (2003) by Age, Race, Sex

**6.b** Expected remaining lifetimes (years) of the general U.S. population & dialysis & transplant patients, by age, gender, & race

general U.S. population, 2002, & prevalent dialysis & transplant patients, 2003

General U.S. population, 2002									ESRD patients, 2003							
Age	All races			White			Black			Age	Dialysis			Transplant		
	All	M	F	All	M	F	All	M	F		All	M	F	All	M	F
0-14	70.9	68.2	73.4	71.3	68.7	73.7	66.4	62.9	69.7	0-14	18.3	19.2	17.3	50.0	50.2	49.9
15-19	61.1	58.4	63.6	61.4	58.9	63.9	56.7	53.3	59.9	15-19	16.0	16.9	15.1	39.7	39.6	39.8
20-24	56.3	53.8	58.7	56.7	54.2	59.0	52.0	48.7	55.0	20-24	13.9	14.8	12.9	36.2	36.1	36.4
25-29	51.6	49.1	53.9	51.9	49.5	54.2	47.4	44.3	50.2	25-29	12.0	12.7	11.3	32.3	32.1	32.6
30-34	46.8	44.4	49.0	47.1	44.8	49.3	42.8	39.8	45.5	30-34	10.5	10.8	10.0	28.5	28.3	28.9
35-39	39.8	44.2	41.5	38.3	35.4	40.8	33.9	31.1	36.3	35-39	9.0	8.7	8.7	25.2	24.8	25.8
40-44	35.2	39.5	37.7	33.9	31.1	36.3	29.7	26.9	32.0	40-44	8.0	7.6	7.6	21.9	21.5	22.7
45-49	30.8	34.9	33.1	29.7	26.9	32.0	25.7	23.1	27.8	45-49	6.0	5.7	5.7	19.0	18.5	19.8
50-54	28.6	26.6	30.4	28.8	26.8	30.5	25.7	23.1	27.8	50-54	5.9	6.0	5.9	16.3	15.7	17.2
55-59	24.4	22.5	26.0	24.5	22.7	26.1	22.0	19.6	23.9	55-59	5.0	5.0	5.0	13.8	13.2	14.7
60-64	20.4	18.7	21.9	20.5	18.8	21.9	18.5	16.4	20.1	60-64	4.3	4.3	4.4	11.5	11.0	12.5
65-69	16.8	15.2	18.0	16.8	15.2	18.0	15.3	13.5	16.7	65-69	3.7	3.6	3.7	9.6	9.1	10.6
70-74	13.4	12.0	14.4	13.4	12.0	14.4	12.4	10.8	13.5	70-74	3.1	3.1	3.1	7.9	7.4	8.9
75-79	10.4	9.3	11.1	10.3	9.2	11.1	9.9	8.6	10.7	75-79	2.6	2.6	2.7	6.7	6.2	7.7
80-84	7.8	6.9	8.3	7.7	6.9	8.2	7.8	6.8	8.3	80-84	2.2	2.2	2.2			
85+	4.3	3.8	4.5	4.2	3.7	4.3	4.6	4.2	4.8	85+	1.8	1.7	1.8			
overall*	25.2	23.4	26.6	25.3	23.5	26.7	23.0	20.8	24.7	overall*	5.5	5.6	5.4	15.1	14.6	15.9

40-44

35.6

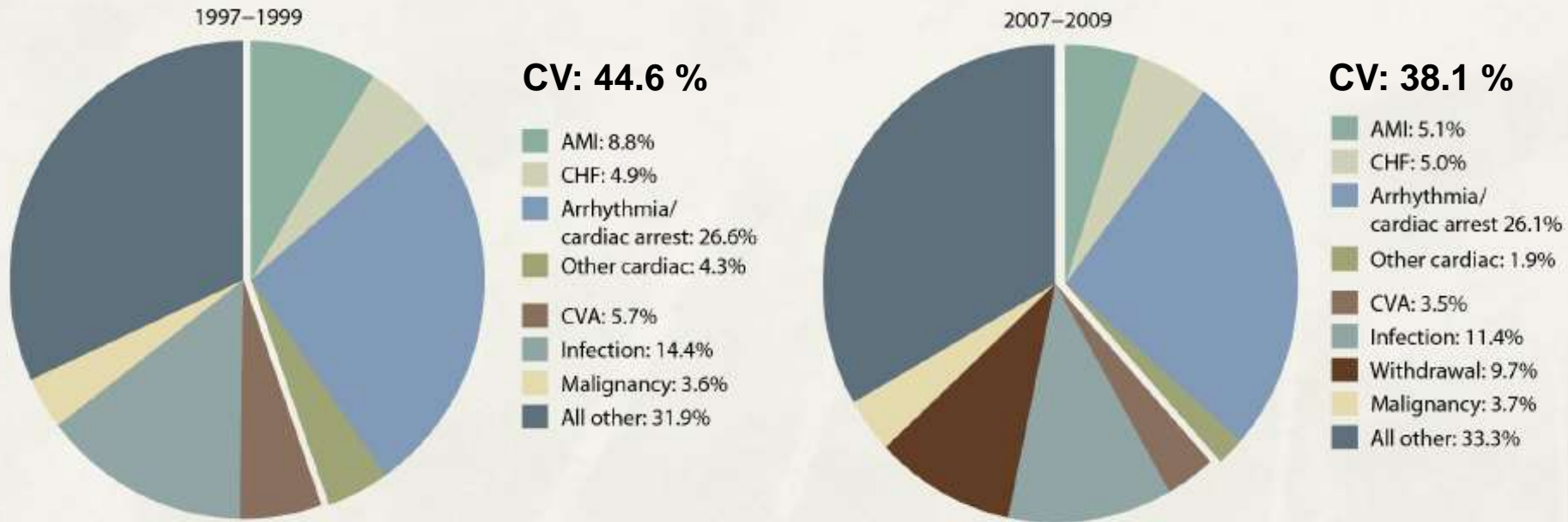
8.0

# Enfermedad cardiovascular y mortalidad



La enfermedad Cardiovascular es la responsable del 40-50% de la mortalidad de los pacientes en diálisis

# Mortality in ESRD



Causes of death among period prevalent dialysis patients 1997-1999 and 2007-2009. Data are from the USRDS Special Session: 'Heart Disease and CKD: is it getting any better? From Charles A. Herzog MD' ([www.usrds.org](http://www.usrds.org))

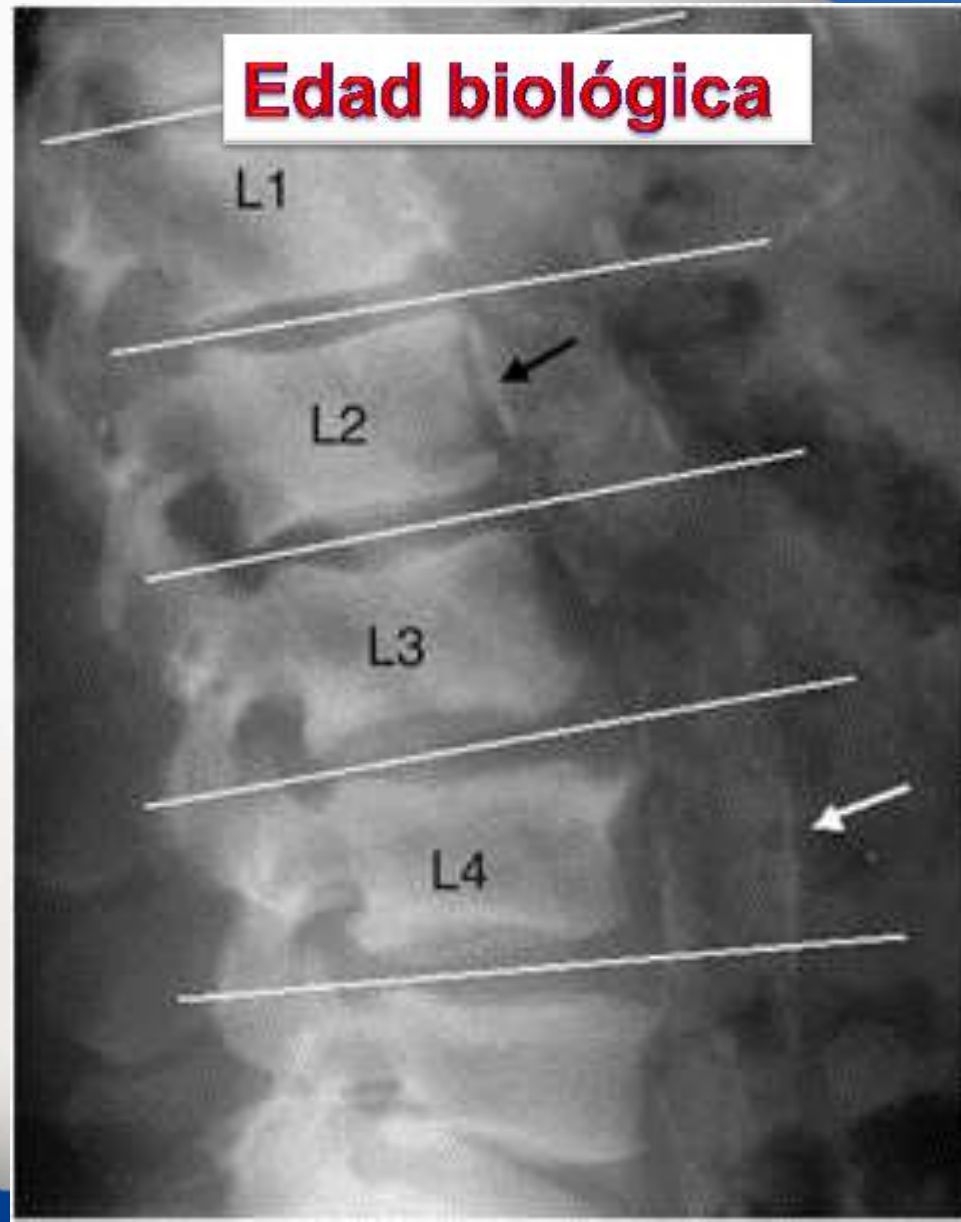


# Envejecimiento vascular: Es más acelerado y precoz

## Edad cronológica



## Edad biológica



# Life-expectancy in USA-population (2002) Compared With Dialysis Patients (2003) by Age, Race, Sex

**6.b** Expected remaining lifetimes (years) of the general U.S. population & dialysis & transplant patients, by age, gender, & race

General U.S. population, 2002										ESRD patients, 2003						
Age	All races			White			Black			Age	Dialysis			Transplant		
	All	M	F	All	M	F	All	M	F		All	M	F	All	M	F
0-14	70.9	68.2	73.4	71.3	68.7	73.7	66.4	62.9	69.7	0-14	18.3	19.2	17.3	50.0	50.2	49.9
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25-29	51.6	49.1	53.9	51.9	49.5	54.2	47.4	44.3	50.2	25-29	12.0	12.7	11.3	32.3	32.1	32.6
30-34	46.8	44.4	49.0	47.1	44.8	49.3	42.8	39.8	45.5	30-34	10.5	10.8	10.0	28.5	28.3	28.9
35-39	39.8	37.7	42.4	37.7	35.6	39.7	33.9	31.1	36.3	35-39	9.0	9.3	8.7	25.2	24.8	25.8
40-44	35.2	33.2	37.7	33.2	31.1	35.1	29.7	26.9	32.0	40-44	8.0	8.3	7.6	21.9	21.5	22.7
45-49	30.8	28.8	33.2	28.8	26.8	30.5	25.7	23.1	27.8	45-49	6.8	7.0	6.7	19.0	18.5	19.8
50-54	28.6	26.6	30.4	26.6	24.5	28.1	22.0	19.6	23.9	50-54	5.9	6.0	5.9	16.3	15.7	17.2
55-59	24.4	22.5	26.0	22.5	20.5	24.4	18.5	16.4	20.1	55-59	5.0	5.0	5.0	13.8	13.2	14.7
60-64	20.4	18.7	21.9	18.7	16.8	21.9	15.3	13.5	16.7	60-64	4.3	4.3	4.4	11.5	11.0	12.5
65-69	16.8	15.2	18.0	15.2	13.5	18.0	12.4	10.8	13.5	65-69	3.7	3.6	3.7	9.6	9.1	10.6
70-74	12.0	11.1	14.4	11.1	9.9	14.4	10.7	8.6	10.7	70-74	3.1	3.1	3.1	7.9	7.4	8.9
75-79	9.3	8.3	11.1	8.3	7.8	11.1	8.3	6.8	8.3	75-79	2.6	2.6	2.7	6.7	6.2	7.7
80-84	6.9	6.9	8.3	6.9	6.2	8.3	4.6	4.2	4.8	80-84	2.2	2.2	2.2			
85+	4.3	3.8	4.5	4.2	3.7	4.5				85+	1.8	1.7	1.8			
overall*	25.2	23.4	26.6	25.3	23.5	26.7	23.0	20.8	24.7	overall*	5.5	5.6	5.4	15.1	14.6	15.9

40-44

8.0

75-79

9.2



'There are some things they don't teach you in medical school. I think you've got one of those things.'



# RISK PREDICTION



# BIOMARKER DEFINITION

**Biological Marker:** A characteristic that is objectively measured as an indicator of normal biological process, pathogenic processes or pharmacological responses to a therapeutic intervention (Type 0, 1 and 2).

**Risk Factor:** A risk factor is associated with a disease because it is in the causal pathway leading to the disease

**Risk Marker:** A marker is associated with the disease (statistically) but may not be causally linked (measure of the disease process itself)



# Traditional Risk Factors for CVD The Framingham Study

Age

Sex

Total Cholesterol

HDL Cholesterol

Systolic Blood Pressure

Smoking status

Diabetes

# Assessing CVD Risk in Men

## Step 1: Age

Years	Points
20-34	-9
35-39	-4
40-44	0
45-49	3
50-54	6
55-59	8
60-64	10
65-69	11
70-74	12
75-79	13

## Step 2: Total Cholesterol

TC (mg/dL)	Points at Age 20-39	Points at Age 40-49	Points at Age 50-59	Points at Age 60-69	Points at Age 70-79
<160	0	0	0	0	0
160-199	4	3	2	1	0
200-239	7	5	3	1	0
240-279	9	6	4	2	1
≥280	11	8	5	3	1

## Step 3: HDL-Cholesterol

HDL-C (mg/dL)	Points
≥60	-1
50-59	0
40-49	1
<40	2

## Step 4: Systolic Blood Pressure

Systolic BP (mm Hg)	Points if Untreated	Points if Treated
<120	0	0
120-129	0	1
130-139	1	2
140-159	1	2
≥160	2	3

## Step 5: Smoking Status

	Points at Age 20-39	Points at Age 40-49	Points at Age 50-59	Points at Age 60-69	Points at Age 70-79
Nonsmoker	0	0	0	0	0
Smoker	8	5	3	1	1

## Step 6: Adding Up the Points

Age	_____
Total cholesterol	_____
HDL-cholesterol	_____
Systolic blood pressure	_____
Smoking status	_____
Point total	_____

## Step 7: CHD Risk

Point Total	10-Year Risk
<0	<1% 11 8%
0	1% 12 10%
1	1% 13 12%
2	1% 14 16%
3	1% 15 20%
4	1% 16 25%
5	2% ≥17 ≥30%
6	2%
7	3%
8	4%
9	5%
10	6%

# The Framingham Prediction Model in CKD

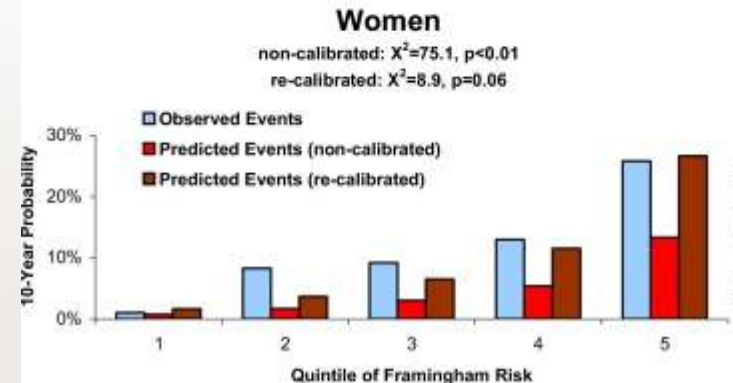
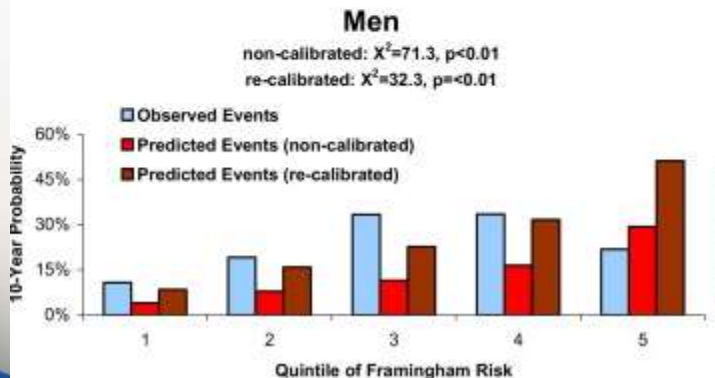
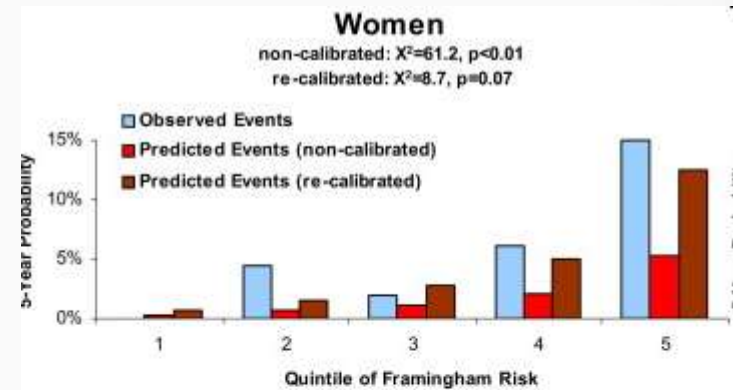
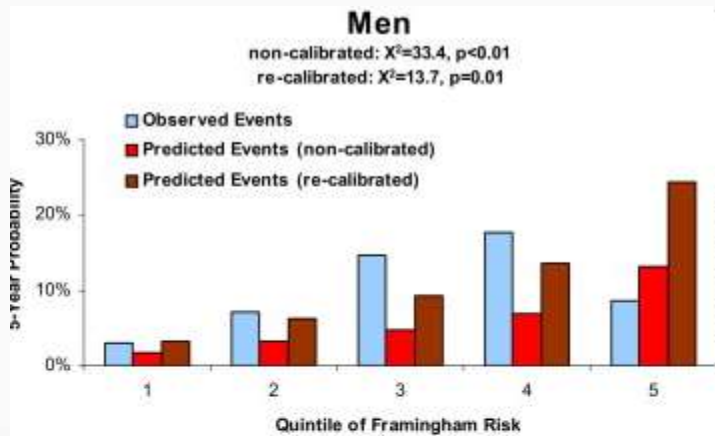
**Table 2**

**Framingham Probabilities and Event Rates for Men and Women in the CKD and Framingham Derivation Cohorts**

	Men		Women	
	CKD (n = 357)	Framingham (n = 2,439)	CKD (n = 577)	Framingham (n = 2,812)
Framingham probability (%)				
5-yr	6.0 ± 4.6	3.5 ± 3.6	1.9 ± 2.2	0.9 ± 1.6
10-yr	13.9 ± 9.8	8.2 ± 7.9	4.8 ± 5.4	2.5 ± 4.0
Outcomes (%)				
5-yr cardiac events	9.8	3.7	5.1	1.4
10-yr cardiac events	20.7	8.0	9.7	2.8
5-yr mortality events	14.8	3.5	9.4	2.3
10-yr mortality events	35.3	9.0	20.8	5.8

Rates were compared using chi-square tests and means using t tests. All testing was 2-sided. All p values <0.001 for gender-specific differences between individuals with chronic kidney disease (CKD) and Framingham subjects. Framingham probabilities and 5- and 10-year mortality data from the derivation cohort for the Framingham equation were not readily available in published data; therefore, these were generated by reproducing the Framingham derivation cohort using limited access patient level data from visit 11 of the Framingham Heart study and the baseline visit of the Framingham Offspring study.

# The Framingham Prediction Model in CKD



Weiner et al. JACC 50:217-224. 2007

# The Framingham Prediction Model in CKD

Traditional risk factors have bigger weight

New risk factors needed for the equation

Inflammation

Anemia

Mineral metabolism

Endothelial dysfunction

Procoagulant state

Volume expansion

Adipokines

Activation of the sympathetic system

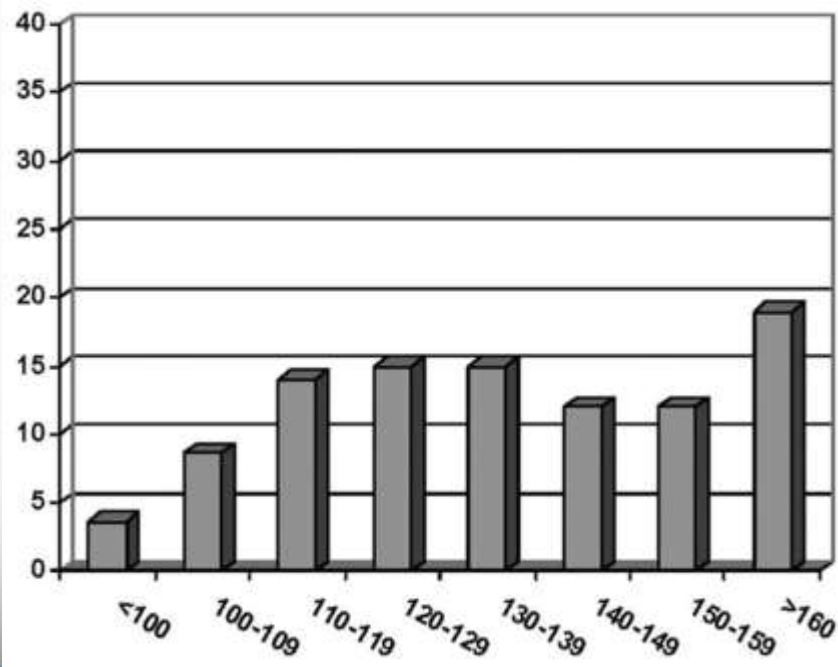
Hypothyroidism



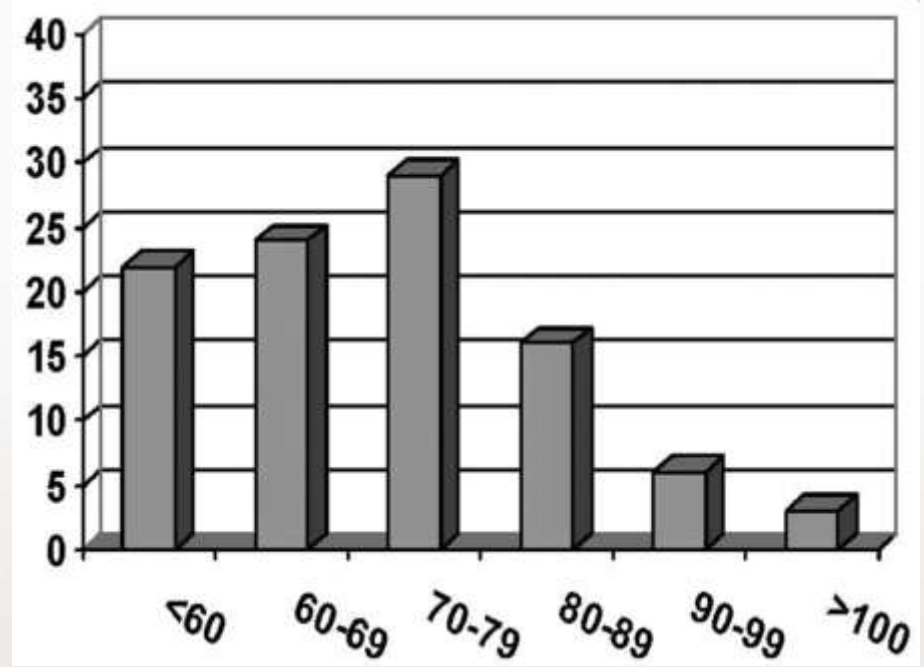
# Traditional Risk Factors

## Hypertension

Poorly controlled in CKD



SBP

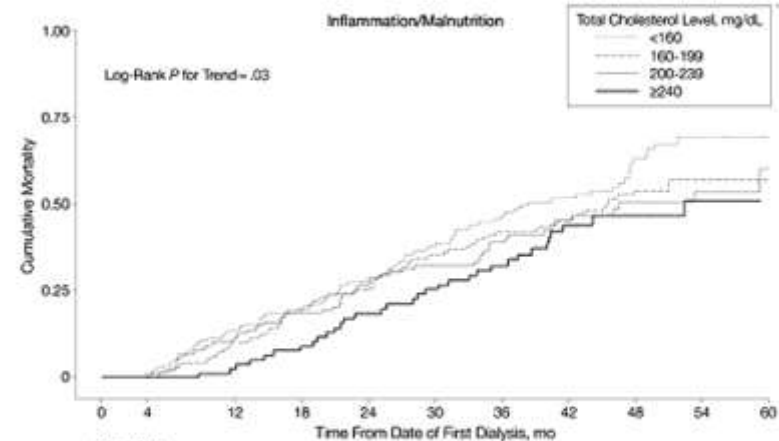


DBP

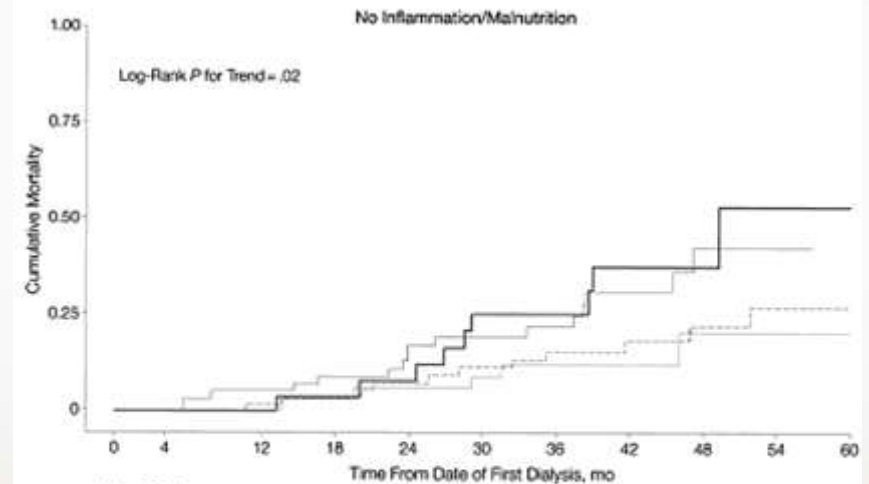
NHANES IV

# Traditional Risk Factors

## Dyslipidemia



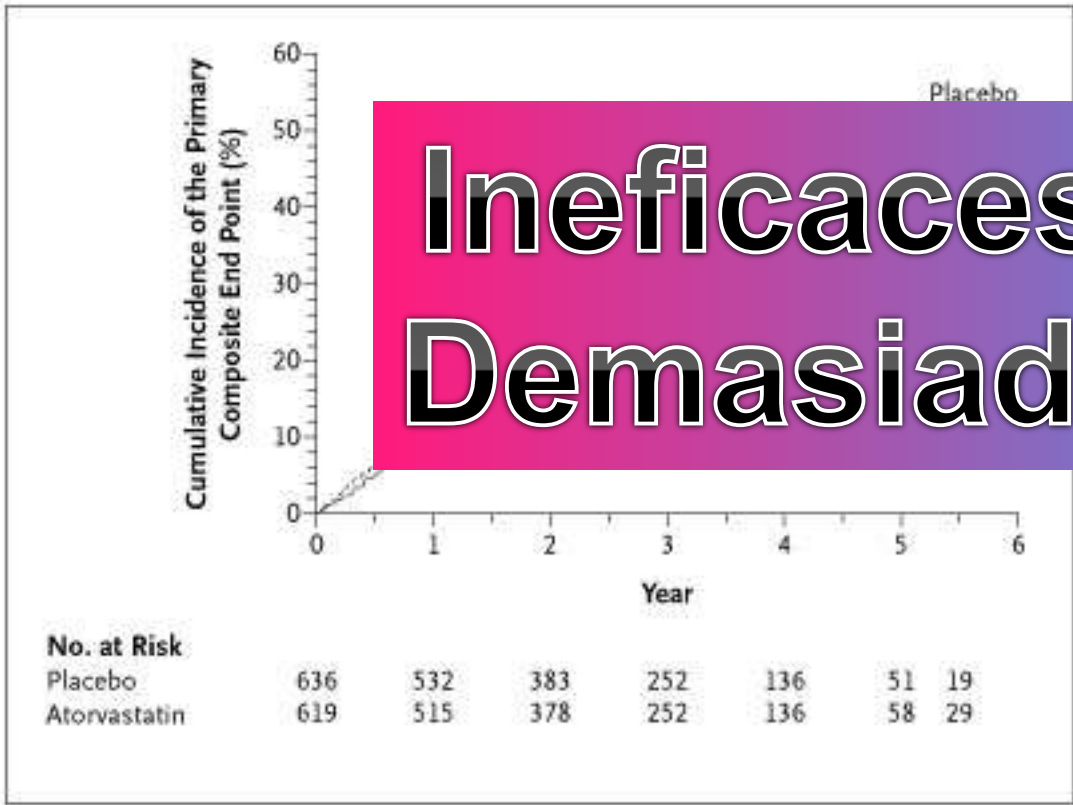
Cholesterol Level, mg/dL	0	12	24	36	48	60
<160	176	136	86	31		
160-199	180	145	92	37		
200-239	107	82	53	27		
≥240	70	59	47	15		



Cholesterol Level, mg/dL	0	12	24	36	48	60
<160	35	34	23	7		
160-199	54	48	40	23		
200-239	47	41	30	9		
≥240	25	23	16	7		

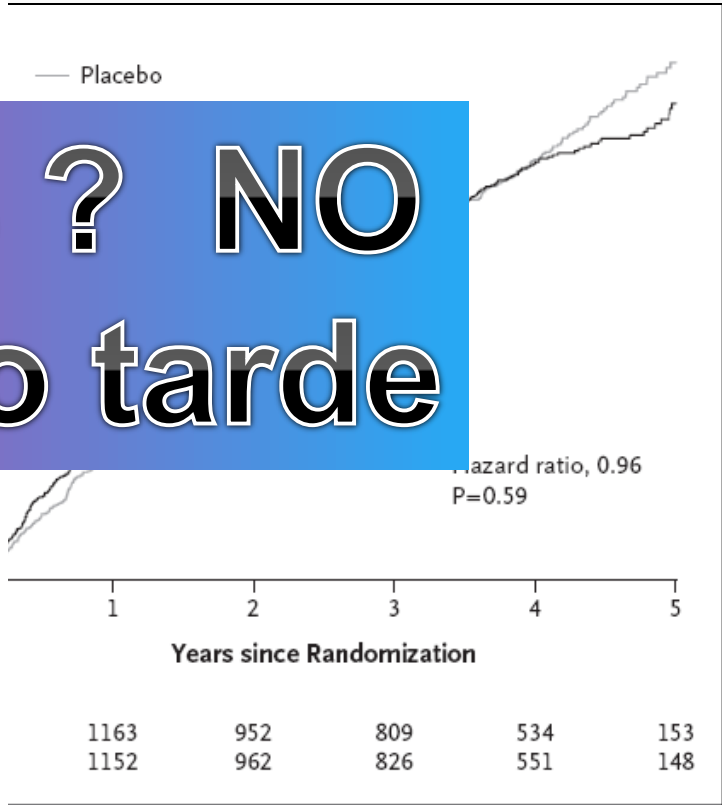
# 4D

1255 randomized 1:1 hemodialysis diabetic patients.  
 Atorvastatin 20 mg/Placebo  
 Primary and Secondary Prevention of CVD



# AURORA

2776 randomized 1:1 hemodialysis patients.  
 Rosuvastatin 10 mg/Placebo  
 Primary and Secondary Prevention of CVD



**Ineficaces ? NO**  
**Demasiado tarde**