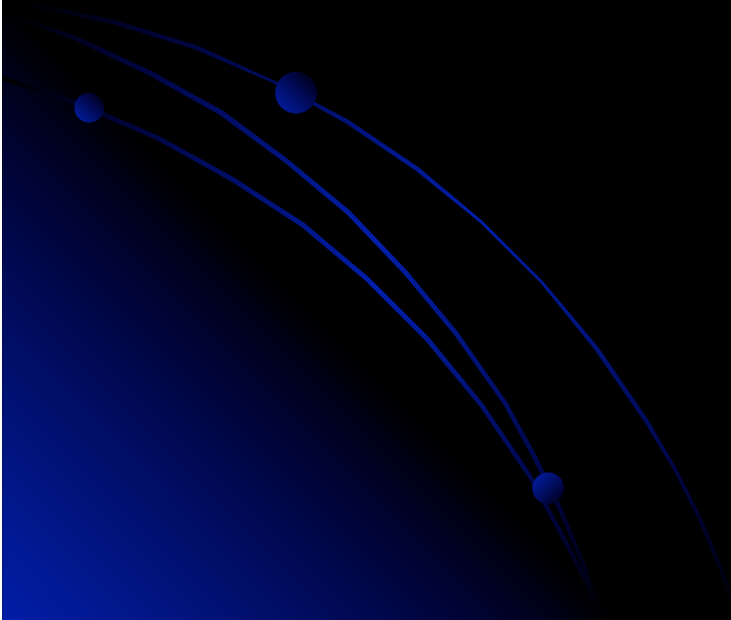



Calcificación Vascular





“Un hombre es tan viejo como sus vasos”

R. Virchow (1821-1902)

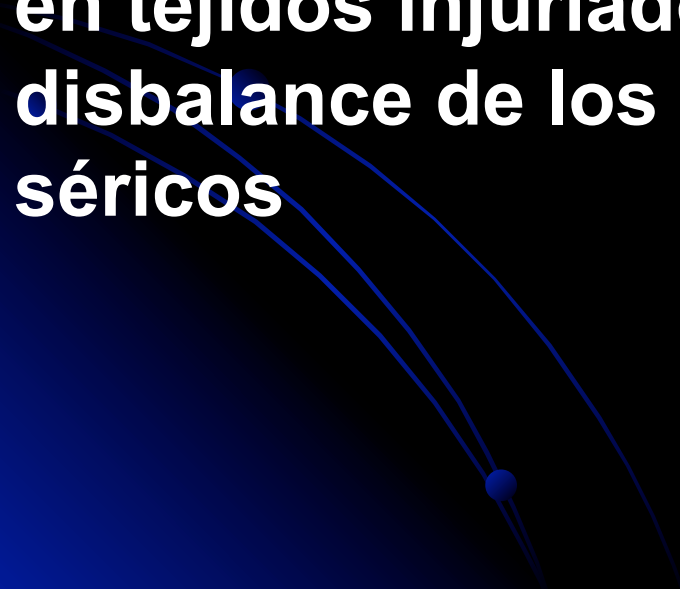
- **Definición**
 - **Epidemiología**
 - **Fisiopatología de las calcificaciones**
 - **Implicancias clínicas**
 - **Tratamiento**
 - **Conclusiones**
- 

• Definición

Las calcificaciones se definen como el anormal depósito de sales de calcio en tejidos blandos

• Calcificaciones metastásicas : las que ocurren en tejidos vitales como consecuencia de la alteración del metabolismo fosfocálcico

• Calcificaciones distróficas : son las que ocurren en tejidos injuriados o necróticos en ausencia de desbalance de los niveles de fósforo y calcio séricos



Calcificaciones Vasculares

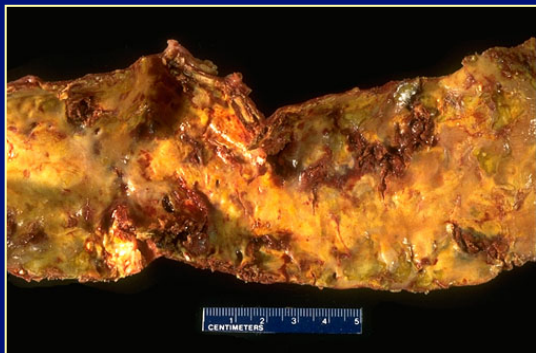
Aterosclerosis : Calcificación de la placa de ateroma

Arterioesclerosis: Calcificación de la capa media muscular

(Esclerosis medial de Monckeberg)

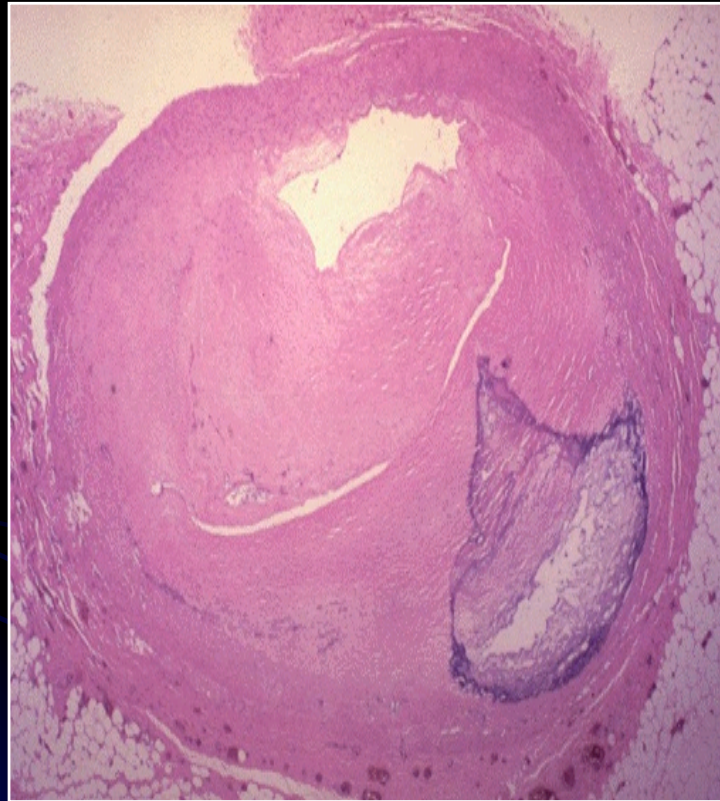


Arteriosclerosis versus Aterosclerosis

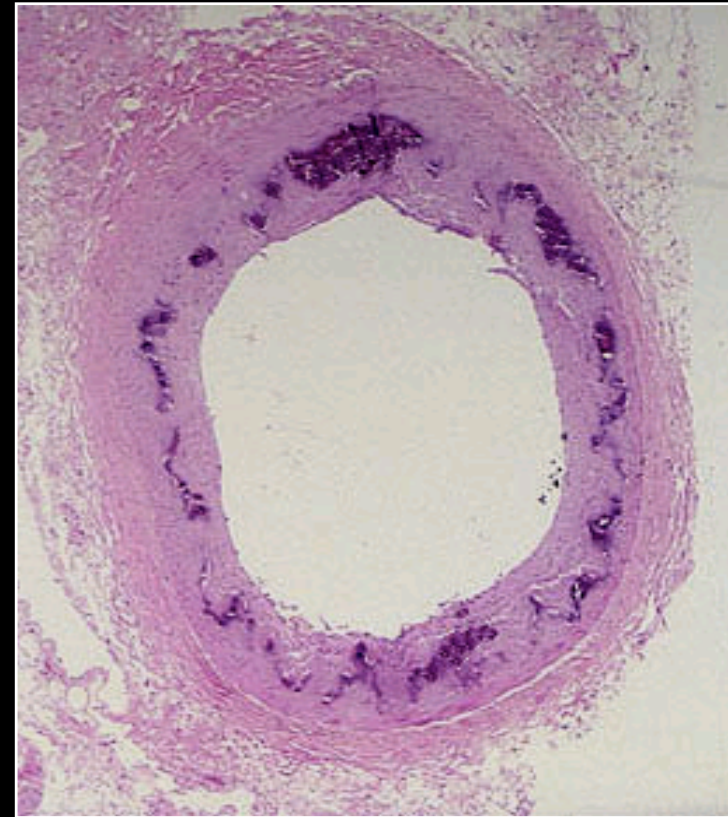


- ATEROSCLEROSIS
 - Caracterizada por la presencia de placas y distribución parcelar
 - Se desarrolla primariamente en la íntima
 - Consecuencia: oclusión y isquemia o infarto distal
 - Factores: dislipemia - estrés mecánico - diabetes - inflamación - tabaco - estrés oxidativo
- ARTERIOSCLEROSIS
 - Caracterizada por remodelado generalizado del árbol arterial
 - Se desarrolla primariamente en la media
 - Consecuencia: rigidez arterial, sobrecarga cardiaca de presión y alteración de la perfusión coronaria
 - Factores: edad - HTA - **uremia** - diabetes - aterosclerosis


Vascular Calcification in ESRD



**Intimal Calcification
Atherosclerosis**

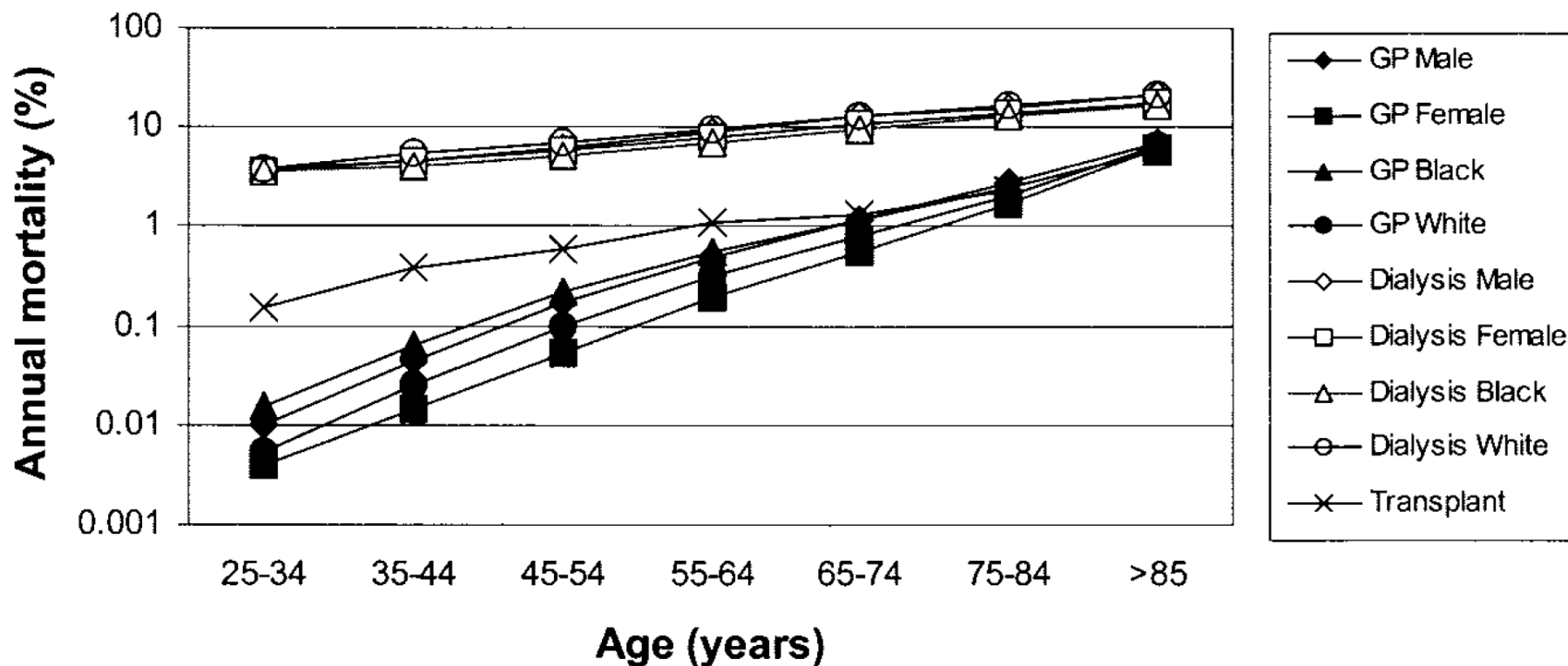


**Medial Calcification
Arteriosclerosis**

- **Definición**
 - **Epidemiología**
 - **Fisiopatología de las calcificaciones**
 - **Implicancias clínicas**
 - **Tratamiento**
 - **Conclusiones**
- 
- Decorative graphic element consisting of three curved blue lines with circular dots at their ends, located in the bottom-left corner of the slide.

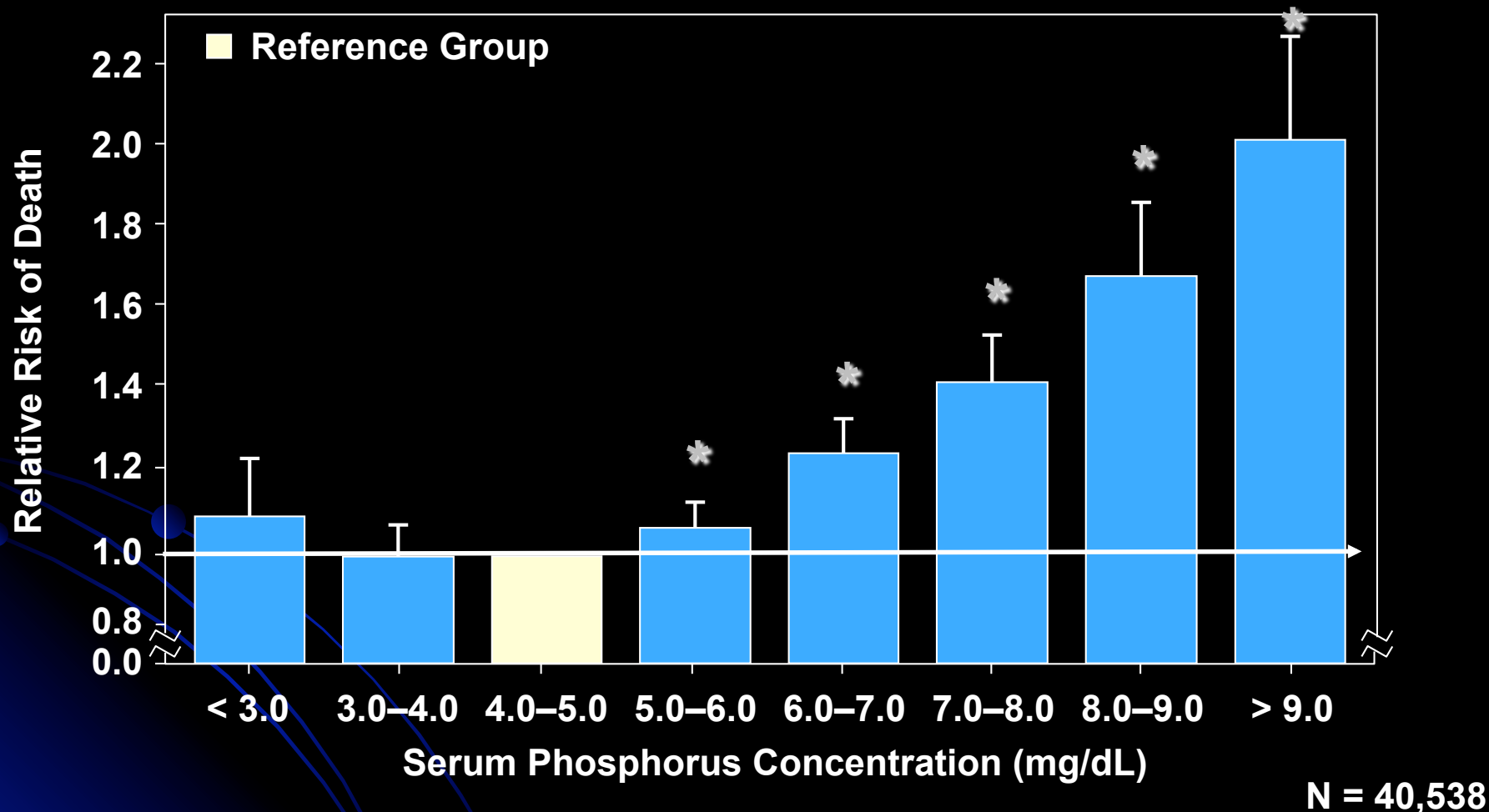
Mortalidad CV en Diálisis vs Población General

Cardiovascular mortality in the general population (NCHS) and in kidney failure treated by dialysis or transplant (USRDS)



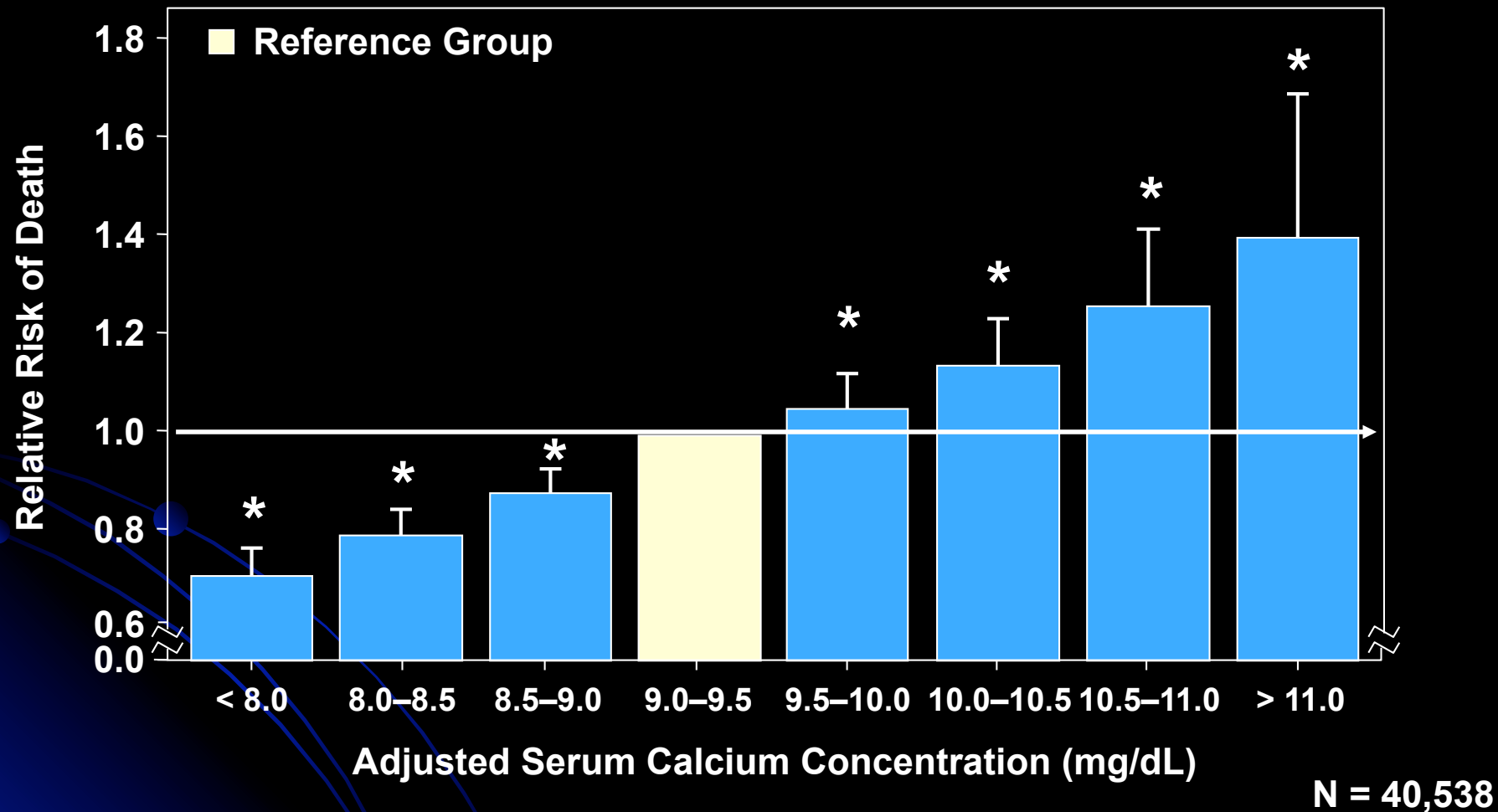
PG: Población general

Multivariable-Adjusted Relative Risk (RR) of Death for Serum Phosphorus



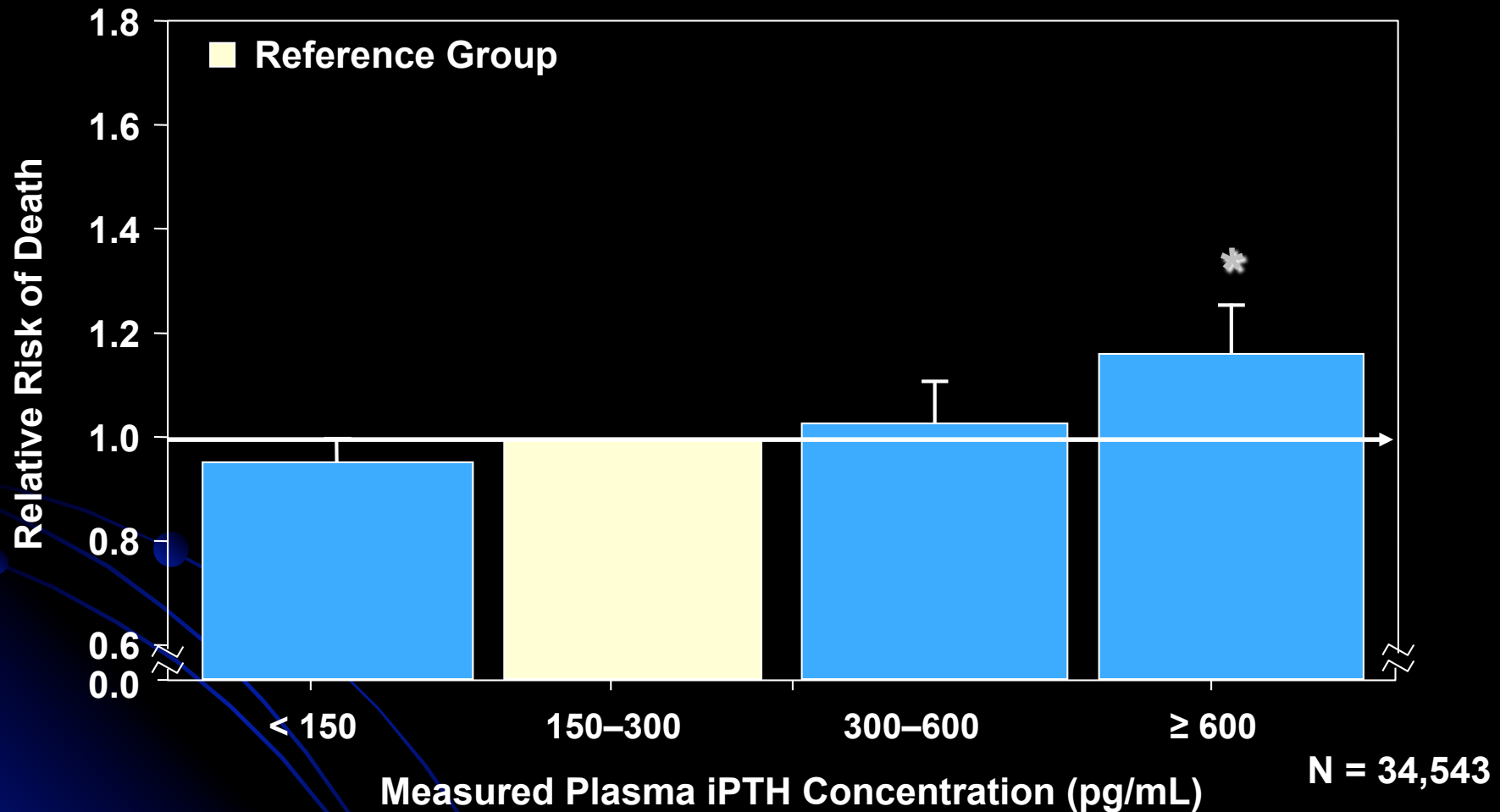
Multivariable analysis adjusted for age, gender, race or ethnicity, diabetes, vintage, body weight, URR, serum albumin, creatinine, predialysis BUN, bicarbonate, cholesterol, hemoglobin, ferritin, and aluminum
 Adapted from Block GA, et al. *J Am Soc Nephrol.* 2004;15:2208-2218.

Multivariable-Adjusted Relative Risk of Death for Adjusted Serum Calcium



Multivariable analysis adjusted for age, gender, race or ethnicity, diabetes, vintage, body weight, URR, serum albumin, creatinine, predialysis BUN, bicarbonate, cholesterol, hemoglobin, ferritin, and aluminum
Adapted from Block GA, et al. *J Am Soc Nephrol.* 2004;15:2208-2218.

Multivariable-Adjusted Relative Risk of Death for iPTH

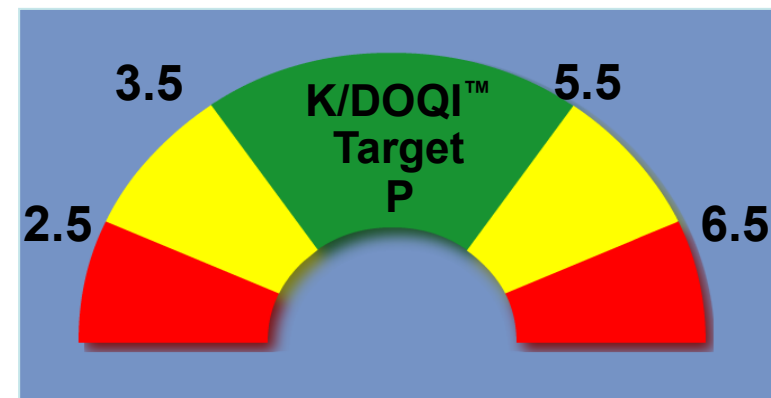
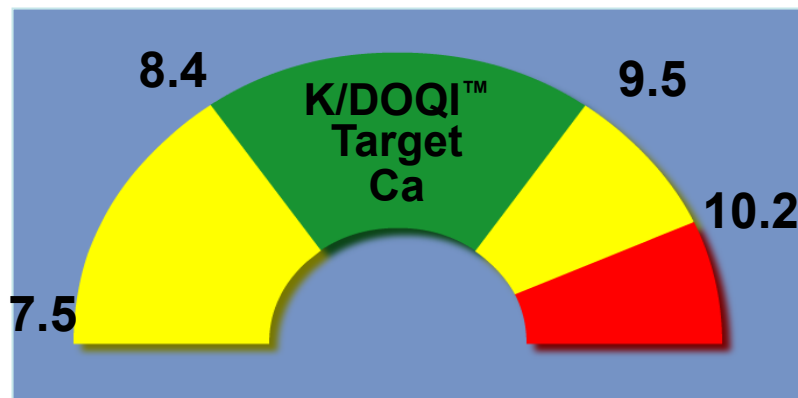
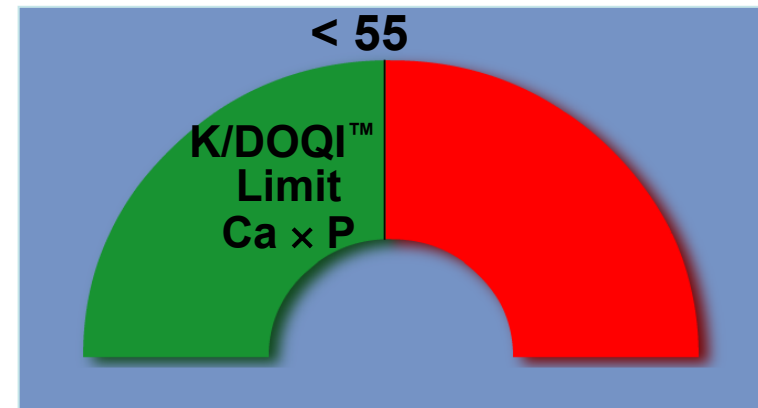
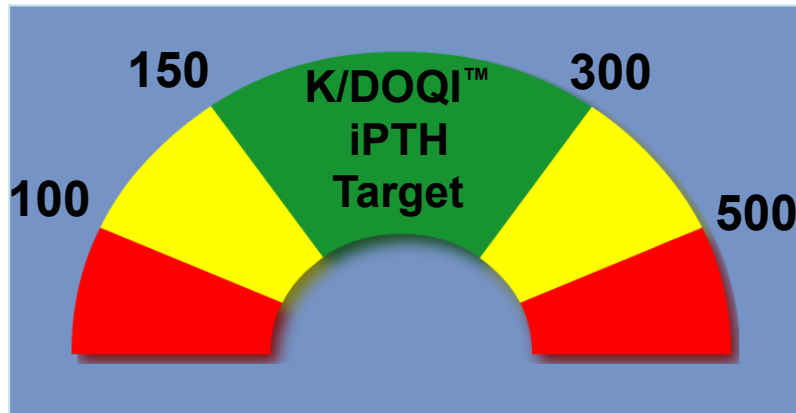


Multivariable analysis adjusted for age, gender, race or ethnicity, diabetes, vintage, body weight, URR, serum albumin, creatinine, predialysis BUN, bicarbonate, cholesterol, hemoglobin, ferritin, and aluminum

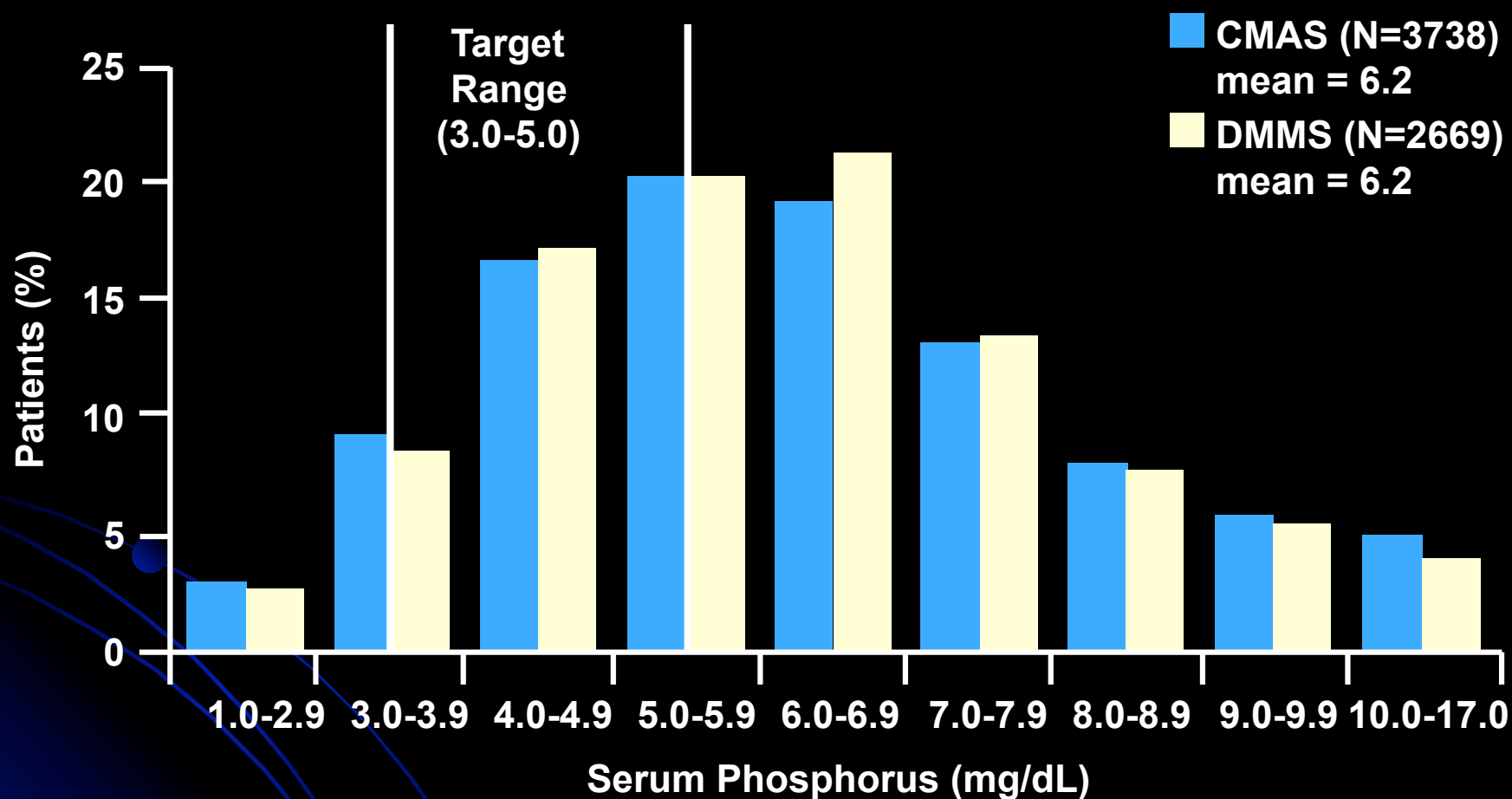
iPTH = intact PTH

Adapted from Block GA, et al. *J Am Soc Nephrol.* 2004;15:2208-2218.

K/DOQI™ Guidelines: Recommended Target Ranges



La mayoría de los pacientes en HD tienen Hiperfosfatemia

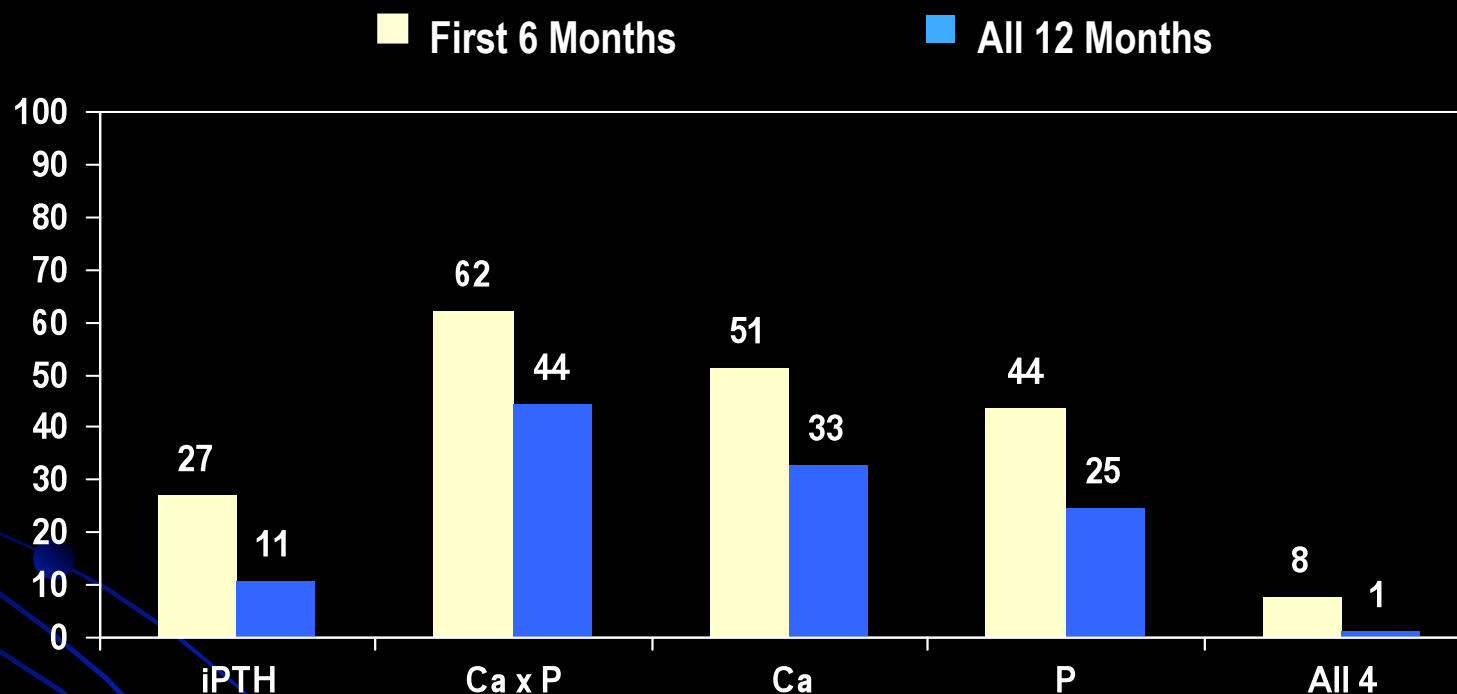


CMAS = Case Mix Adequacy Study;
DMMA = Dialysis Morbidity and Mortality Study.

Block GA et al. *Am J Kidney Dis.* 1998;31:607-617.
Block GA. *Clin Nephrol.* 2000;54:318-324.

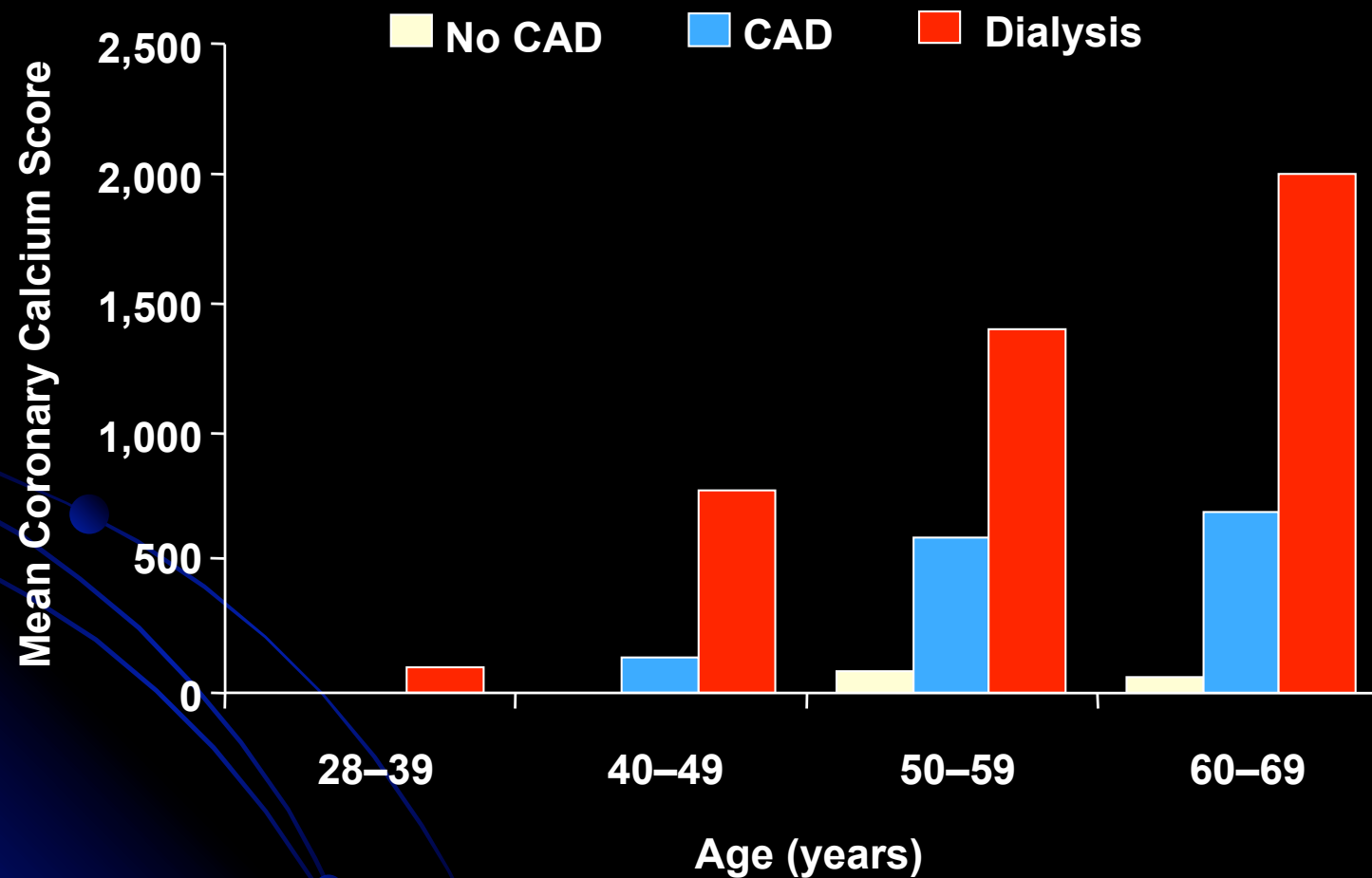
Achievement and Maintenance of K/DOQI Targets: US DOPPS Database

Percentage of Patients in Target

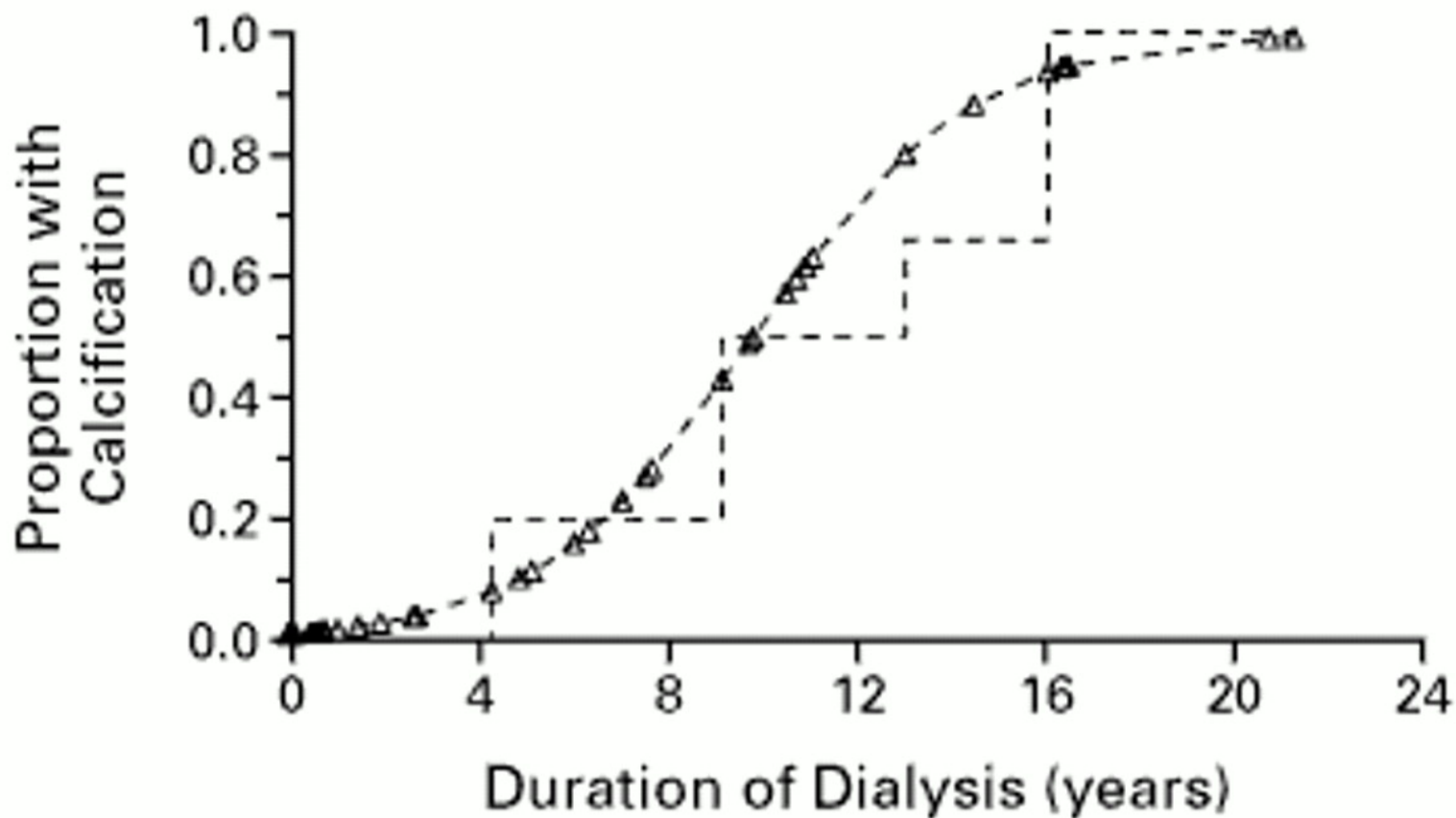


N ~ 4,000

Increased Risk of Cardiovascular Calcification in Dialysis Patients



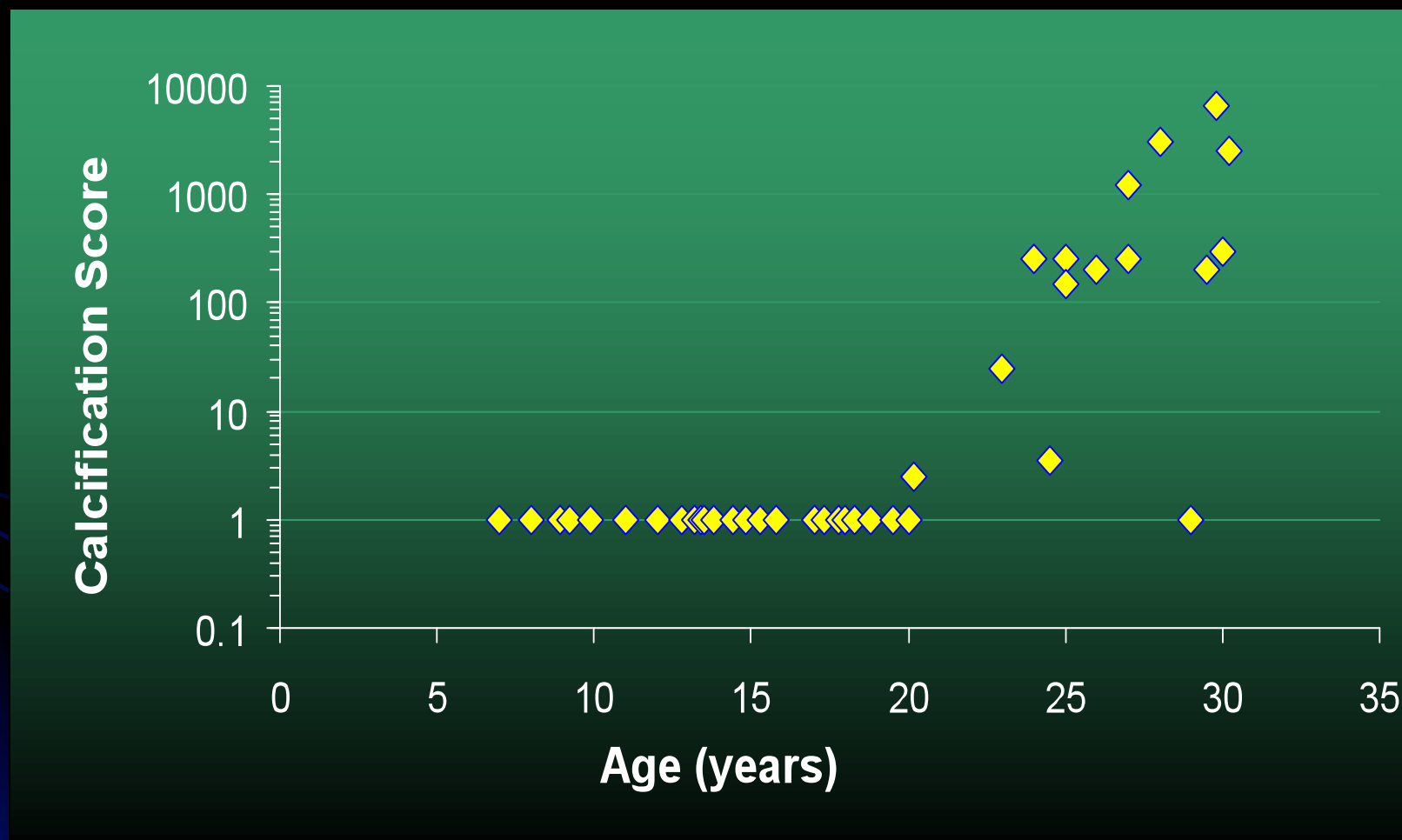
Adapted from Braun J, et al. *Am J Kidney Dis.* 1996;27:394-401.



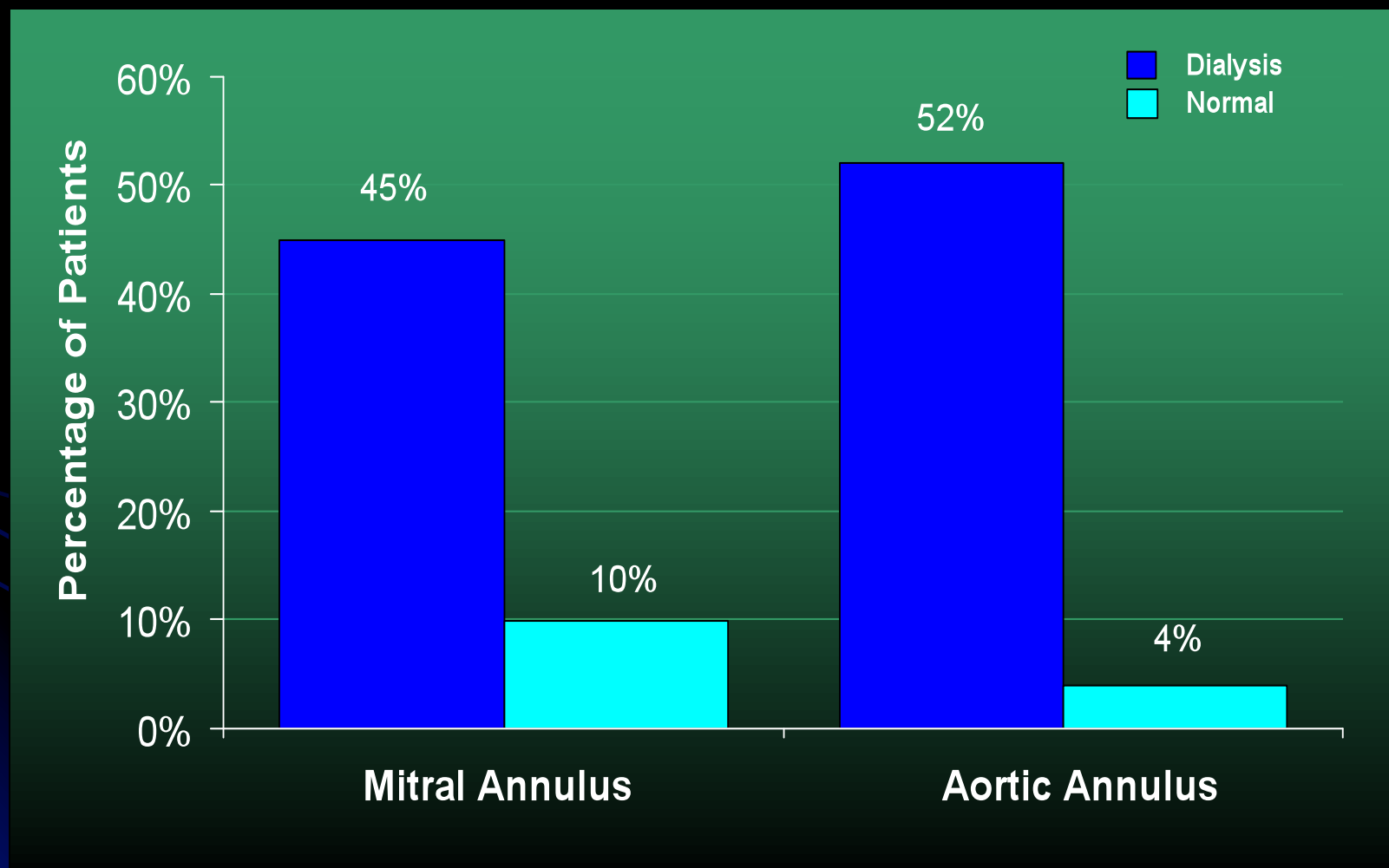
Prevalence of Coronary-Artery Calcification among 39 Patients with End-Stage Renal Disease, According to the Duration of Treatment with Dialysis.

Coronary-artery calcification was assessed by electron-beam computed tomography. All patients were 30 years of age or younger when they were first evaluated by electron-beam computed tomography.

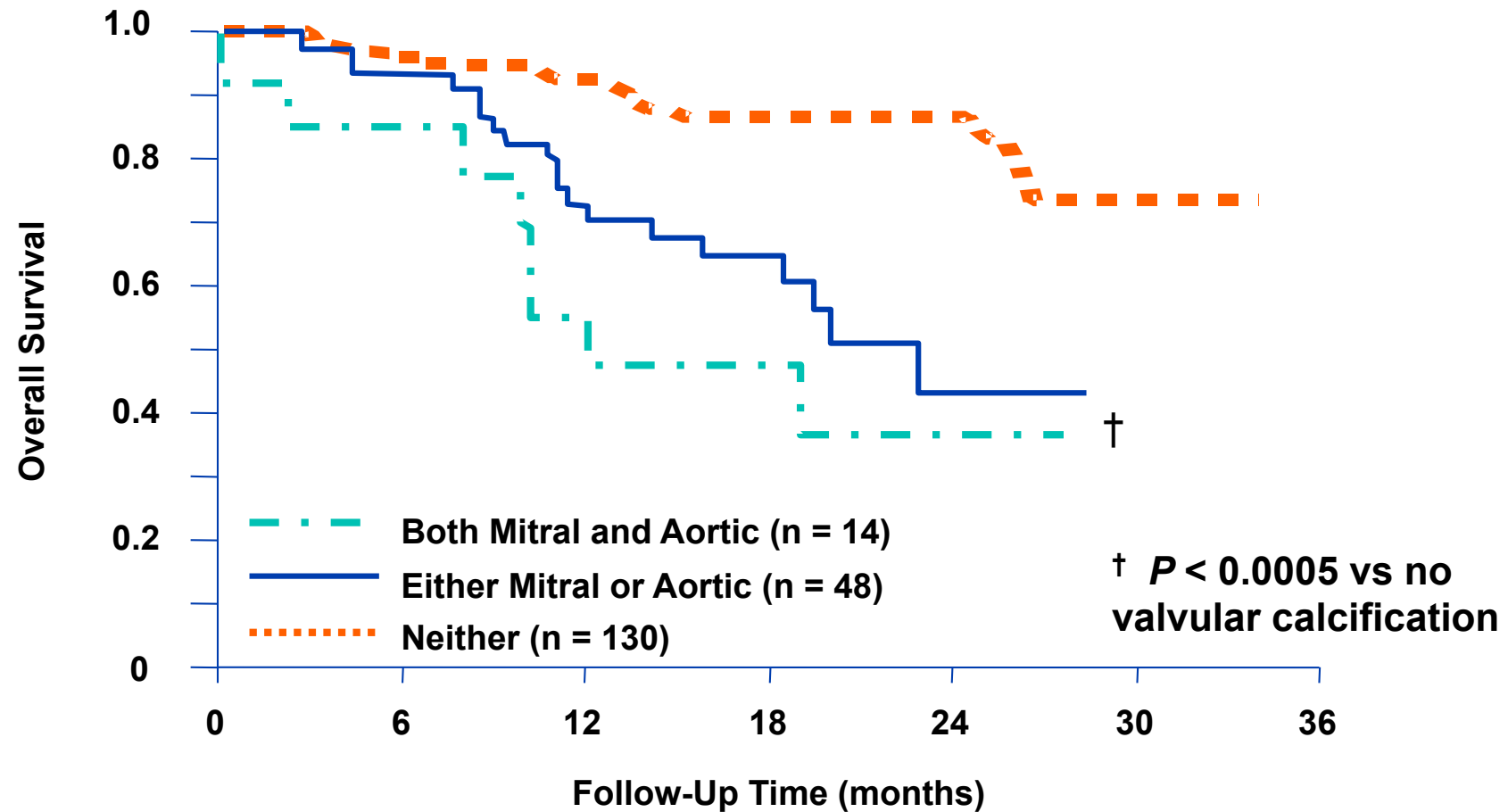
Coronary Artery Calcification in Young Dialysis Patients



Presence of Valvular Calcification¹




Valvular Calcification and Mortality





El Hombre de Pompeya

- **Definición**
 - **Epidemiología**
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 - **Implicancias clínicas**
 - **Tratamiento**
 - **Conclusiones**
- 

Calcificación – Balance de Fuerzas

Edad

Diabetes mellitus

Enf Renal

Hiperfosfatemia
Warfarin
Hipercalcemia



Injuria

Calcificación de la Media

Fosfatasa Alcalina
Sialoproteína Osea
BMP2 (prot morfogenética ósea)
Colageno tipo 2

Osteoprotegerina
Proteína GLA de matriz (MGP)
Osteopontina
BMP-7
Fetuina

Calcification Normal

Formación

Inhibición

Fisiopatología de la calcificación del músculo liso

- Valores elevados de Ca y P aumentan la actividad del cotransporte Na-P Pit-1

P induce un up-regulation de los pit-1

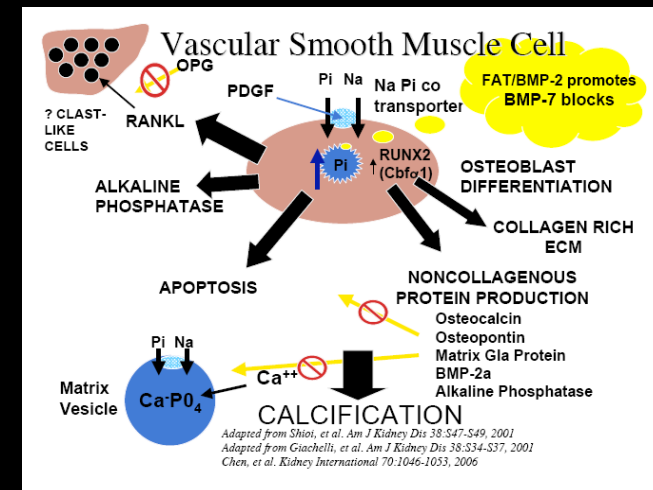
Ca induce mayor expresión RNAm Pit-1

} > P intracelular

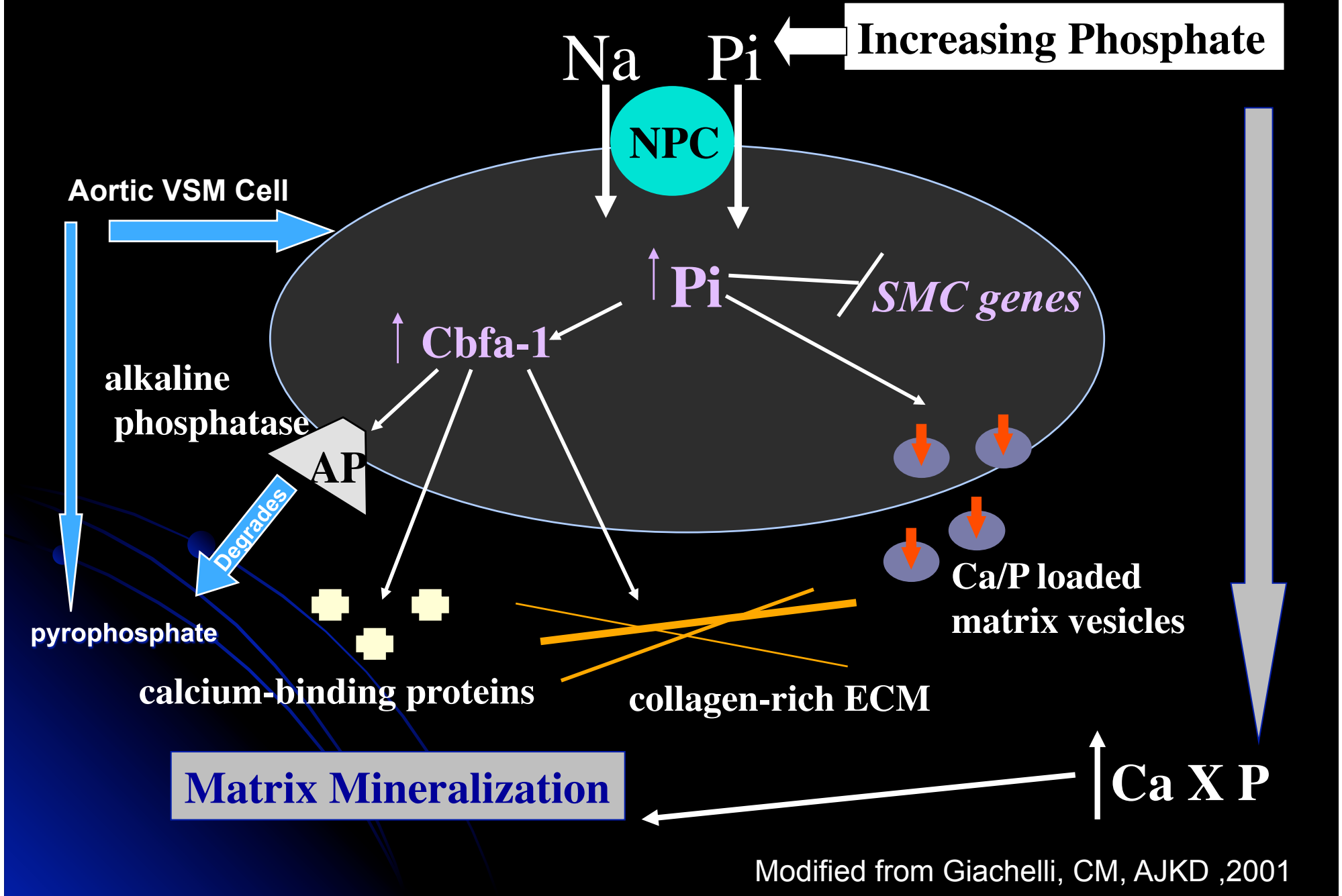
- Valores elevados de P genera una modulación fenotípica de Cbfa-1 (factor de transcripción 1), generando un up-regulation de genes osteogénicos (Runx2, osteocalcina, fosfatasa alcalina)

- Desdiferenciación a células osteoblasticas o condrocitos

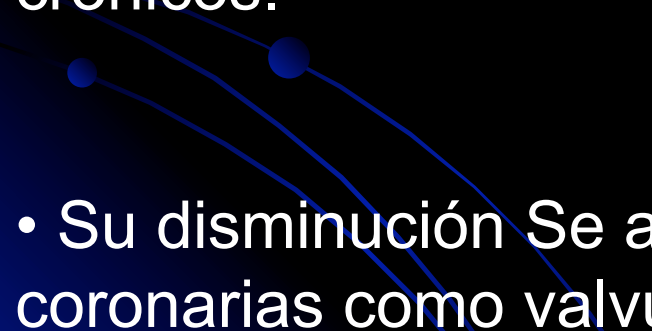
- Existe una salida de vesículas de matriz con Ca y P de las células Musculares lisas y aumento de secreción de moléculas que nuclean minerales, dando como resultado final el depósito de hidroxapatita.



Theories Regarding Molecular Mechanism for Vascular Calcification



Fetulina A

- La fetulina A es una glicoproteína de 60 kDa sintetizada por los hepatocitos.
 - Es un potente inhibidor de la calcificación y formación de hidroxiapatita.
 - Reacciona como un reactante negativo de fase aguda y se produce su down-regulation en procesos inflamatorios agudos o crónicos.
 - Su disminución se asocia con un aumento de las calcificaciones coronarias como valvulares.
- 

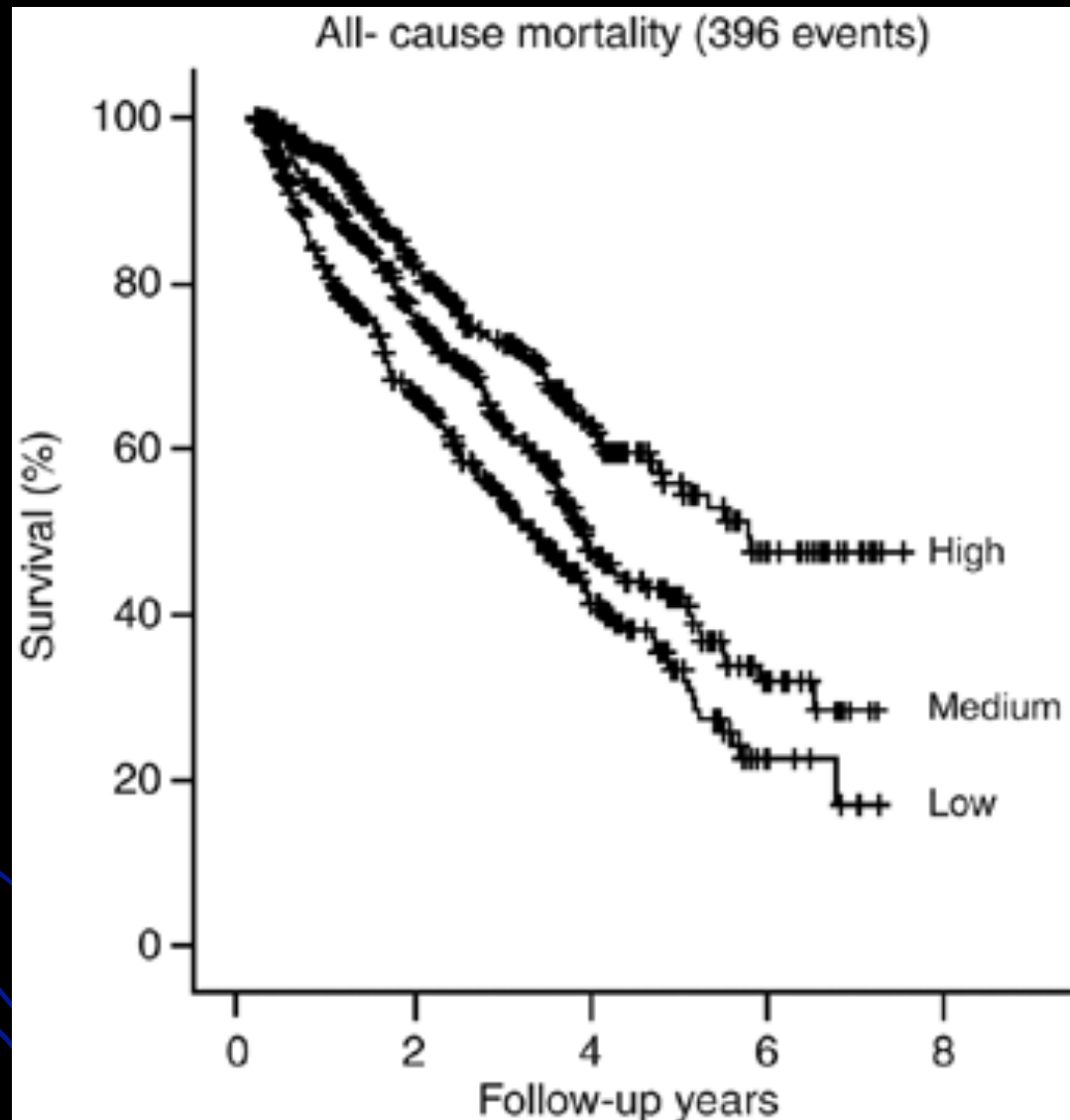
Emerging role for fetuin-A as contributor to morbidity and mortality in chronic kidney disease

R Mehrotra^{1,2}

Vascular calcification (VC) is an important reason for the high burden of vascular disease among chronic dialysis patients. Chronic kidney disease (CKD) is associated with increased promoters and decreased inhibitors of VC. The circulating levels of fetuin-A, a well-described inhibitor of calcification, regulate the cell-dependent process of osteogenesis. It is not surprising that the low circulating fetuin-A levels are associated with a greater prevalence and/or severity of VC and increased risk for all-cause and cardiovascular mortality. However, high circulating fetuin-A levels appear to induce insulin resistance and, in non-dialyzed subjects with diabetic nephropathy, are directly related to VC burden. These findings underscore the need to further clarify the multiple, systemic effects of fetuin-A and its role in health and various stages of CKD.

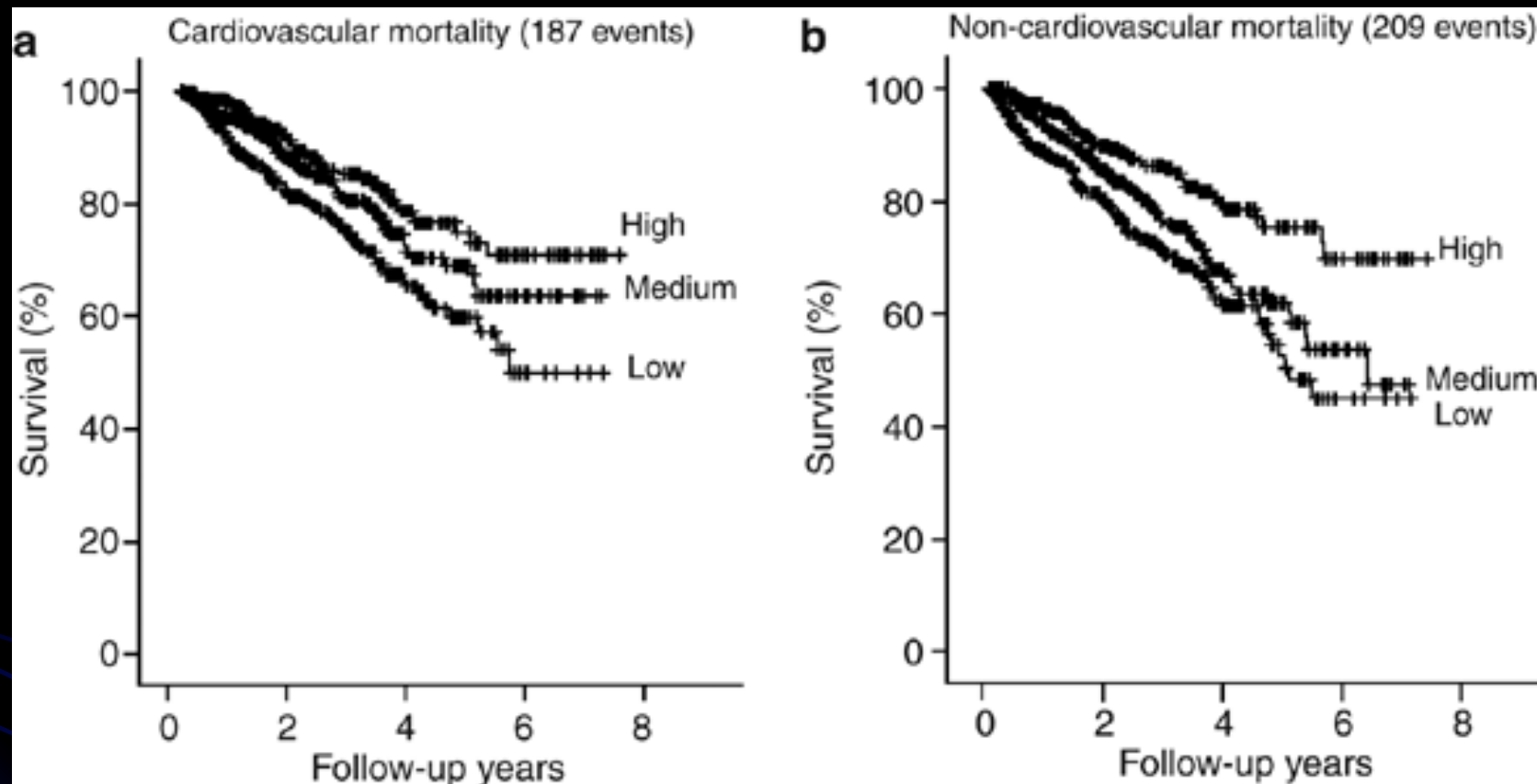
Kidney International (2007) **72**, 137–140. doi:10.1038/sj.ki.5002355

Concentración de Fetuina A y mortalidad global



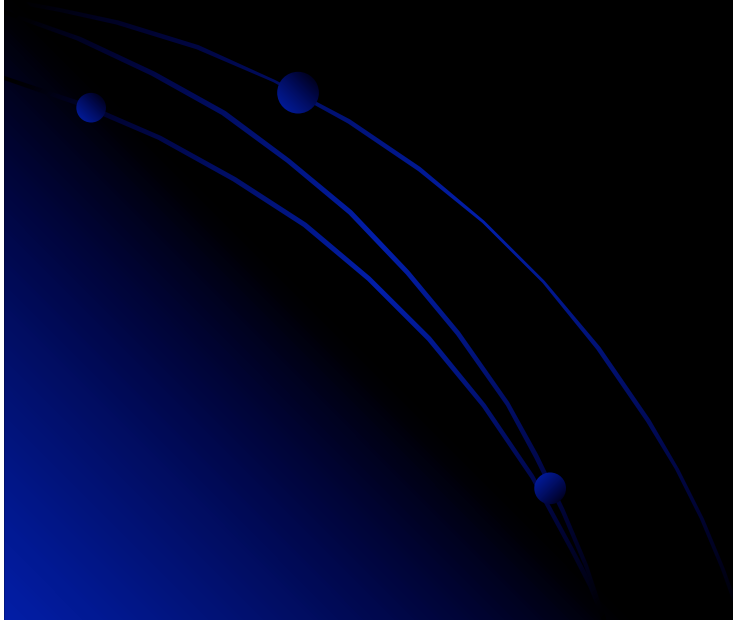
Kaplan-Meier curve showing all-cause mortality, by tertile of serum fetuin-A concentration (low (0.25–0.55 g/l), median (0.56–0.69 g/l), and high (0.70–1.53 g/l)) in all dialysis patients.

Concentración de Fetuina A , mortalidad CV y no CV

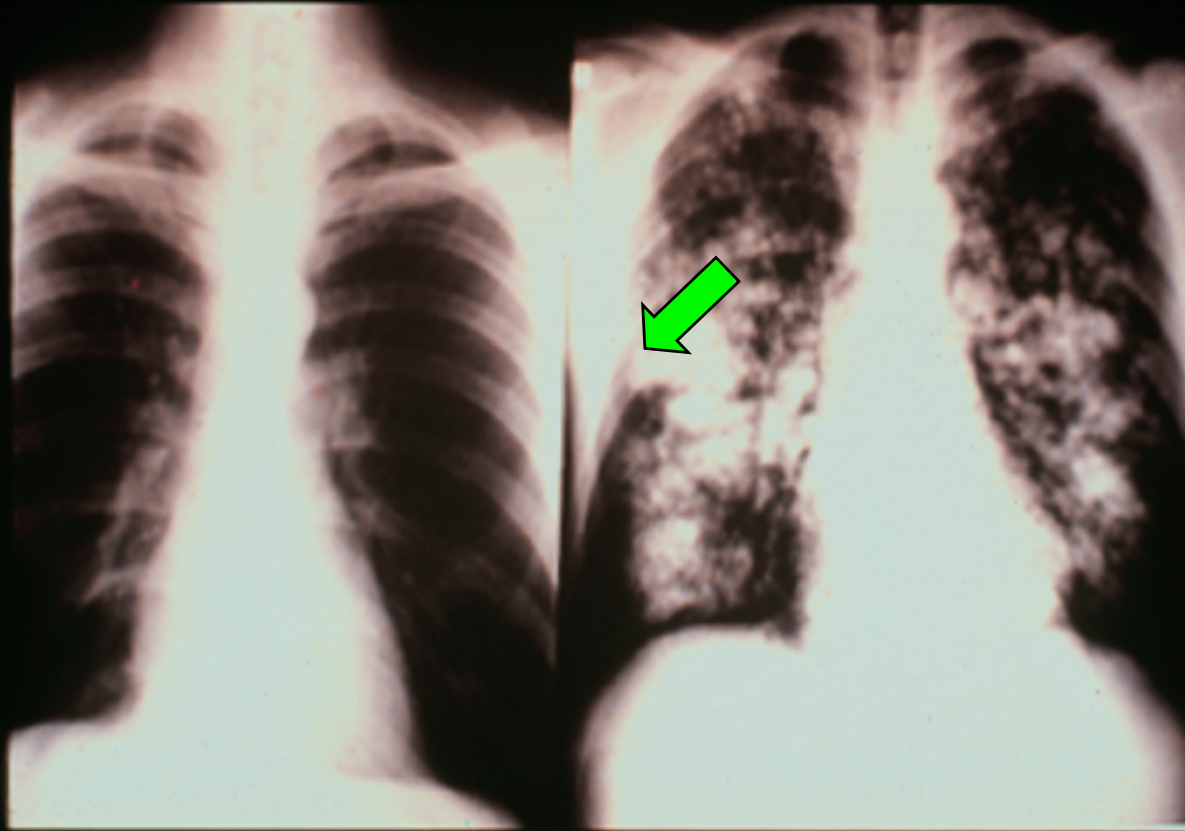


Kaplan–Meier curve showing CV mortality (a) and non-CV mortality (b), by tertile of serum fetuin-A concentration (low (0.25–0.55 g/l), median (0.56–0.69 g/l), and high (0.70–1.53 g/l)) in all dialysis patients.

Calcificaciones metastásicas



Calcification of the Lung



Noncalcified

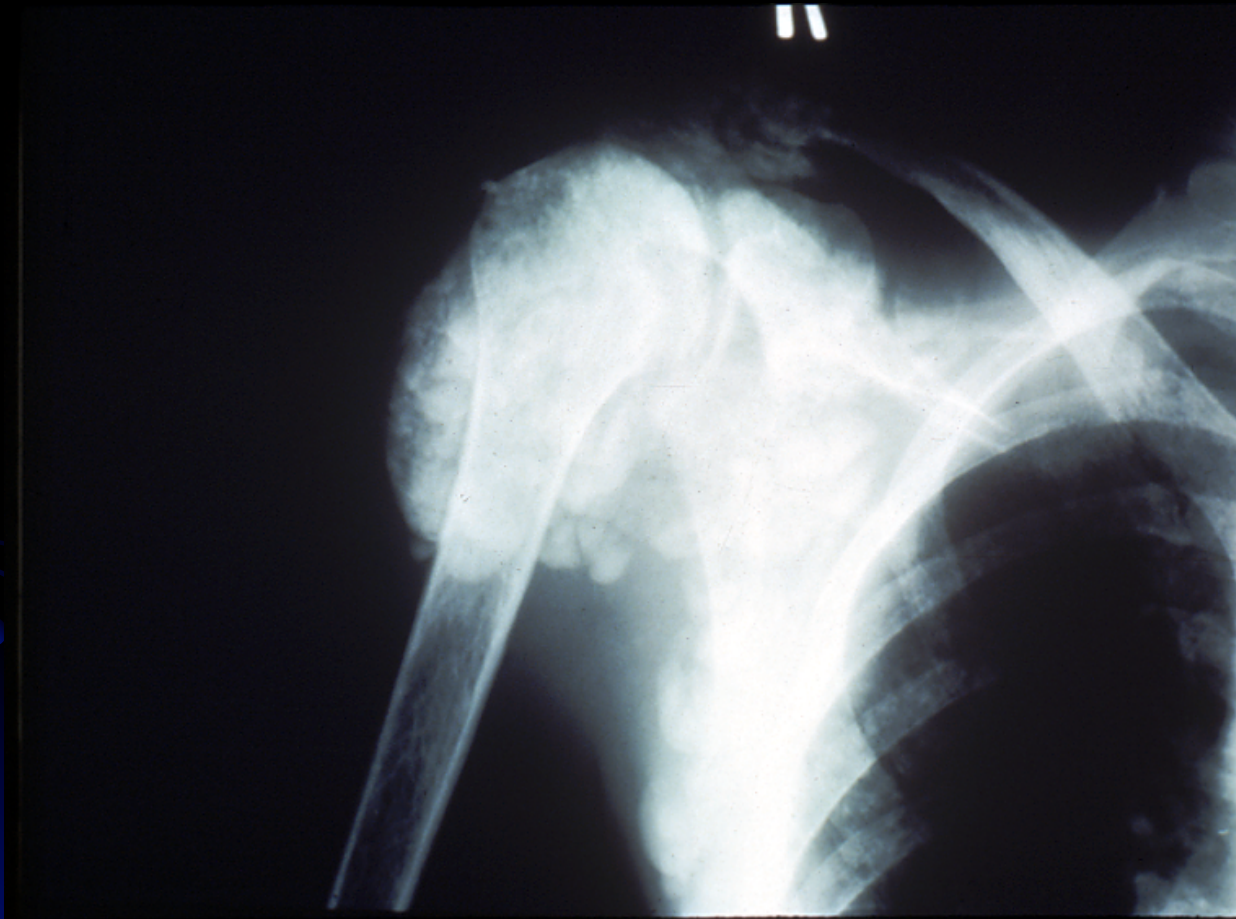
Calcified

Sanders C, et al. *Am J Roentgenol.*
1987;149:881-887.

Kuzela DC, et al. *Am J Pathol.* 1977;86:403-424.

Slide courtesy of E. Slatopolsky.

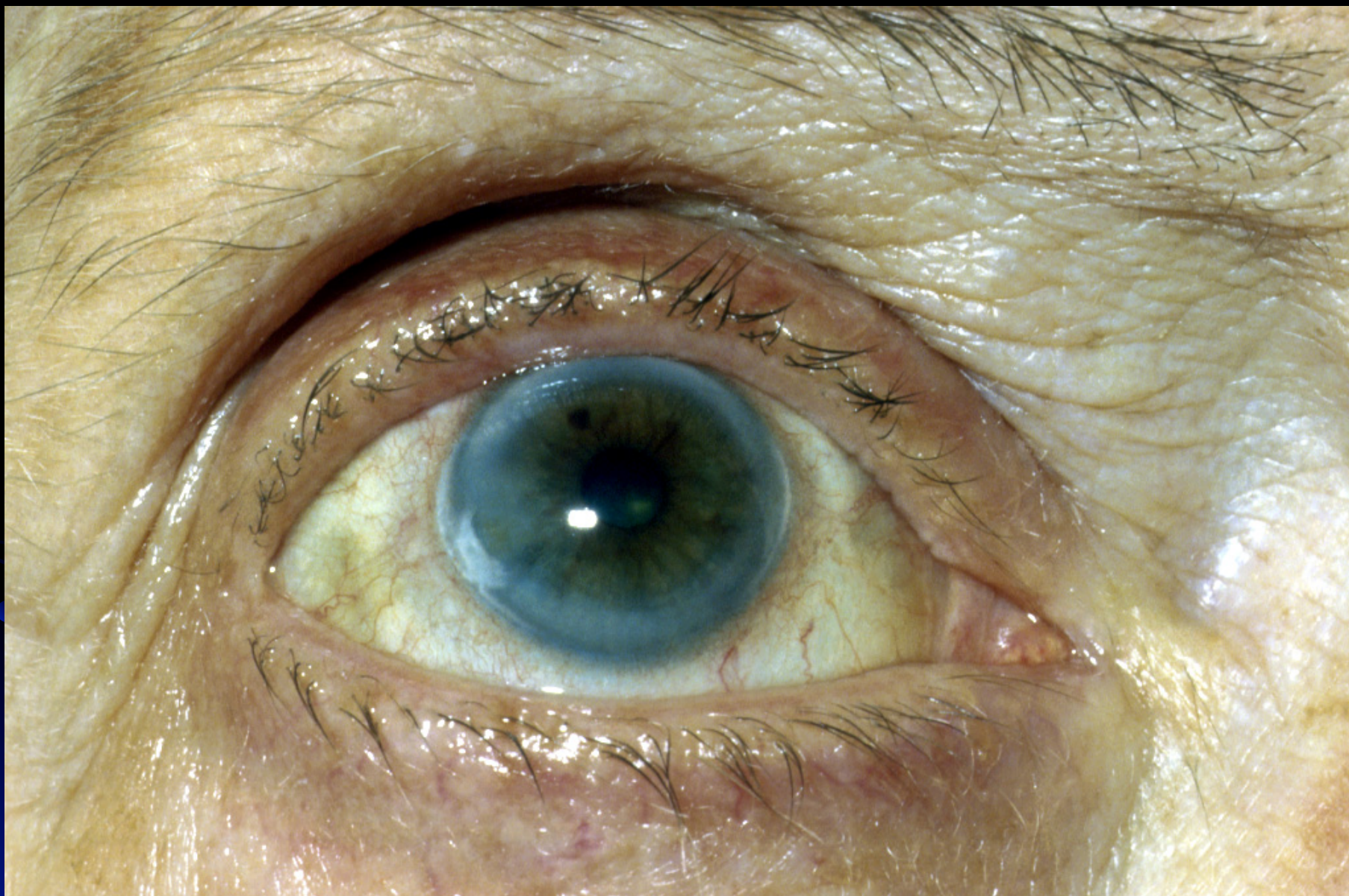
Periarticular Calcification



Slide courtesy of D. Sherrard.



Metastatic calcification Hand radiograph showing metastatic calcification in a patient with calciphylaxis. Courtesy of Peter H Schur MD.



Cutaneous/Subcutaneous Calcification



Slide courtesy of H. Malluche.



Calciphylaxis Calciphylaxis of the leg in a patient with end-stage renal disease. Ischemic necrosis has led to both violaceous lesions and black, leathery eschar-like lesions.



Calcificación vascular en la IRC

Factores asociados a la IR

(uremia, alteraciones met. Ca-P)

