Hiperfosfatemia

y

Riesgo Cardiovascular en Diálisis

Quelantes Cálcicos vs Quelantes no Cálcicos

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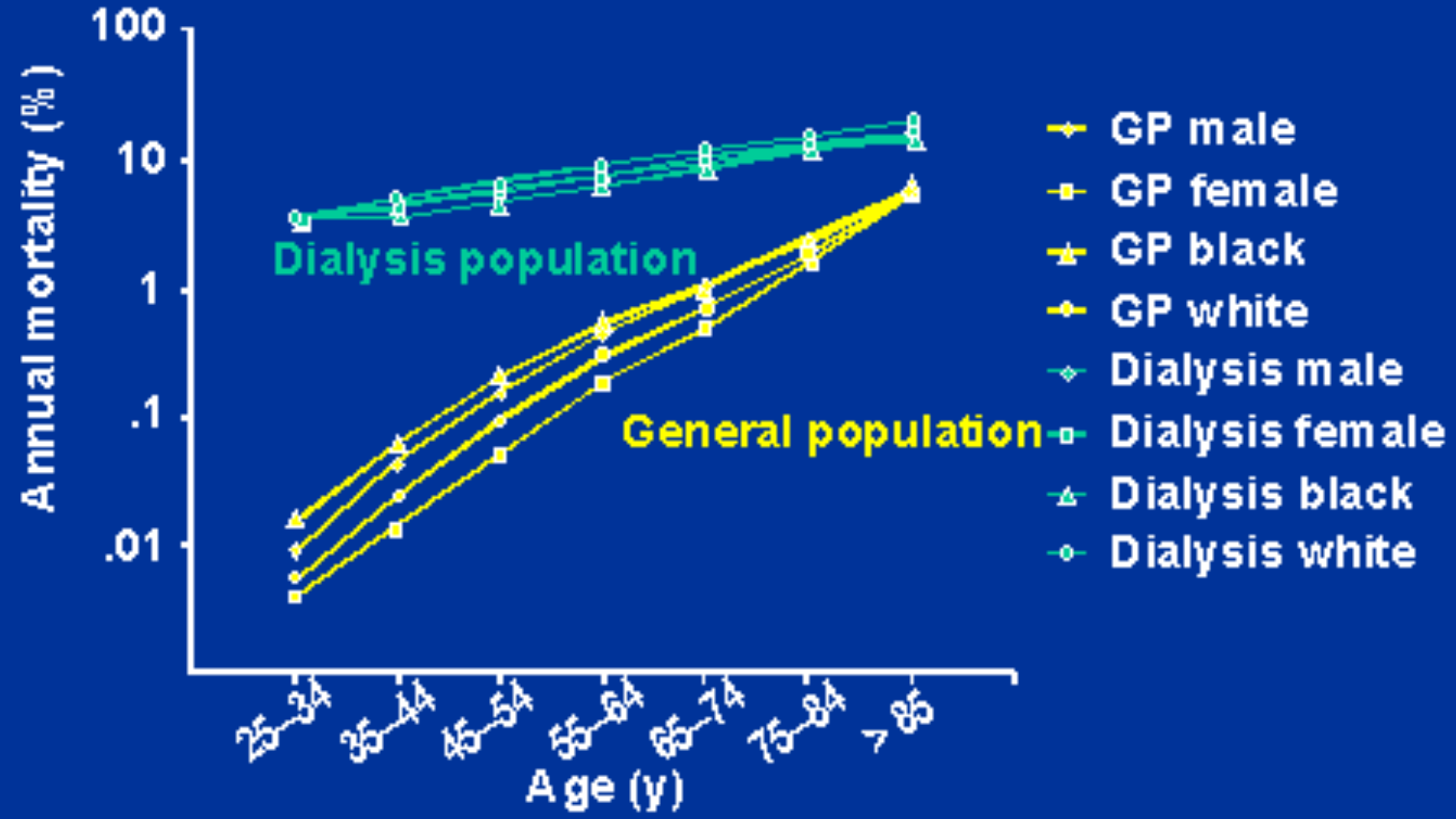
HOSPITAL BRITANICO
DE BUENOS AIRES

Mortalidad en hemodializados vs población general



Meyer KB, Levey AS. *J Am Soc Nephrol.* 1998;9(suppl):S31-S42.

Enfermedad Cardiovascular y ERC

- La enfermedad CV contribuye con el 40-50% de las muertes en ERC
- La incidencia es 15 veces mayor que la población general
- 40% de los pacientes que inician diálisis tienen evidencia de enfermedad coronaria
- Solo 15% tiene función ventricular normal

Factores de riesgo cardiovascular en la IRC

Tradicionales

Edad

Sexo varón

Hipertensión arterial

LDL-C elevado

HDL-C bajo

Diabetes

Tabaquismo

Inactividad física

Historia familiar ECV

HVI

Menopausia

No tradicionales y propios uremia

Albuminuria

Homocisteína

Lipoproteína(a) e isoformas de apo(a)

Remanentes lipoproteínas

Resistencia insulina

Hiperactividad simpática

Anemia

Alteración met Ca-P y Calcific vascul.

Hipervolemia

Alteraciones electrolíticas

↑ Estrés oxidativo

Inflamación/malnutrición

↑ Velocidad onda de pulso

↑ Factores trombogénicos

Alteraciones del sueño

Patrón “non deeper”

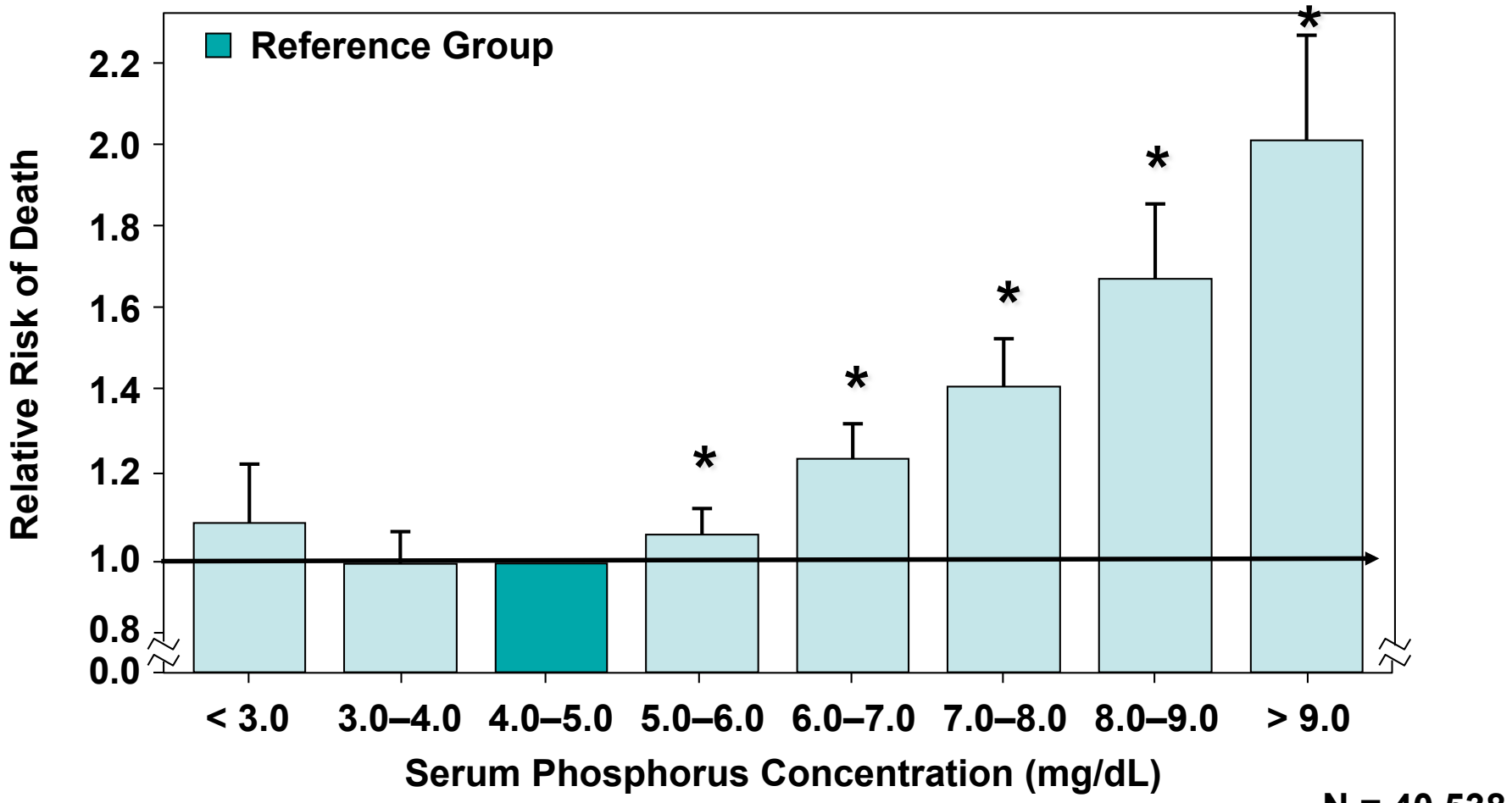
Alteración balance óxido nítrico/ET

Modificado de Sarnak MJ et al. Hypertension 2003

Mortalidad Cardiovascular Calcificaciones Vasculares y Fosfato

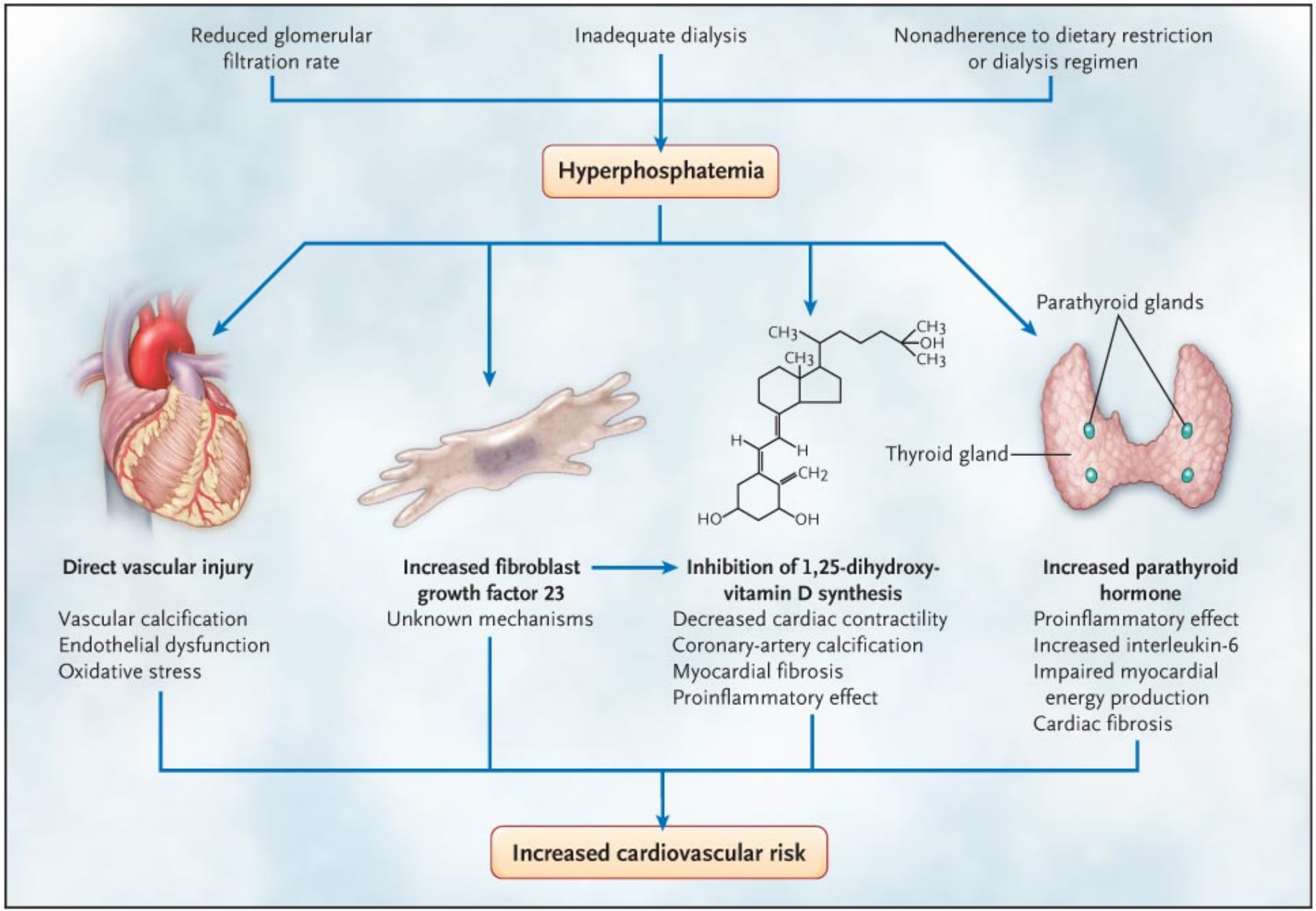
1. El riesgo de muerte CV en IRC es mayor que en población general *(Foley, 1998)*.
2. El 70% de los pacientes en diálisis tienen niveles de fósforo sérico > 5 mg/dl *(Block, 1998)*.
3. El aumento del fósforo y producto P x Ca se correlacionan con aumento de la mortalidad *(Block, 1998)*.
4. El aumento del producto P x Ca se asocia con calcificación aórtica y valvular *(Hutin, 1994; Ribeiro, 1998)*.
5. La calcificación coronaria es frecuente y progresiva en niños y jóvenes con IRC correlacionándose con fosforemia P x Ca, e ingesta de Calcio *(Goodman, 2000)*.

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



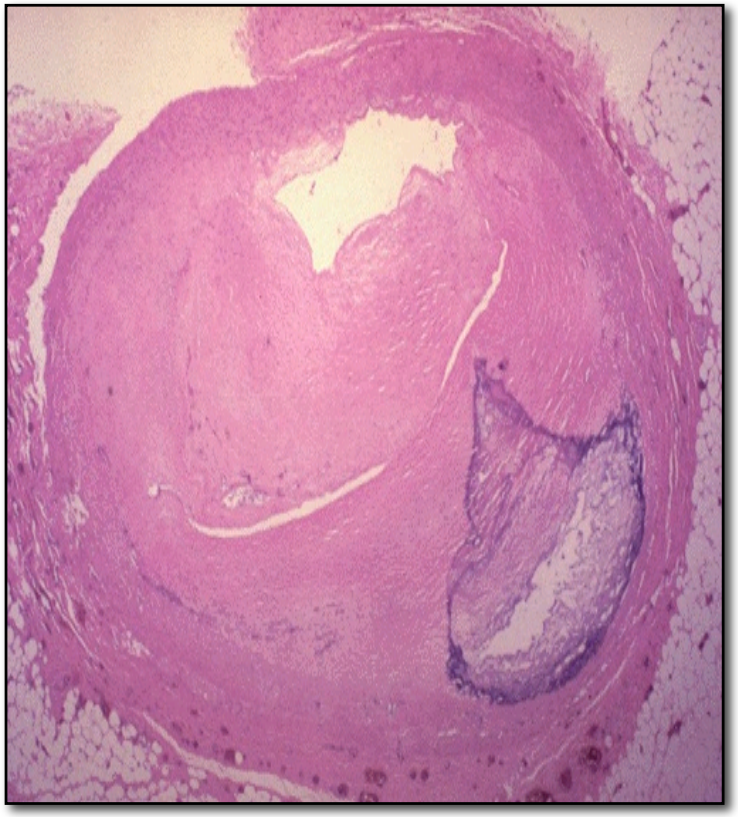
N = 40,538

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.

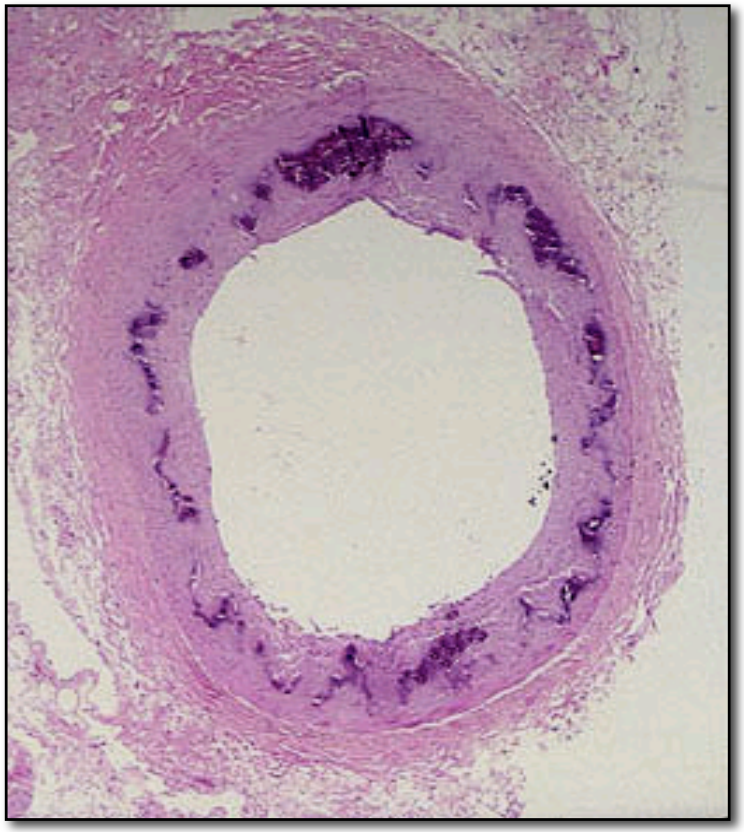


N Engl J Med 2010;362:1312-24.

Calcificación Vascular en la IRC



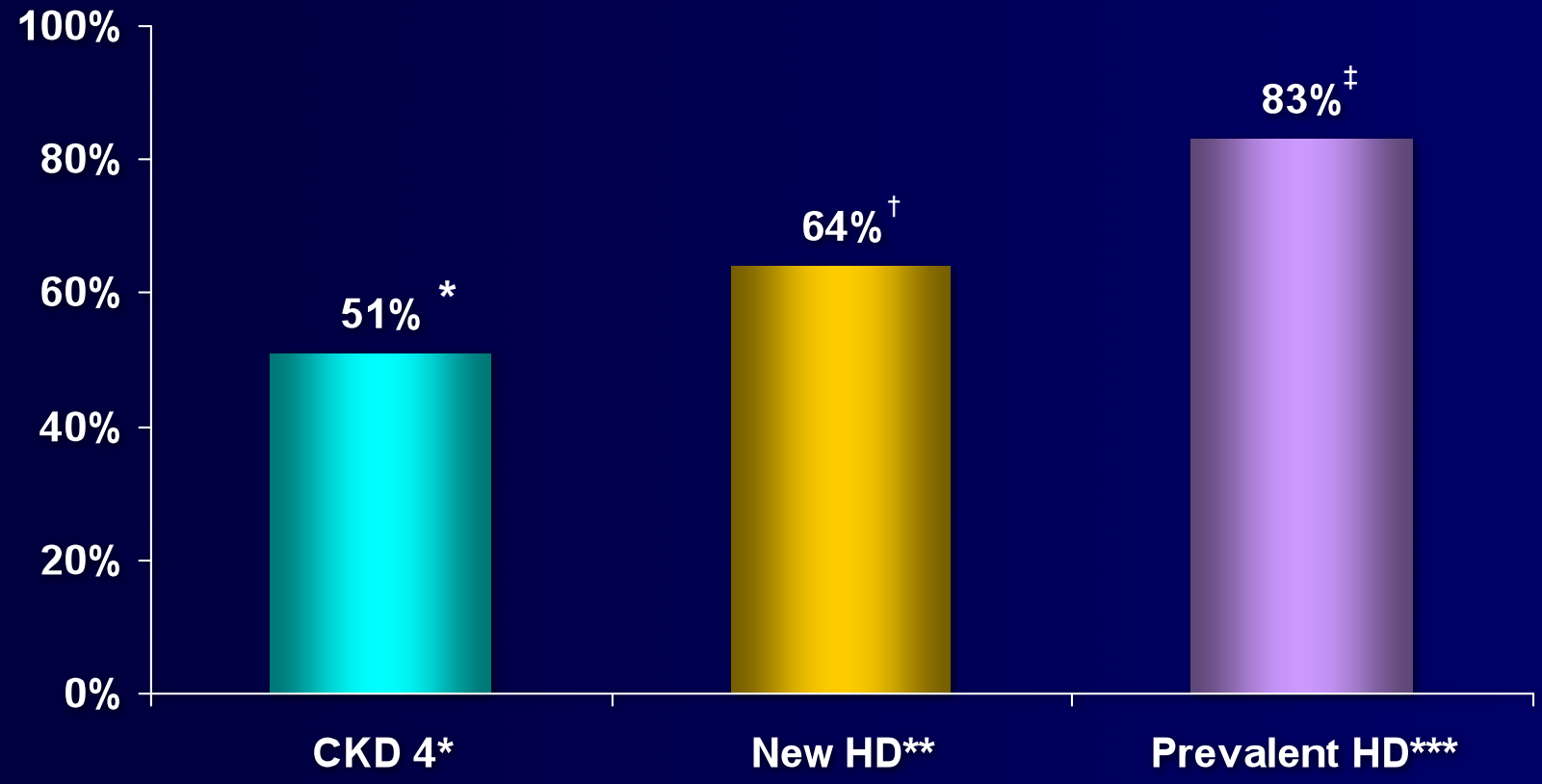
Calcificación intimal



Calcificación medial

Available at: http://library.med.utah.edu/WebPath/CVHTML/CV007.html. Accessed May 2007.

Prevalencia de calcificación vascular en la Insuficiencia renal

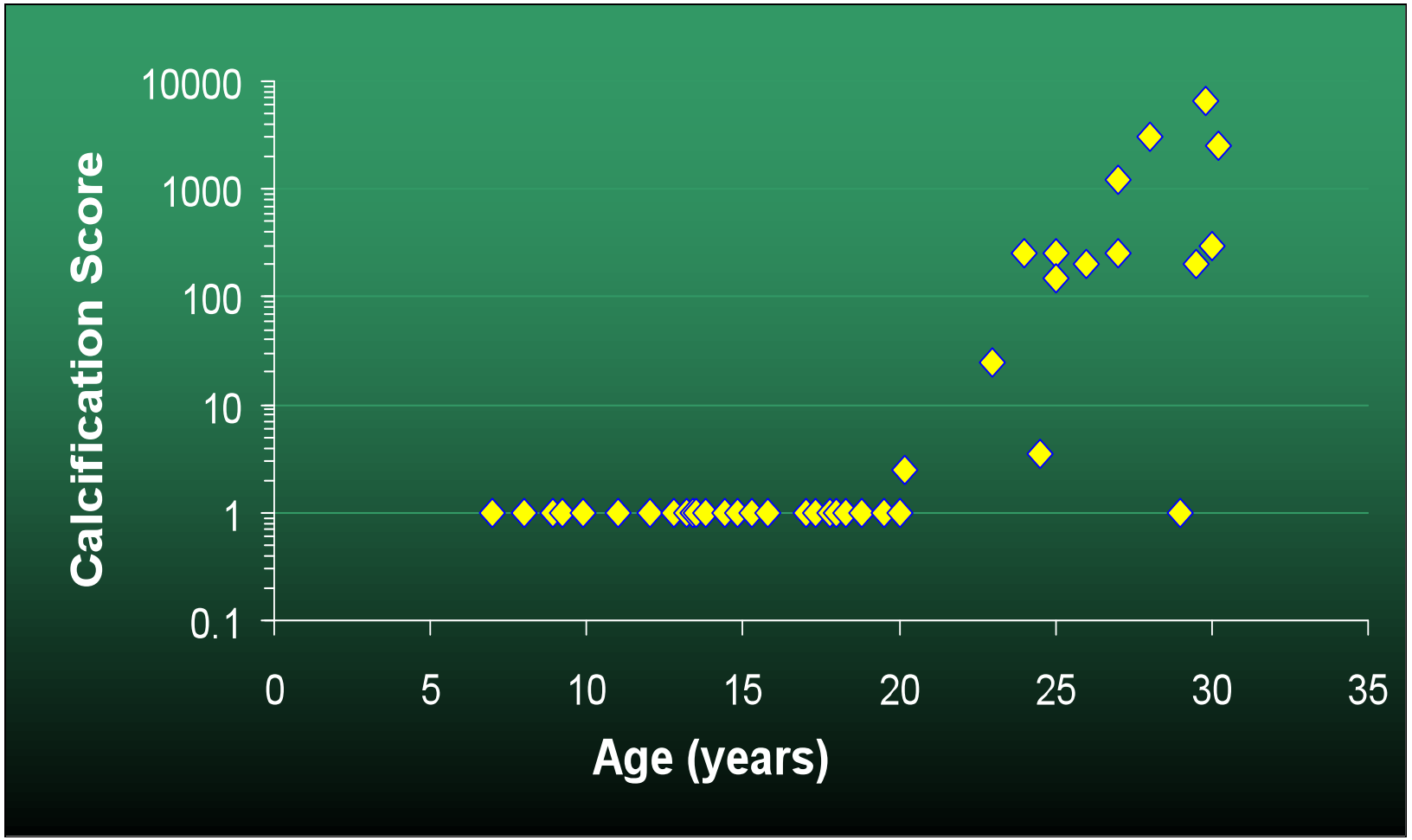


*Russo D, Corrao S, Miranda I, et al. Progression of coronary artery calcification in predialysis patients. *Am J Nephrol.* 2007;27:152-158.

†Spiegel DM, Raggi P, Mehta R, et al. Coronary and aortic calcifications in patients new to dialysis. *Hemodialysis Int.* 2004;8:265-272.

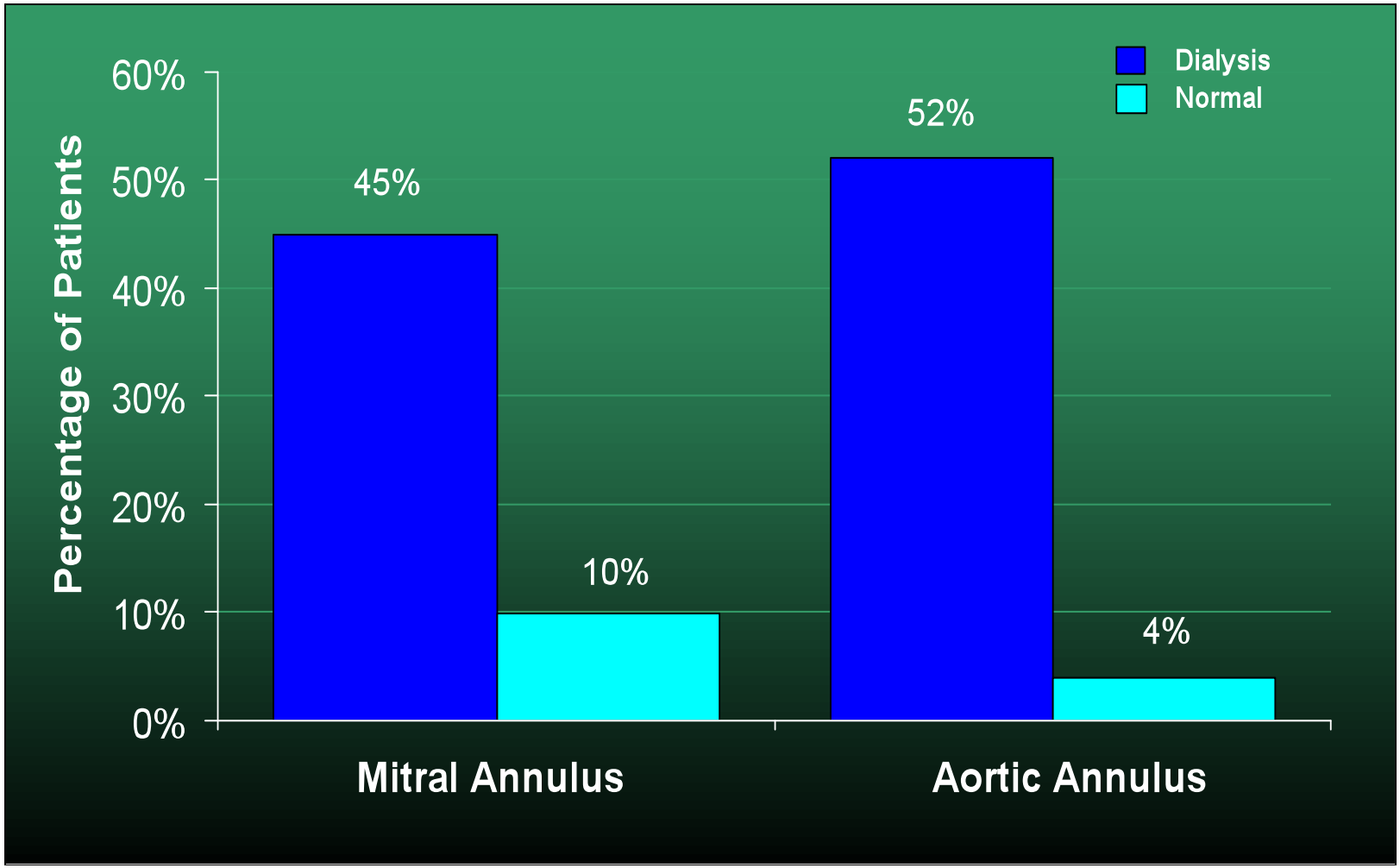
‡Chertow GM, Burke SK, Raggi P; for Treat to Goal Working Group. Sevelamer attenuates the progression of coronary and aortic calcification in hemodialysis patients. *Kidney Int.* 2002;62:245-252.

Calcificación coronaria en pacientes jóvenes en Hemodiálisis



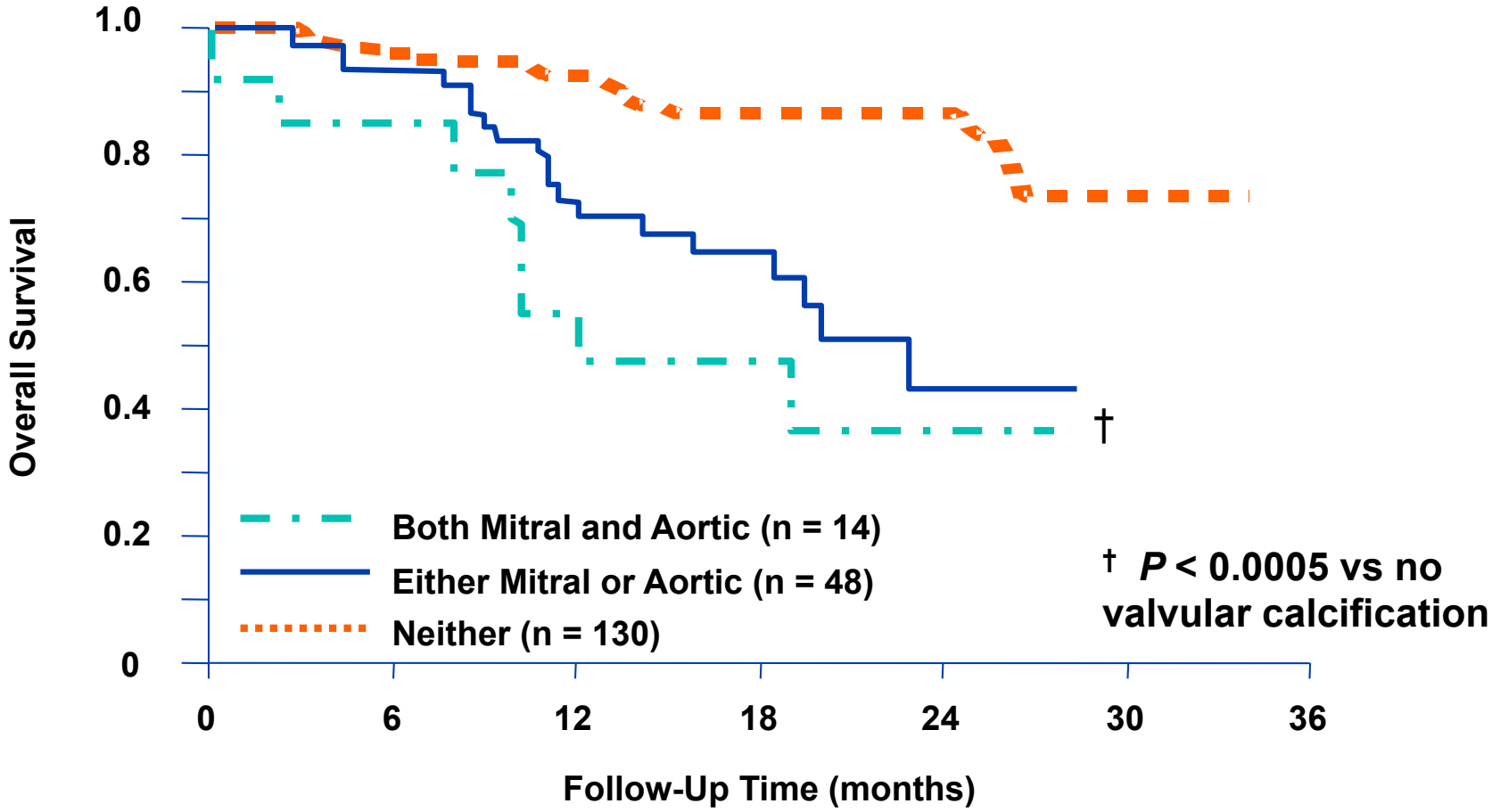
Adapted from Goodman WG, et al. *N Engl J Med*. 2000;342:1478-1483.

Calcificación Valvular



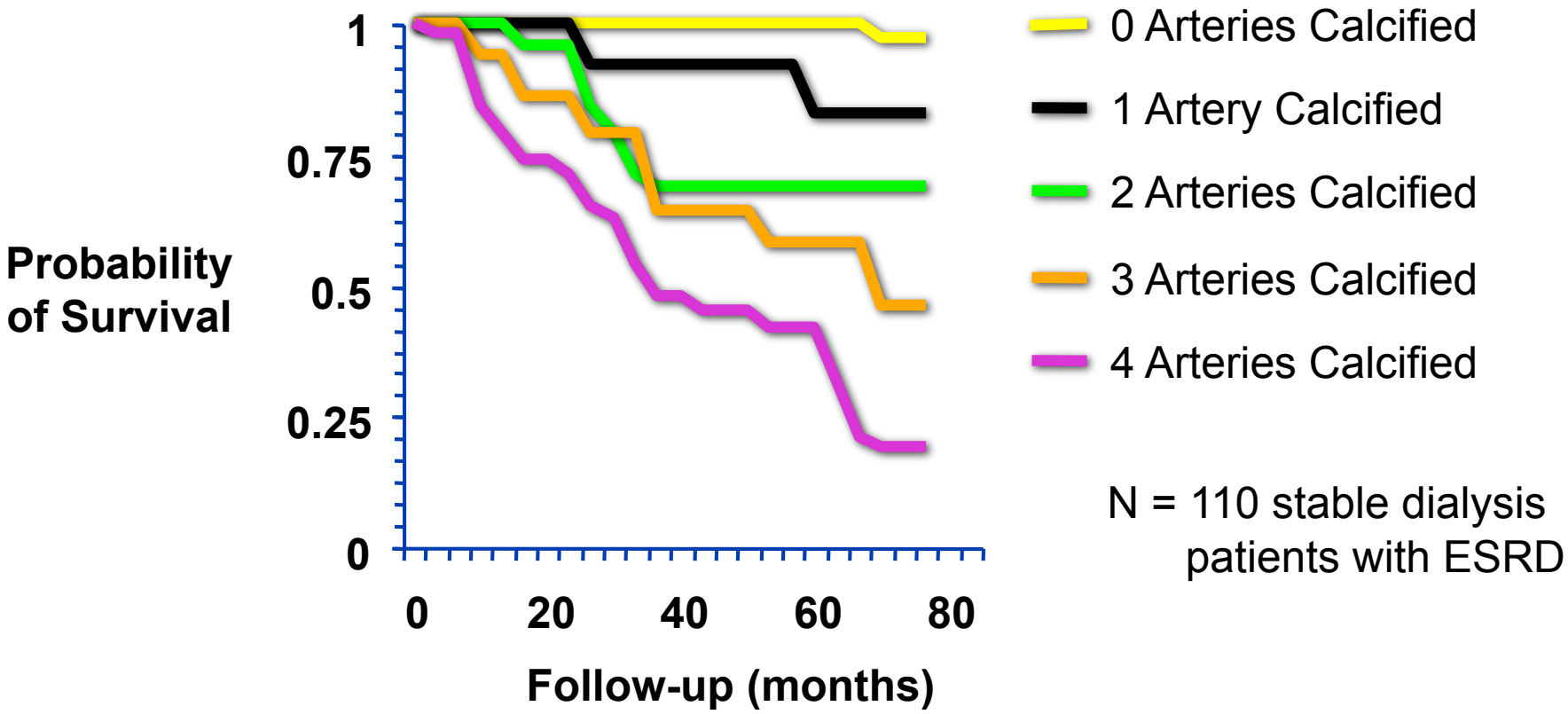
1. Ribeiro S, et al. *Nephrol Dial Transplant.* 1998;13:2037-2040.

Calcificación valvular y mortalidad



Wang A, et al. *J Am Soc Nephrol.* 2003;14:159-168.

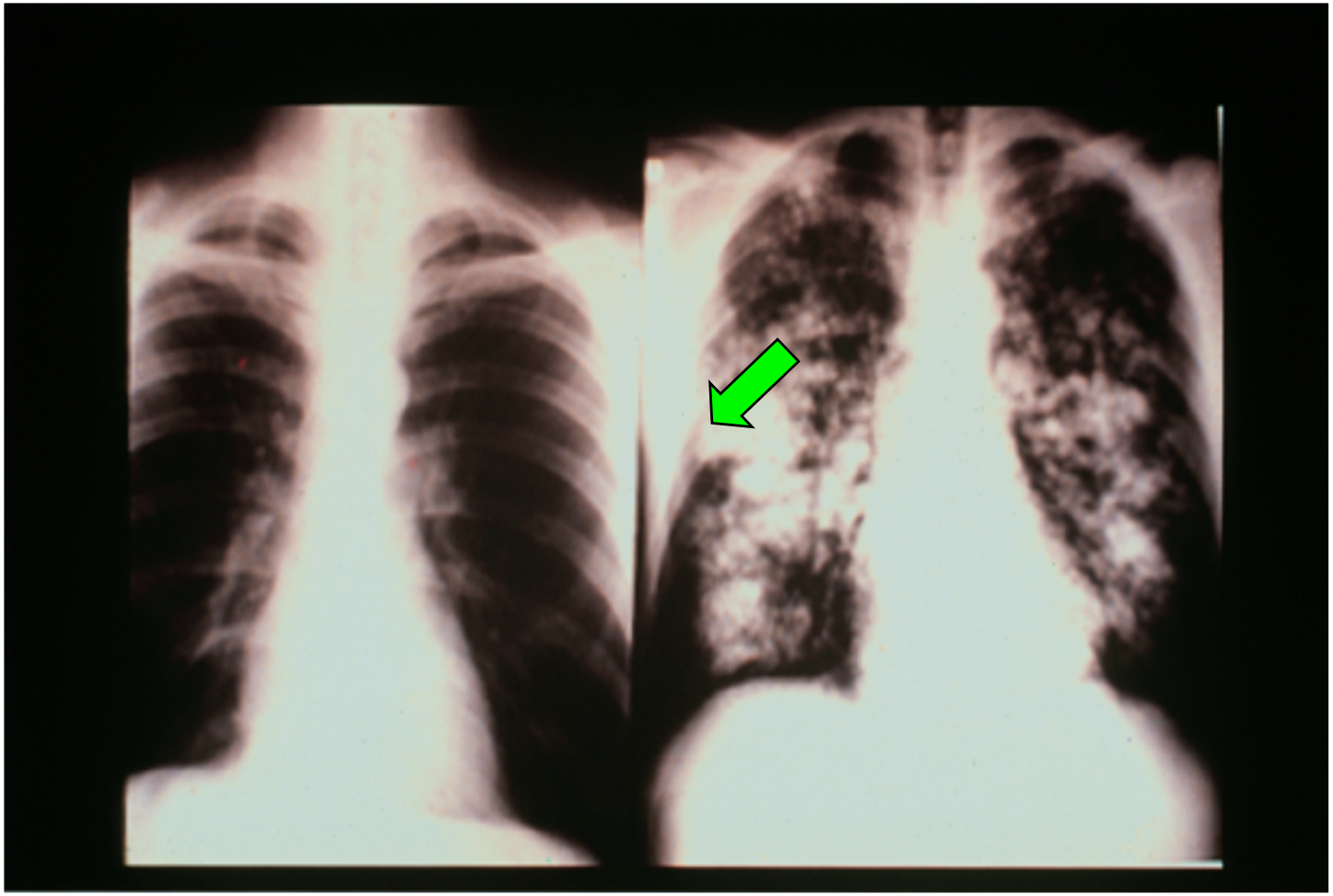
La probabilidad de sobrevida baja al aumentar la calcificación arterial



P < 0.0001 comparison among groups

Blacher J, et al. *Hypertension*. 2001;38:938-942.

Calcificación Pulmonar



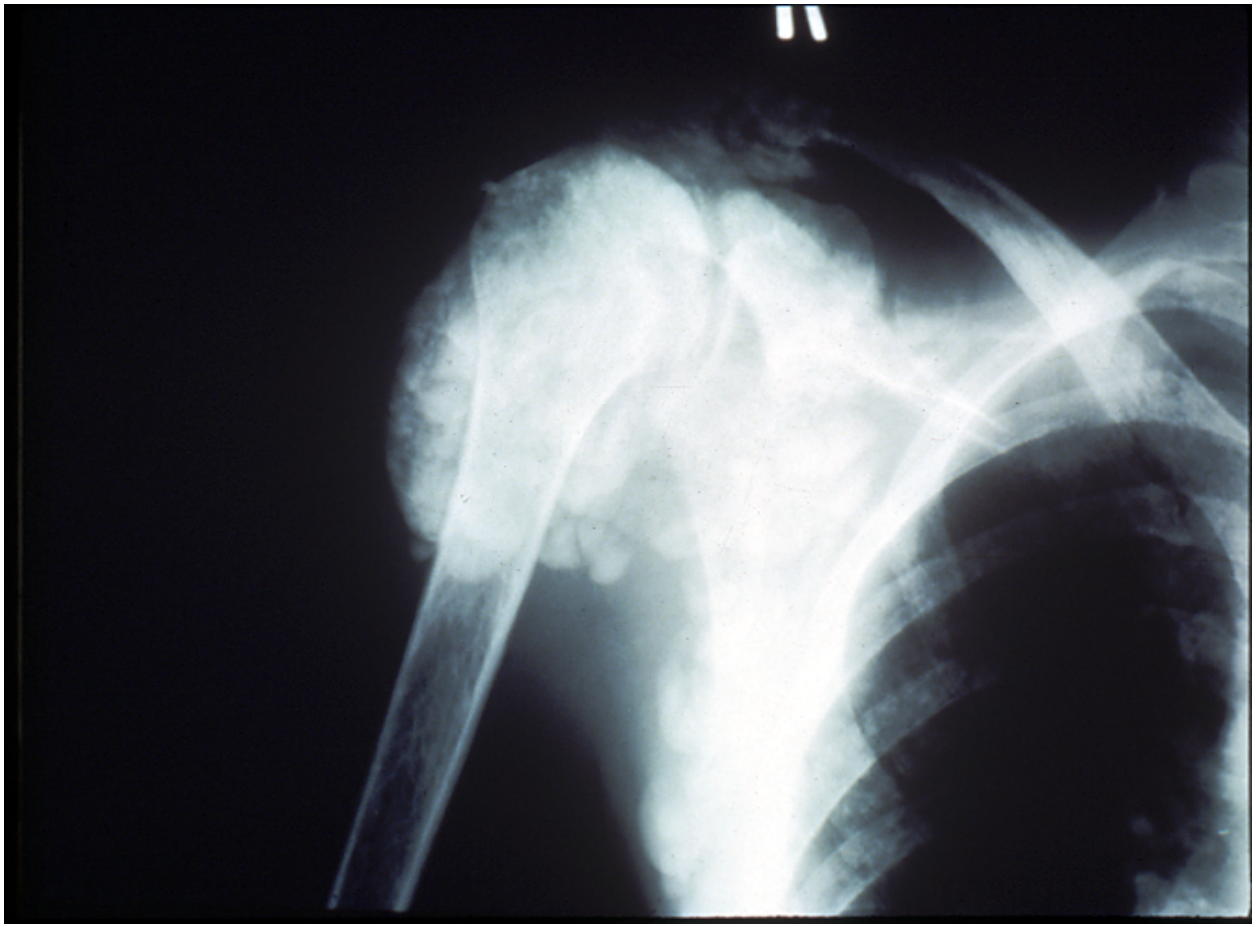
Noncalcified **Calcified**

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.

Calcificación Periarticular

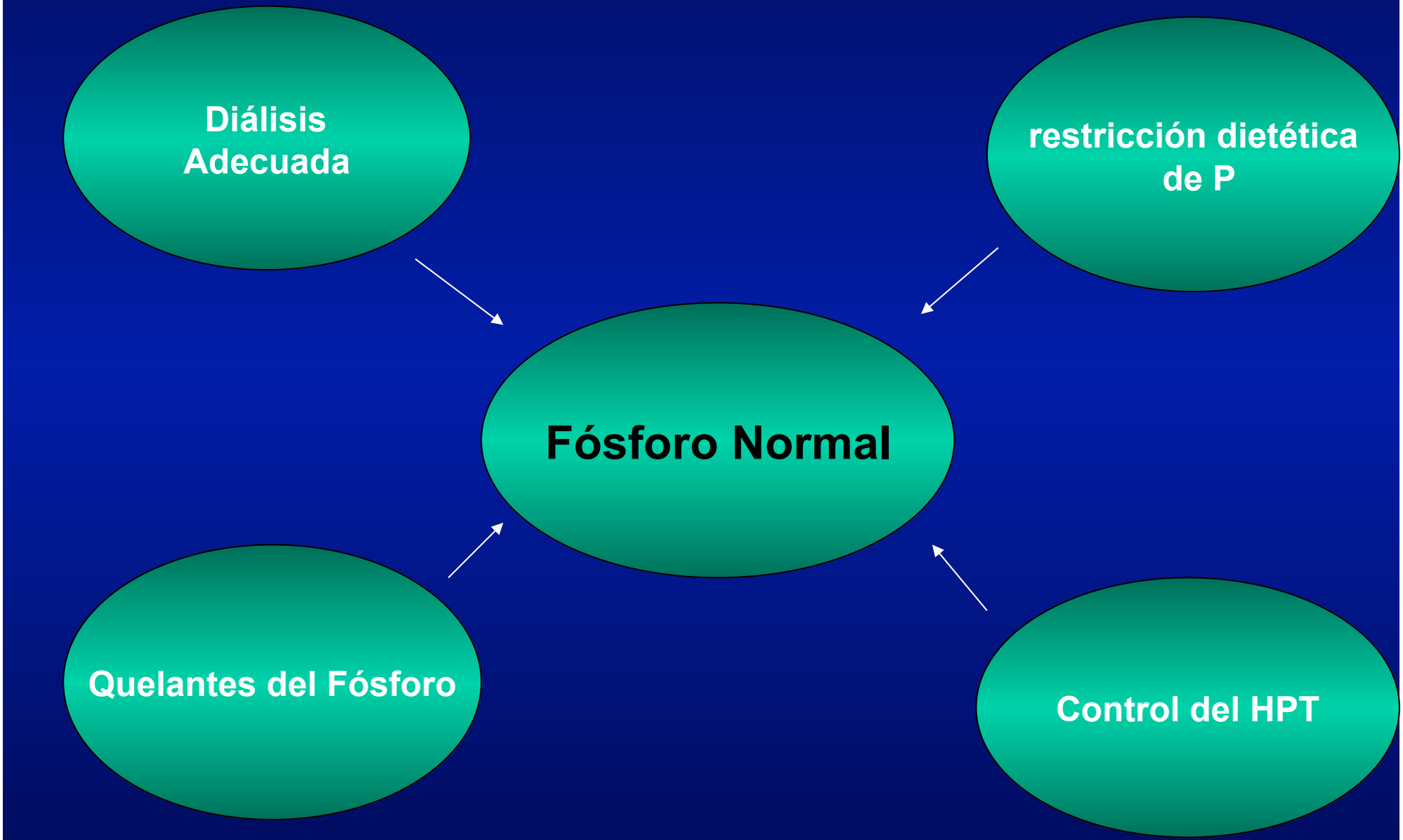


Slide courtesy of D. Sherrard.

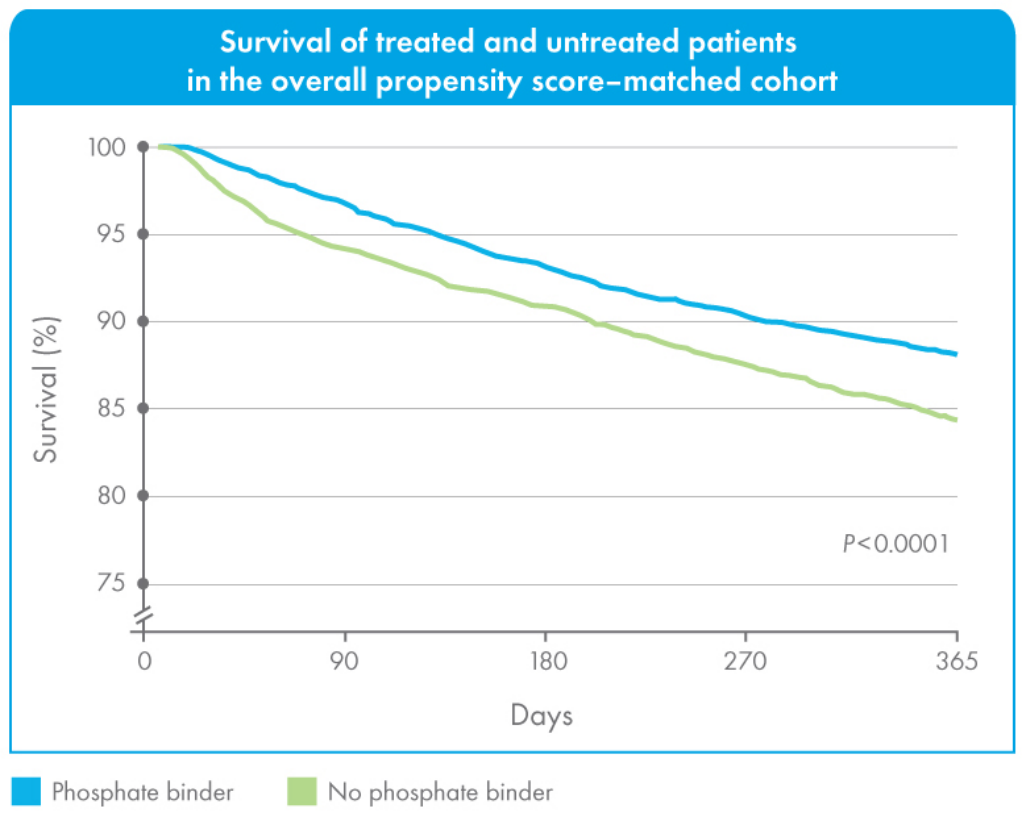
Calcificación subcutánea

Slide courtesy of H. Malluche.

Control de la Hiperfosfatemia



El tratamiento con quelantes del fósforo se asocia en forma independiente a una mejor sobrevida en pacientes en diálisis .



- **Estudio de cohorte prospectivo en 10,004 pacientes incidentes en hemodiálisis ,comparando la mortalidad global al año en pacientes en tratamiento o no con quelantes del fósforo .**
- **Loa pacientes tratados presentaban una reducción significativa de la mortalidad comparado con el grupo de pacientes no tratados . (*P*<0.0001)**
- **En 1,434 pacientes que einiciaron el tratamiento con quelantes del fosforo predialisis presentaban una mayor sobrevida comparado con 5,055 pacientes que fueron tratados en los primeros 90 dias de dialsis (*P*=0.0008)**

Isakova T, Gutiérrez OM, Chang Y, et al. Phosphorus binders
hemodialysis. *J Am Soc Nephrol.* 2009;20:388-396.

Características ideales de un quelante de fósforo

- Gran poder de quelación
- Gran afinidad con el fósforo (requerimiento de baja dosis)
- Escasa absorción sistémica (o nula)
- No toxico
- Vía oral en forma sólida
- Agradable al gusto y que genere mayor compliance

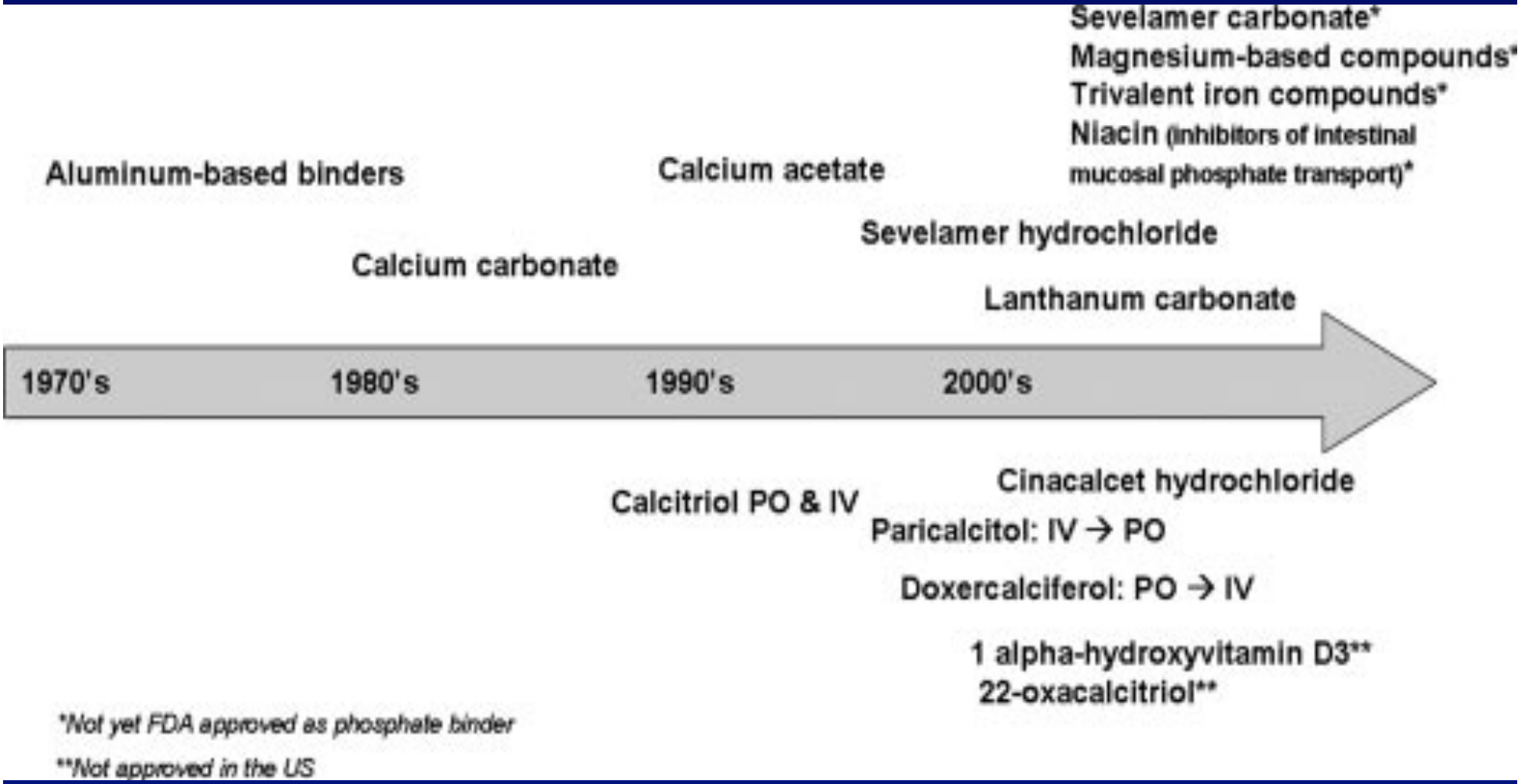
Ligantes

Cálcicos

- Carbonato
- Acetato

No-Cálcicos

- Aluminio
- Magnesio
- Sales de Hierro
- Sevelamer
- Lantano



Historia del tratamiento del disordenes del metabolismo mineral en la IRC

Table 19 | Phosphate-binding compounds

Binder source	Rx	Forms	Content (mineral/metal/element)	Potential advantages	Potential disadvantages
Aluminum hydroxide	No	Liquid, tablet, capsule	Aluminum content varies from 100 to >200 mg (per tablet)	Very effective phosphate-binding capacity; variety of forms	Potential for aluminum toxicity; altered bone mineralization, dementia; GI side effects
Calcium acetate	Yes/no	Capsule, tablet	Contains 25% elemental Ca^{2+} (169 mg elemental Ca^{2+} per 667 mg cap)	Effective phosphate-binding, potentially for enhanced phosphate-binding capability over $CaCO_3$ potentially less calcium absorption	Potential for hypercalcemia-associated risks including extraskeletal calcification and PTH suppression; more costly than $CaCO_3$; GI side effects
Calcium carbonate	No	Liquid, tablet, chewable, capsule, gum	Contains 40% elemental Ca^{2+} (200 mg elemental Ca^{2+} per 500 mg $CaCO_3$)	Effective, inexpensive, readily available	Potential for hypercalcemia-associated risks including extraskeletal calcification and PTH suppression; GI side effects
Calcium citrate	No	Tablet, liquid, capsule	Contains 22% elemental Ca^{2+}	Not recommended in CKD	Enhancement of aluminum absorption; GI side effects
Calcium ketoglutarate					Similar to other calcium salts, costly, GI side effects, potentially less hypercalcemic than calcium carbonate or acetate, not well studied
Calcium gluconate		Tablet, powder			Similar to other calcium salts, not well studied
Ferric citrate					GI side effects, not well studied
Magnesium/calcium carbonate	No	Tablet	Approx 28% Mg^{2+} (85 mg) per total mg carbonate and 25% elemental Ca^{2+} (100 mg) per total $CaCO_3$	Effective; potential for lower calcium load than pure calcium-based binders	GI side effects, potential for hypermagnesemia, not well studied
Magnesium carbonate/ calcium acetate	Yes	Tablet			Lack of availability worldwide; assumed to have similar effects of its components
Sevelamer-HCl	Yes	Caplet	None	Effective; no calcium/metal; not absorbed; potential for reduced coronary/aortic calcification when compared with calcium-based binders in some studies; reduces plasma concentration of LDL-C	Cost; potential for decreased bicarbonate levels; may require calcium supplement in presence of hypocalcemia; GI side effects
Sevelamer carbonate	Yes	Caplet, powder	None	Effective; no calcium/metal; not absorbed; assumed to have similar advantages as sevelamer-HCl; potentially improved acid–base balance	Cost; may require calcium supplement in the presence of hypocalcemia; GI side effects
Lanthanum carbonate	Yes	Wafer, chewable	Contains 250, 500, or 1000 mg elemental lanthanum per wafer	Effective; no calcium; chewable	Cost; potential for accumulation of lanthanum due to GI absorption, although long-term clinical consequences unknown; GI side effects

CKD, chronic kidney disease; GI, gastrointestinal; LDL-C, low-density lipoprotein cholesterol; PTH, parathyroid hormone.

KDIGO. *Kid Int.* 2009; 76 (Suppl 113):S1-S130

Quelantes del Fósforo

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KDIGO. *Kid Int.* 2009; 76 (Suppl 113):S1-S130

Hidróxido de aluminio

Binder source	Rx	Forms	Content (mineral/metal/element)	Potential advantages	Potential disadvantages
Aluminum hydroxide	No	Liquid, tablet, capsule	Aluminum content varies from 100 to >200 mg (per tablet)	Very effective phosphate-binding capacity; variety of forms	Potential for aluminum toxicity; altered bone mineralization, dementia; GI side effects

KDIGO. *Kid Int.* 2009; 76 (Suppl 113):S1-S130

Uso de captores alumínicos en hemodiálisis en la era del agua ultrapura

M.ª D. Arenas, T. Malek, M. T. Gil, A. Moledous, C. Núñez y F. Álvarez-Ude

[1]*Hospital Perpetuo Socorro. Alicante.* [2]*Hospital General de Segovia.*

Nefrología 2008; 28 **(2)** 168-173

Su uso
encefa

Sin em de aluminio en el agua de hemodialisis previo al uso sistemático de ósmosis inversa.

Actualmente ,no existen estudios randomizados prospectivos que demuestren la toxicidad del aluminio en dosis via oral adecuadas y con concentraciones de aluminio inferiores a 5 ug/l en el agua tratada.

Nefrología 2008;28 (2) 129-134

Carbonato de Calcio

Binder source	Rx	Forms	Content (mineral/metal/element)	Potential advantages	Potential disadvantages
Calcium carbonate	No	Liquid, tablet, chewable, capsule, gum	Contains 40% elemental Ca^{2+} (200 mg elemental Ca^{2+} per 500 mg $CaCO_3$)	Effective, inexpensive, readily available	Potential for hypercalcemia-associated risks including extraskeletal calcification and PTH suppression; GI side effects

KDIGO. *Kid Int.* 2009; 76 (Suppl 113):S1-S130

- **Se disuelve en medio acido y se liga al fósforo en un PH elevado**
- **Contiene alta proporción de calcio elemental (40%)**
- **Predispone a la hipercalcemia, y se asocia a las calcificaciones vasculares, a la supresión de la PTH**
- **Trastornos gastrointestinales y regular compliance**

Acetato de Calcio

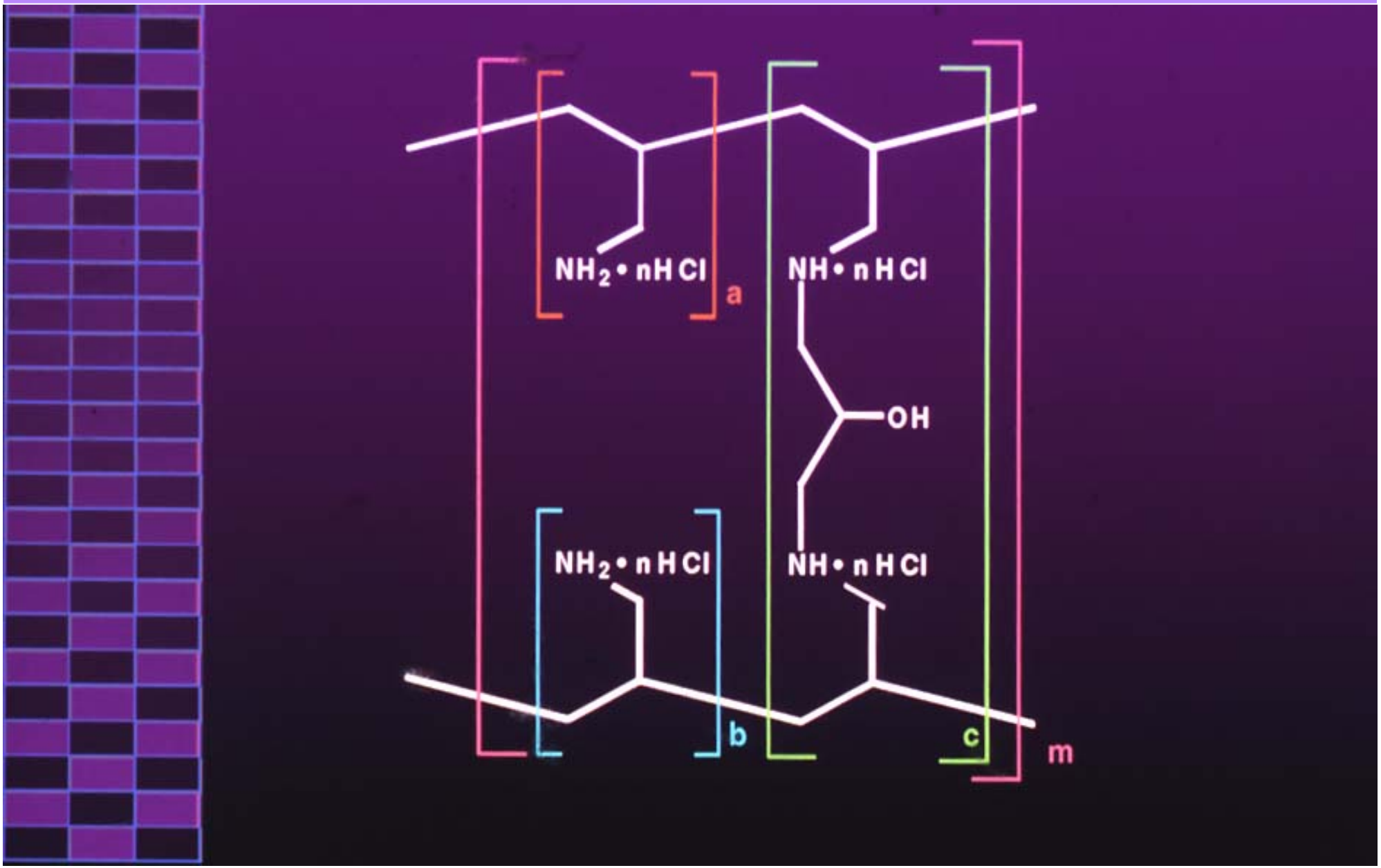
Binder source	Rx	Forms	Content (mineral/metal/element)	Potential advantages	Potential disadvantages
Calcium acetate	Yes/no	Capsule, tablet	Contains 25% elemental Ca^{2+} (169 mg elemental Ca^{2+} per 667 mg cap)	Effective phosphate-binding, potentially for enhanced phosphate-binding capability over $CaCO_3$ potentially less calcium absorption	Potential for hypercalcemia-associated risks including extraskeletal calcification and PTH suppression; more costly than $CaCO_3$; GI side effects

KDIGO. *Kid Int.* 2009; 76 (Suppl 113):S1-S130

- **Contiene 25 % de calcio elemental**
- **Tiene buena solubilidad en medio acido y en medio alcalino**
- **Mejor capacidad de quelación que el carbonato de calcio**

Quelantes

Sevelamer



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Sevelamer carbonate	Yes	Caplet, powder	None	Effective; no calcium/metal; not absorbed; assumed to have similar advantages as sevelamer-HCl; potentially improved acid-base balance	Cost; may require calcium supplement in the presence of hypocalcemia; GI side effects

Polímero no absorbible que no contiene calcio ni aluminio y que liga al fosfato a través de un intercambio iónico.

Droga utilizada en mas del 20% de la población dialítica en USA

Effects of sevelamer and calcium on coronary artery calcification in patients new to hemodialysis

- 129 patients new to hemodialysis in Denver, Colorado
- Randomized to receive calcium containing phosphate binders or sevelamer
- Subjects underwent electron beam computed tomography scanning (EBCT)

  at entry into the study

  and again at 6, 12, and 18 months
- 109 underwent baseline + at least one additional assessment of coronary calcification

Block et al. 2005;68:1815-1824

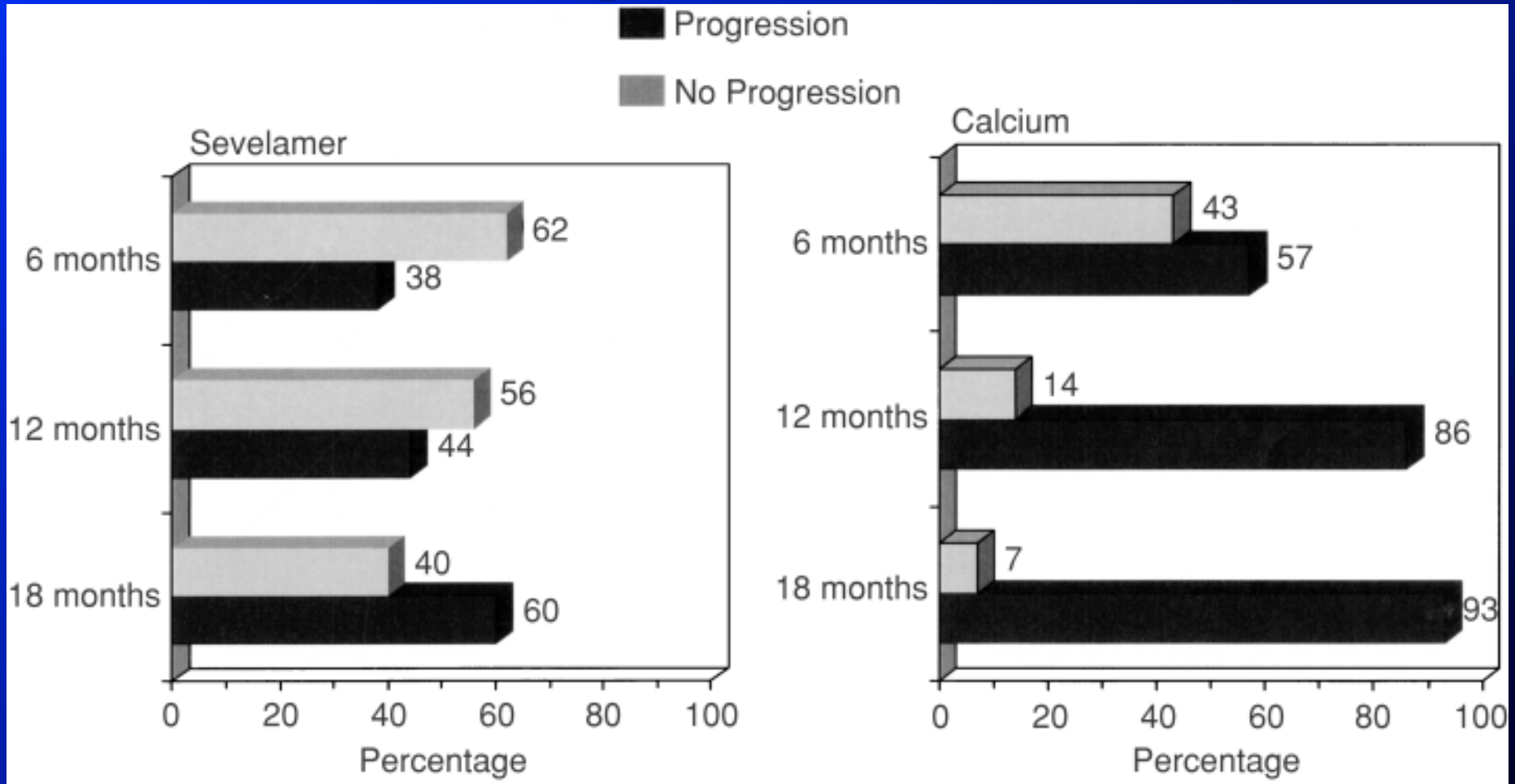
Effects of sevelamer and calcium on coronary artery calcification in patients new to hemodialysis

At baseline:

- 37% of sevelamer treated and 31% of calcium treated patients had no evidence of coronary calcification
- No subject with a zero coronary artery calcium score (CACS) at baseline progressed to a CACS >30 over 18 months
- Subjects with a CACS > 30 at baseline showed progressive increases in CACS in both treatment arms ($P < 0.05$ for each time point in both groups)
- Subjects treated with calcium containing phosphate binders showed more rapid and more severe increases in CACS when compared with those receiving sevelamer hydrochloride ($P = 0.056$ at 12 months, $P = 0.01$ at 18 months).
- Subjects with diabetes progressed more rapidly

Block et al. 2005;68:1815-1824

Effects of sevelamer and calcium on coronary artery calcification in patients new to hemodialysis



*Progression of CACS = greater that 15% increase from baseline

† Fisher exact test *P* value < 0.05 for between group differences at 12 and 18 months

Block et al. 2005;68:1815-1824

Sevelamer atenúa la progresión de la calcificación coronaria y aórtica en pacientes en hemodiálisis

- Ensayo clínico, multicéntrico, aleatorizado de 2 brazos (Sevelamer *vs* quelantes de P basados en calcio) en 200 pacientes en hemodiálisis.
- El objetivo primario fue la reducción significativa del producto Ca x P.
- Se analizaron las calcificaciones vasculares mediante TC en haz de electrones (EBCT), basal a las 26 y a las 52 semanas.

	Sevelamer	Calcio	P
	N= 99	N= 101	
Fósforo (mg/dl)	5,1 ± 1,2	5,1 ± 1,4	0,33
Cálcio (mg/dl)	9,5 ± 0,6	9,7 ± 0,7	0,002
Hipercalcemia (%)	5	16	0,04
CaxP	48 ± 12	49 ± 14	0,12
PTHi (pg/ml)	224	138	0,11
Colesterol (mg/dl)	141 ± 28	182 ± 49	< 0,0001
LDL (mg/dl)	65 ± 21	103 ± 43	< 0,0001

El tratamiento con Sevelamer se asocia a una clara reducción de los episodios de hipercalcemia, del colesterol total y LDL.

Chertow GM *et al, KI* 2002

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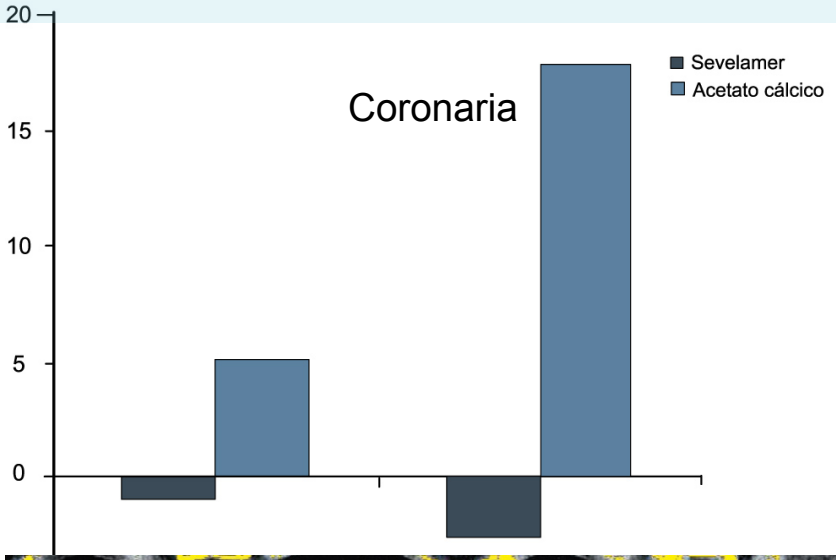
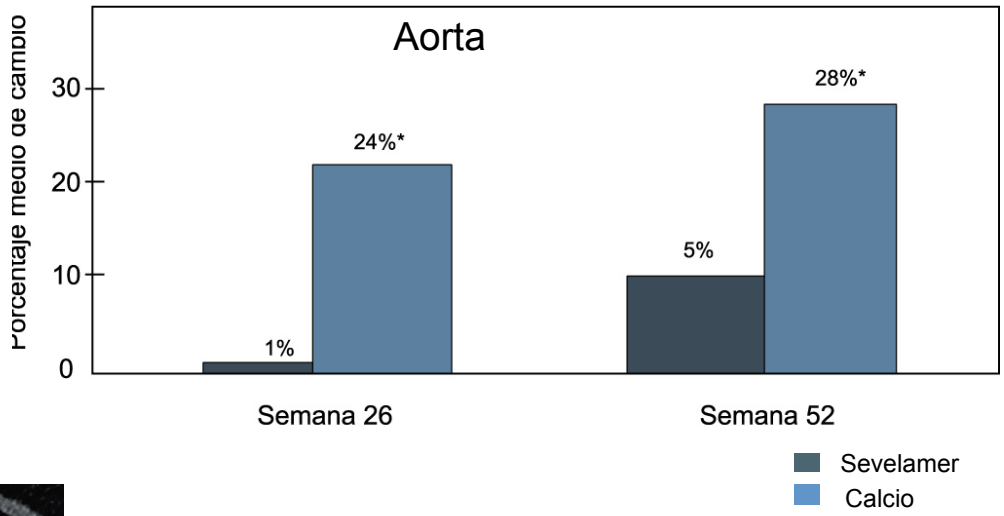
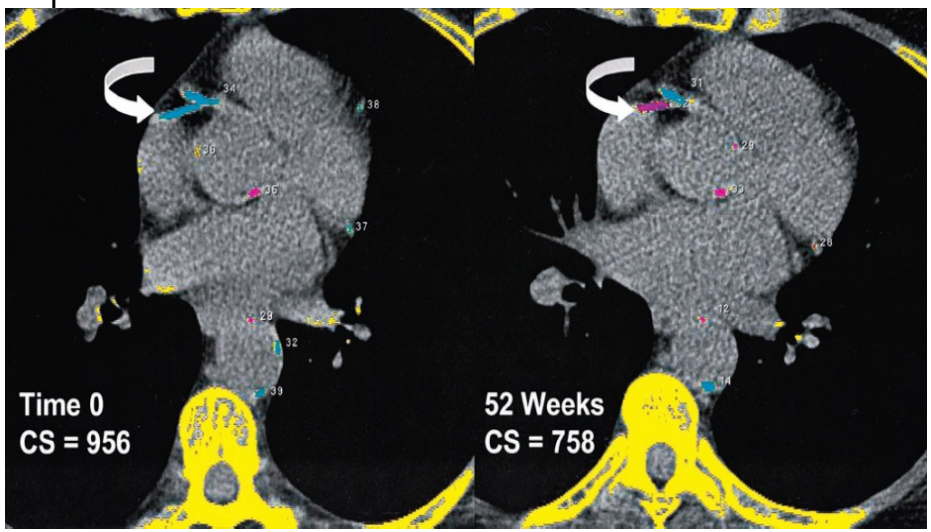
Sevelamer previene la progresión de la calcificación coronaria y aórtica en pacientes en hemodiálisis







Ejemplo de regresión de calcificación coronaria tras 52 semanas de tratamiento (el color cambia de azul a rojo-azul por reducción de la densidad de calcio en la pared arterial).

Chertow GM *et al, KI* 2002

CONCLUSIONES

- El control del P fue´similar en los dos grupos.
- Los pacientes con sales de Ca presentaron más episodios de hipercalcemia
- Las calcificaciones coronarias progresaron significativamente menos en los tratados con sevelamer.
- El efecto del Sevelamer puede ser secundario a menor hipercalcemia asociado a la disminución del LDL colesterol.

Chertow GM *et al, KI* 2002

Efecto favorable de Sevelamer sobre los lípidos y marcadores de inflamación

	Sevelamer	Calcio	P
Colesterol total (mg/dl	135 ± 0,32	175 ± 0,49	< 0,0001
Colesterol LDL (mg/dl)	64 ± 20	97 ± 44	< 0,0001
Colesterol HDL (mg/dl)	43 ± 11	44 ± 12	0,03
Apo B (mg/l)	62 ± 15	78 ± 27	< 0,0001
PCR hs (mg/l)	3,3 (1,2-9,7)	4,3 (1,6-17,4)	0,014

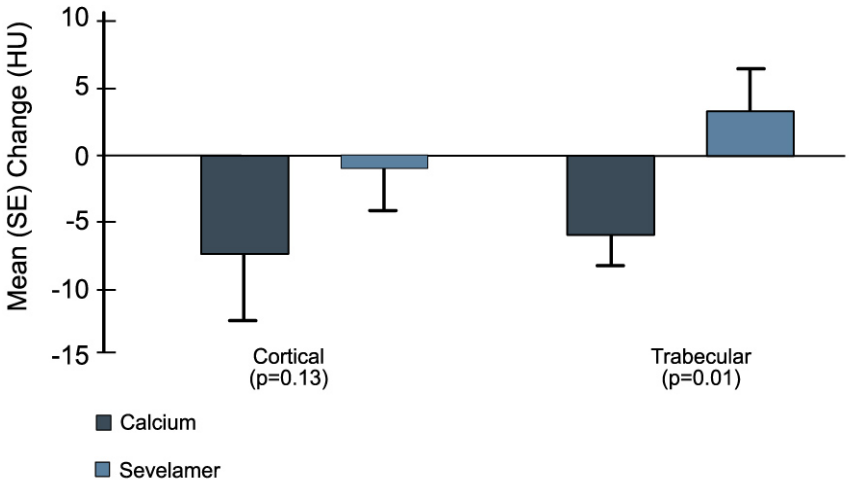
El tratamiento con Sevelamer si se compara con acetato cálcico reduce de forma significativa los niveles de colesterol total, colesterol LDL y Apo B.

El tratamiento con Sevelamer reduce la proteína C reactiva en mayor medida que el tratamiento con acetato cálcico.

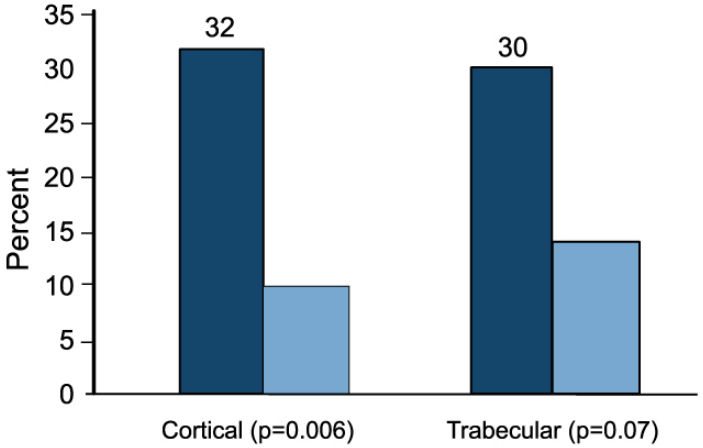
Chertow GM *et al, AIN* 2003

Reducción de la atenuación ósea vertebral en pacientes tratados con quelantes de fósforo a base de calcio en hemodiálisis

Cambios en la atenuación del hueso cortical y trabecular



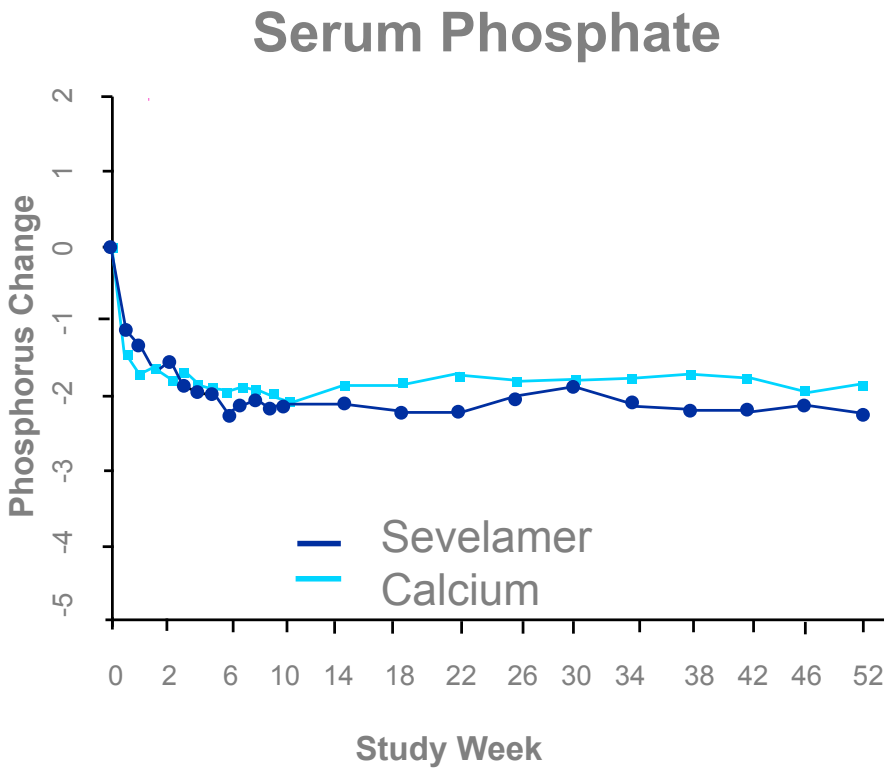
Proporción de pacientes con una reducción >10% de la atenuación del hueso trabecular y cortical

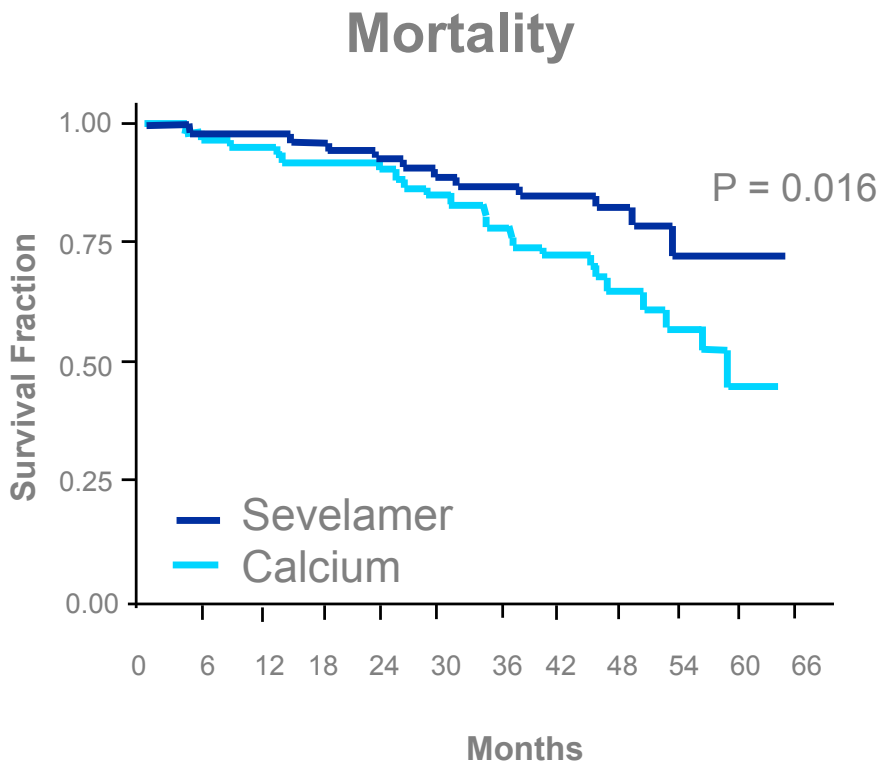


- Existió un descenso significativo en la atenuación del hueso trabecular en los pacientes tratados con sales de calcio, mientras que la atenuación no se modificaba en sevelamer. Este efecto era muy consistente pues persistía después del ajuste multivariante para edad, sexo, raza, diabetes y tiempo en hemodiálisis.
- Los pacientes tratados con sales de calcio experimentan una reducción del 10% o superior en la atenuación del hueso cortical si los comparamos con los tratados con Sevelamer.

Raggi P *et al, J Bone Miner Res* 2005

Managing Mineral Balance: Phosphate Binders





127 Pac Incidentes en HD

Tiempo 44 meses

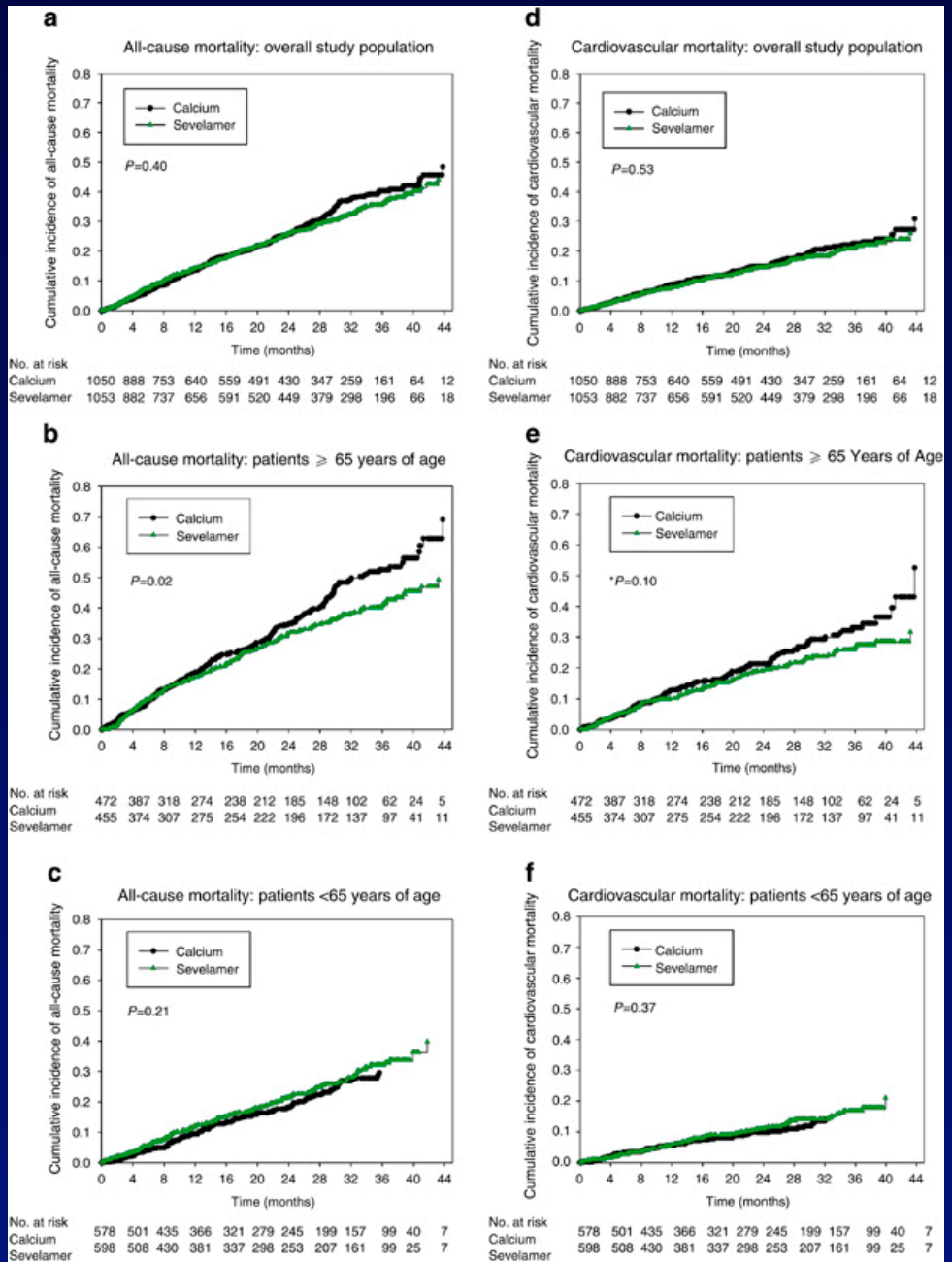
Sevelamer label: http://www.renagel.com/docs/renagel_pi.pdf
Block GA, et al. *Kidney Int.* 2007;71(5):438-441.

DCOR—Study Overview[1]

- Open-label, randomized study in a total of 2103 US ESRD patients on dialysis
- Study hypothesis:
  - **Mortality rate would be lower with Sevelamer by avoiding calcium in the calcium binders**
  - Study was powered to pick up a 22% reduction in all-cause mortality (primary endpoint) - this would also demonstrate reduction in cardiovascular deaths (the parameter sevelamer was expected to reduce)
  - Cardiovascular deaths represented a pre-specified secondary endpoint
- Patients randomized to sevelamer or calcium-based phosphate binders [.CBPBs: PhosLo (73%) or calcium carbonate (27%)]
- Choice of phosphate binder at investigators discretion - no limitation on calcium intake
- Calcium supplementation allowed (but not recorded) in sevelamer group at discretion of investigator
- No control of dialysate Ca or Vitamin D

[1] Suki, et al. Journal of American Society of Nephrology, Volume 16, 2005. Poster. American Society of Nephrology Renal Week. Pennsylvania Convention Center, Philadelphia, PA. November 9-13, 2005.

Estudio DCOR: Sevelamer vs quelantes con calcio. Efecto sobre mortalidad total y CV



N=2103

Hospitalizaciones

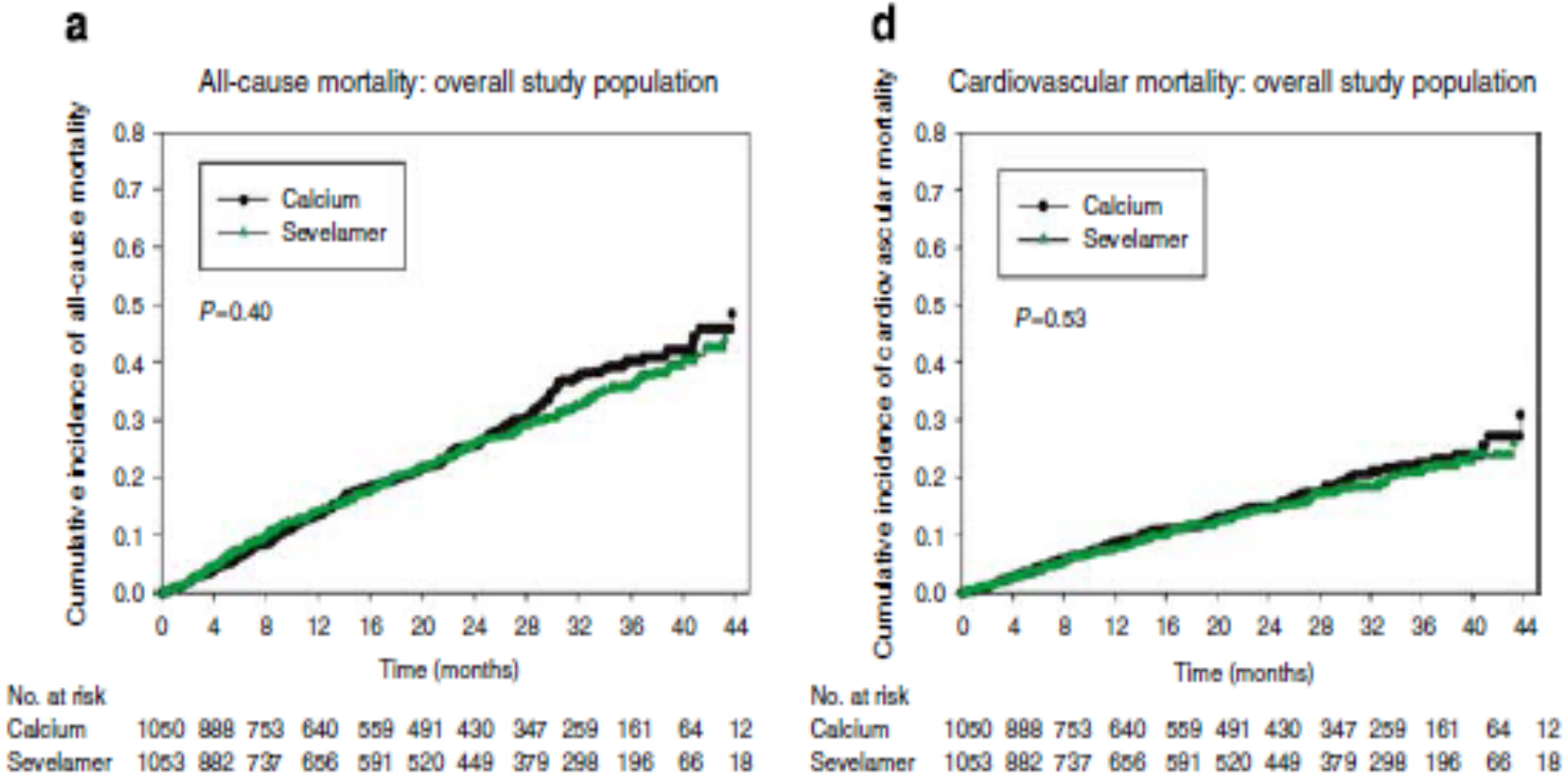
S 2.1 vs Ca 2.3 (p=0.0738)

Dias hospitalización

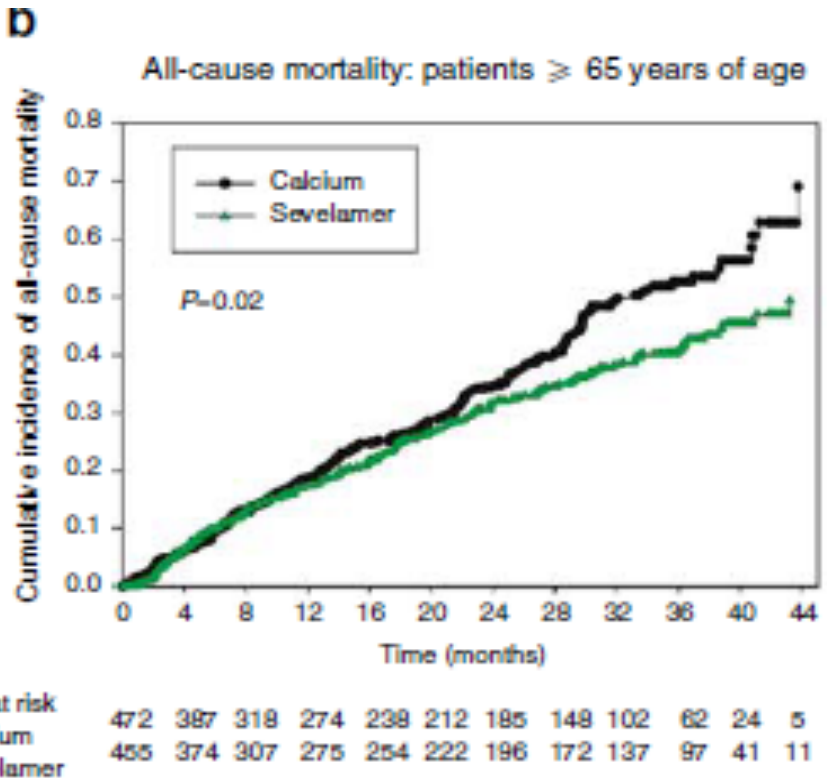
S 14.8 vs Ca 17.4 (p=0.0897)

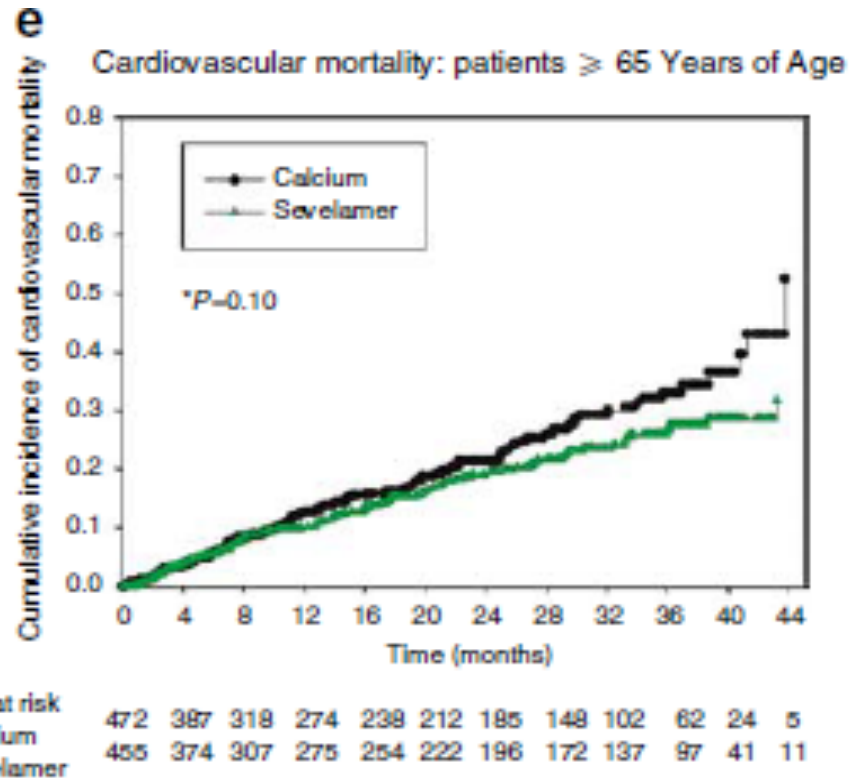
Suki WN. KI 2007; 72: 1130-7

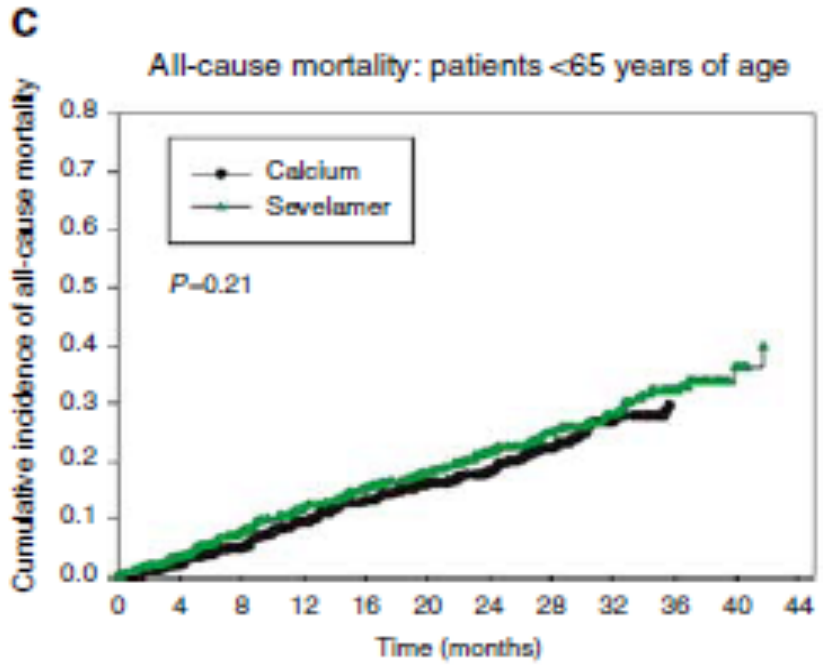
The DCOR (Dialysis Clinical Outcomes Revisited)

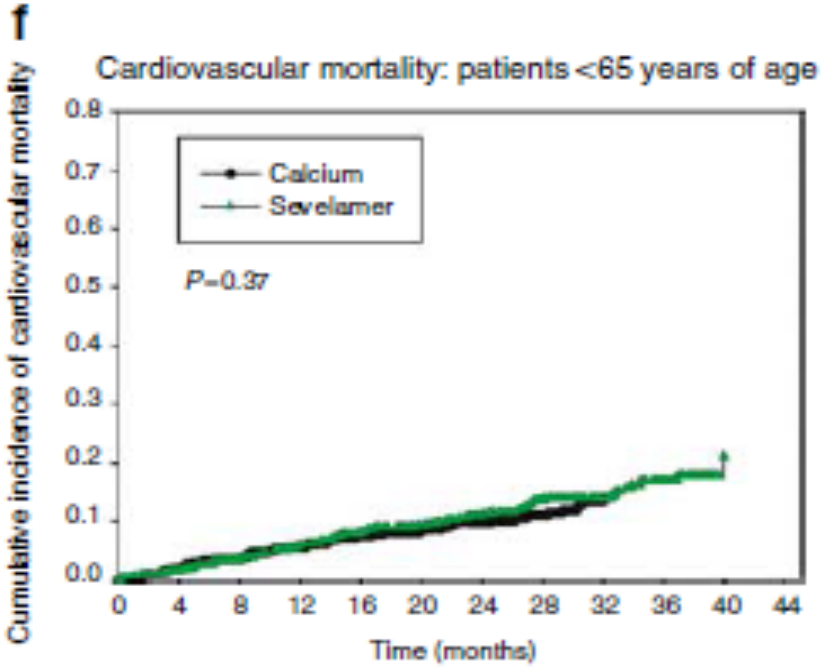


Kidney International (2007) **72**, 1130–1137


b
All-cause mortality: patients ⩾ 65 years of age
Cumulative incidence of all-cause mortality
Calcium
Sevelamer
P=0.02
Time (months)
No. at risk
Calcium 472 387 318 274 239 212 185 148 102 62 24 5
Sevelamer 455 374 307 275 254 222 196 172 137 97 41 11


e
Cardiovascular mortality: patients ⩾ 65 Years of Age
Cumulative incidence of cardiovascular mortality
Calcium
Sevelamer
*P=0.10
Time (months)
No. at risk
Calcium 472 387 318 274 239 212 185 148 102 62 24 5
Sevelamer 455 374 307 275 254 222 196 172 137 97 41 11


c
All-cause mortality: patients <65 years of age
Cumulative incidence of all-cause mortality
Calcium
Sevelamer
P=0.21
Time (months)
No. at risk
Calcium 578 501 435 366 321 279 245 199 157 99 40 7


f
Cardiovascular mortality: patients <65 years of age
Cumulative incidence of cardiovascular mortality
Calcium
Sevelamer
P=0.37
Time (months)
No. at risk
Calcium 578 501 435 366 321 279 245 199 157 99 40 7

Limitaciones del sevelamer

- Requiere un elevado número de pastillas diaria (6-8 comp)
- Menor poder de quelación que el acetato de calcio
- Podría afectar la absorción de Vit K y Vit D
- En altas dosis puede generar trastornos gastrointestinales
- Alto costo

Systematic review of the clinical efficacy and safety of sevelamer in dialysis patients

Marcello Tonelli[1,2,3,4], Natasha Wiebe[1], Bruce Culleton[5], Helen Lee[6], Scott Klarenbach[1,3,4], Fiona Shrive[6] and Braden Manns[3,5,6] for the Alberta Kidney Disease Network

Table 1. Characteristics of included studies

Study									
Studies in									
Bleyer *et*									te
Block *et a*									
							2.3 g/day		
RIND									
Chertow 2002 [29]	US, Germany, Austria	HD	median 3.2 years	RCT	52 weeks	6.5	Calcium acetate (US) 4.6 g/day or calcium carbonate (EUR) 3.9 g/day	200	Calcium phosphate product
Treat-to-Goal									
De Santo *et al.* [30]	Italy	HD	6-10 months	X-RCT	24 weeks	Initial 4.8, 7.2	Calcium carbonate, dose NR	16	Serum bicarbonate
Hervas *et al.* [31]	Spain	HD	57 months	RCT	32 weeks	4.1	Calcium acetate 3.9 g/day	51	Serum phosphate
Kinugasa and Koshikawa [32] Abstract	Japan	HD	–	RCT	8 weeks	4.7	Calcium carbonate 2.8 g/day	230	–
Qunibi *et al.* [33] CARE	US	HD	4.3 years	DB RCT	8 weeks	Final 6.9	Calcium acetate 7.1 g/day	98	Serum phosphate
Sadek *et al.* [34]	France	–	–	RCT	5 months	Final 4.4	Calcium carbonate 4.8 g/day	42	–
Shaheen *et al.* [35]	Saudi Arabia	HD	3.4 years	X-RCT	8 weeks	Final 5.2	Calcium carbonate ending 9.0 g/day	20	–
Suki *et al.* [36] DCOR Poster	US	HD	38 months	RCT	Median <2 years	Dose NR	Calcium acetate or calcium carbonate dose NR	2040	All-cause mortality
Additional studies included in the safety analysis									
Akizawa *et al.* [38]	Japan	HD	–	RCT	6 weeks	1.5, 3.0, 6.0 and 7.5 (4 groups)	–	94	–
Abstract									
Almirall *et al.* [39]	Spain	HD	69 months	SAT	6 months	3.5	–	34	–
Borras *et al.* [40]	Spain	PD	–	SAT	6 months	2.8	–	13	Bicarbonate levels
Castro *et al.* [41]	Portugal	HD	8.8 years	SAT	12 weeks	2.7	–	18	–
Chertow *et al.* [24]	US	HD	>3 months	DB RCT	8 weeks	3.6	Placebo	36	Serum phosphate
Chertow *et al.* [23]	US	HD	3.8 years	SAT	46 weeks	6.3	–	192	–
Chertow *et al.* [25]	US	HD	3.0 years	RCT	12 weeks	Final 4.7	Sevelamer with 900 mg of calcium	71	–
Fischer *et al.* [42]	US	HD	2.9 years	X-RCT	4 weeks	6.7	–	21	Serum phosphate
Gallieni *et al.* [43]	Italy	HD	>3 months	SAT	6 weeks	Initial 2.8	–	19	Serum phosphate and calcium phosphate product
Goldberg *et al.* [44]	US	HD	–	SAT	8 weeks	4.1	–	48	–

Nephrol Dial Transplant (2007) 22: 2856–2866
doi:10.1093/ndt/gfm421

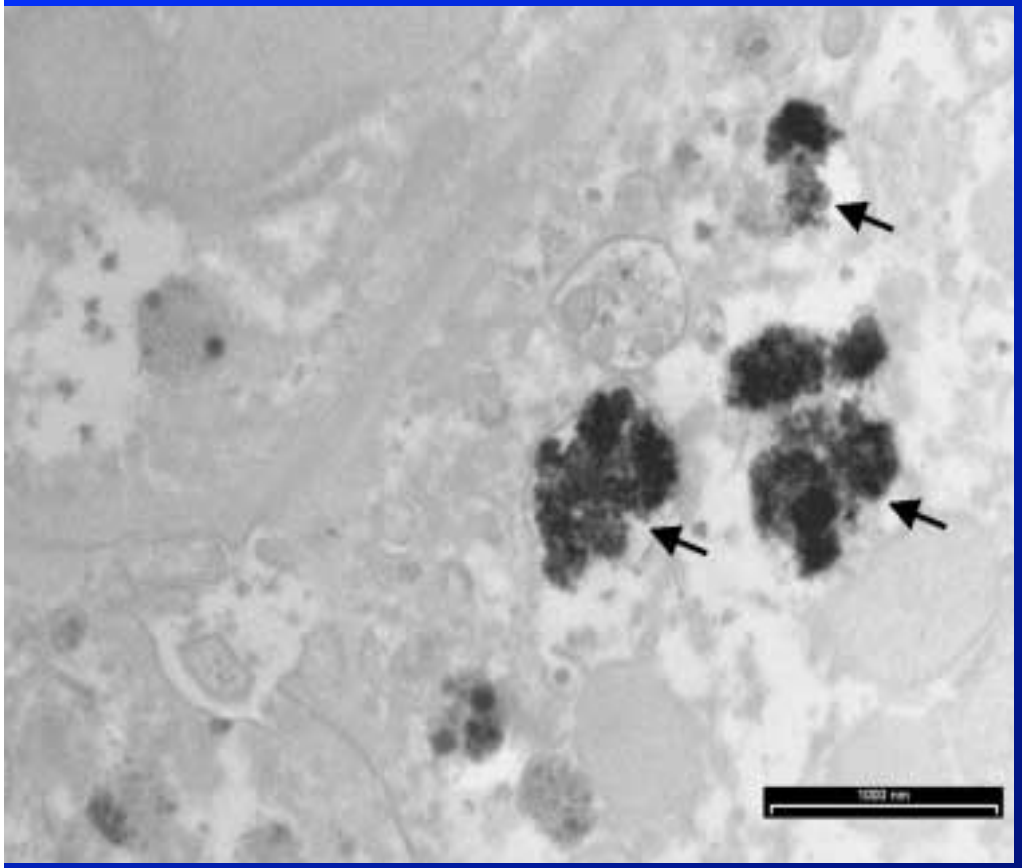
Lanthanum

- A rare earth element
- Atomic number 57
- Atomic weight 139
- Valency 3, binds phosphate ionically
- Present in tap water (very low levels)
- Various salts bind phosphate avidly
- Lanthanum phosphate very insoluble
- Lanthanum carbonate least soluble salt

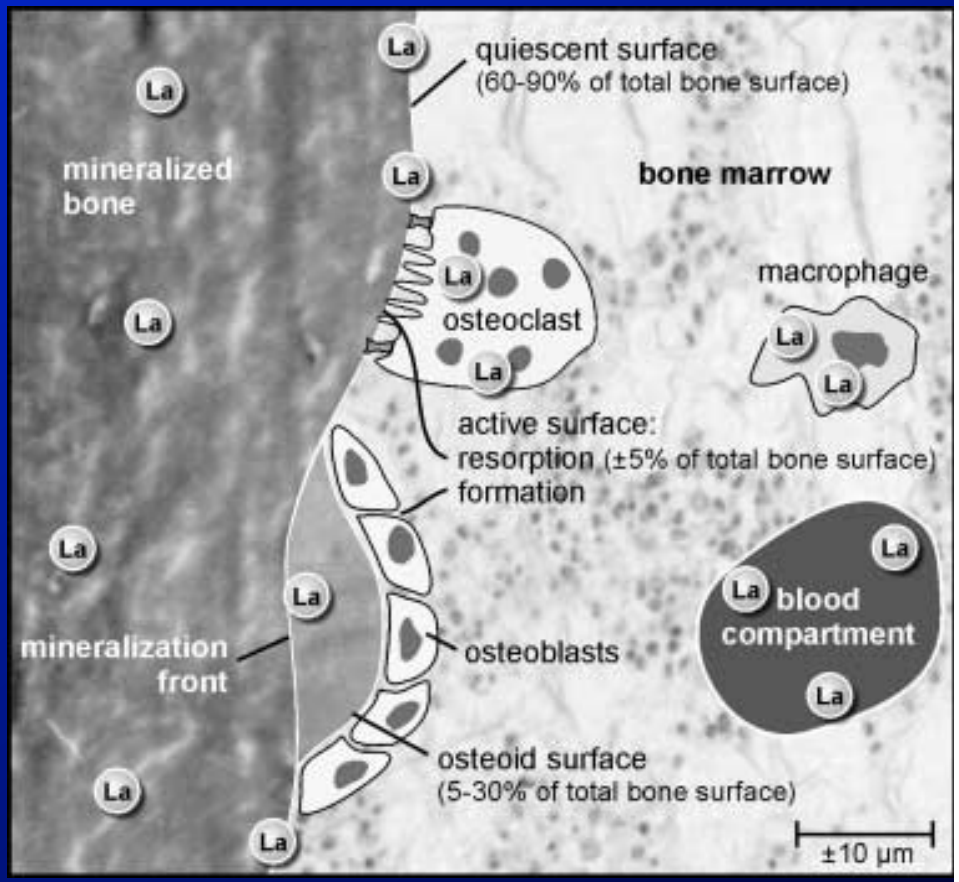
Carbonato de lantano

Binder source	Rx	Forms	Content (mineral/metal/element)	Potential advantages	Potential disadvantages
Lanthanum carbonate	Yes	Wafer, chewable	Contains 250, 500, or 1000 mg elemental lanthanum per wafer	Effective; no calcium; chewable	Cost; potential for accumulation of lanthanum due to GI absorption, although long-term clinical consequences unknown; GI side effects

- Metal Raro
- Potente, incluso en monoterapia
- Pocos efectos secundarios
- No cálcico y alto precio
- Bajo número de pastillas, que deben masticarse
- Radiopaco. Causa estreñimiento.
- Riesgo acumulación a largo plazo del Lantano



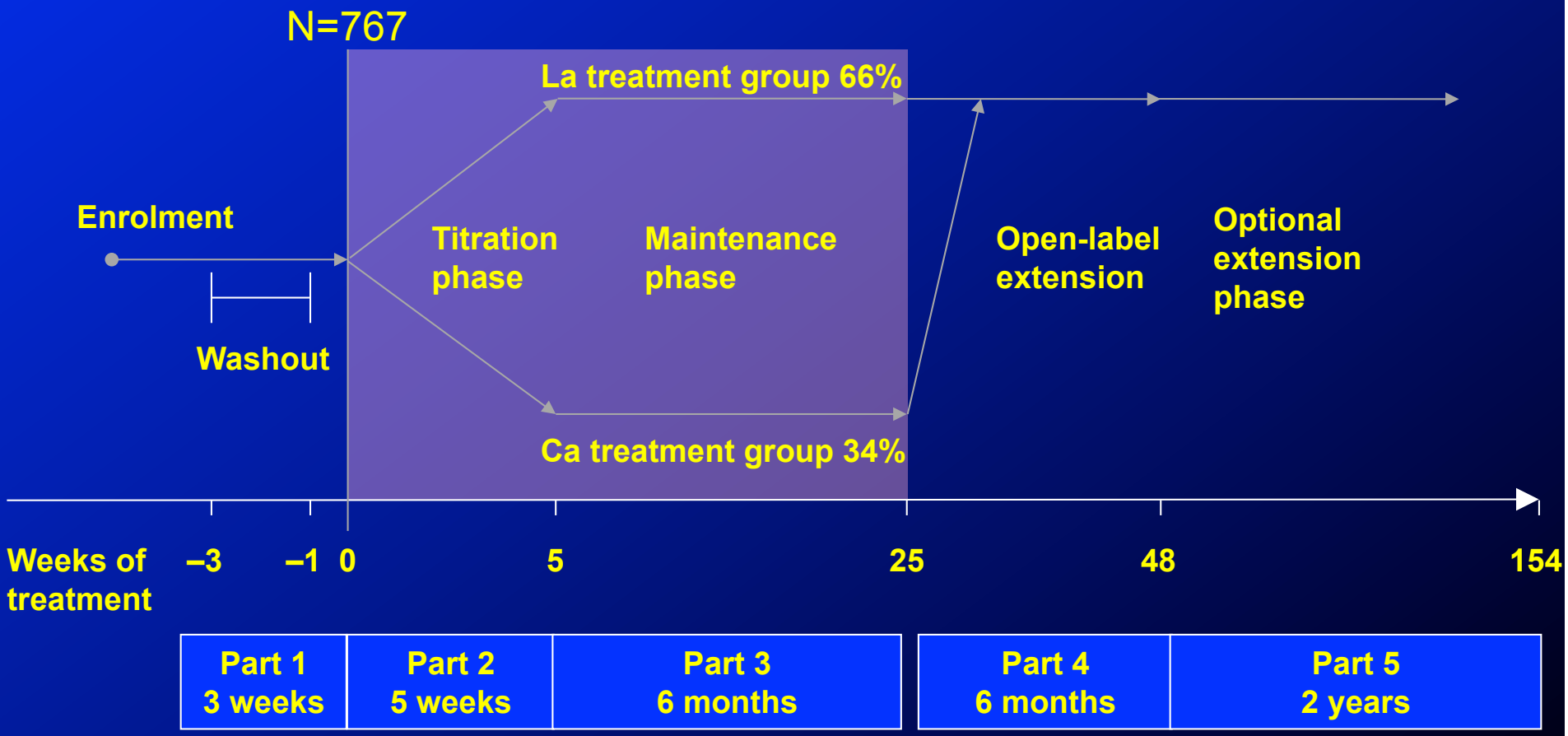
LANTANO EN LISOSOSMAS DE HEPATOCITOS



LANTANO EN HUESO

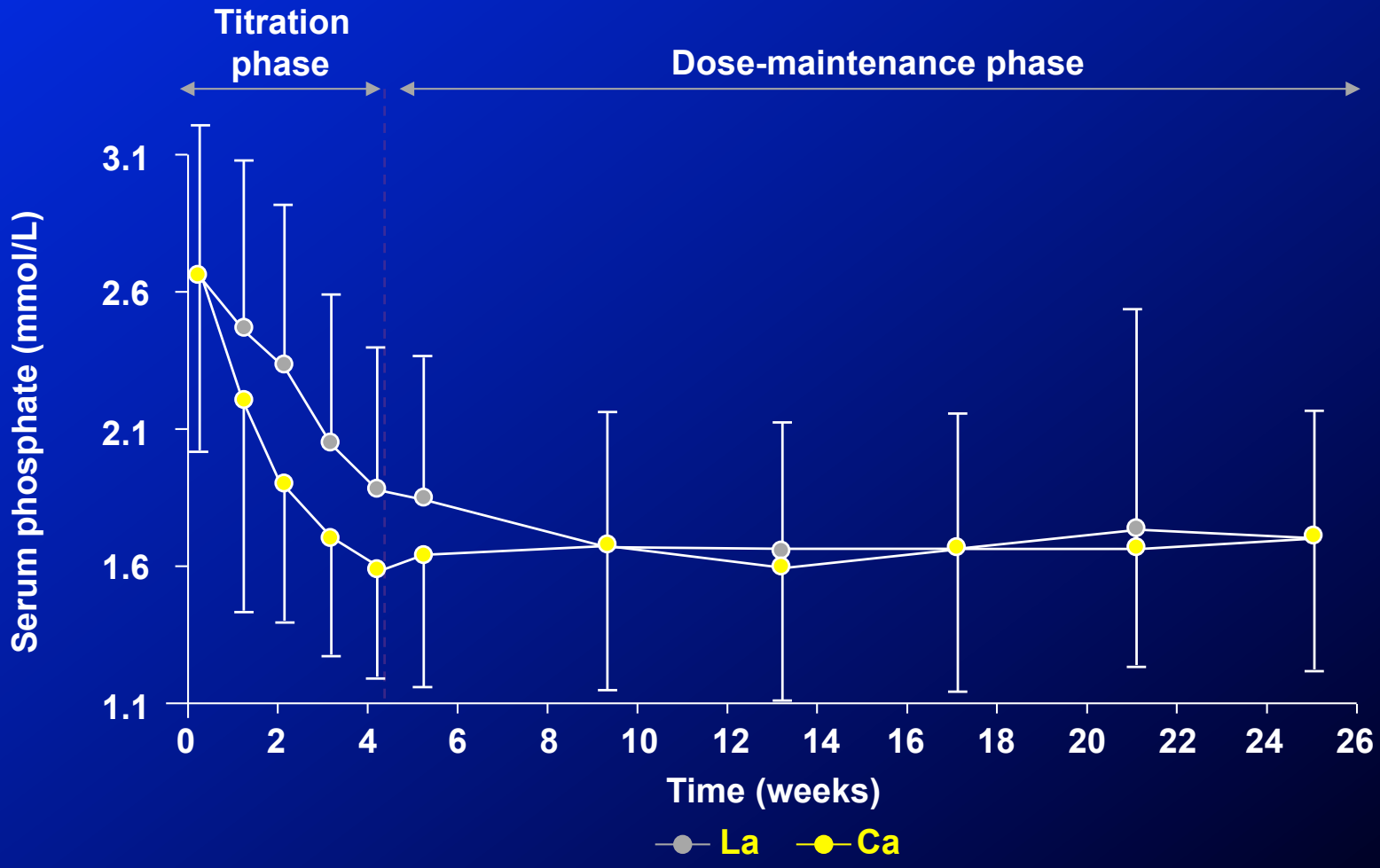
Current Opinion in Nephrology and Hypertension 2004, 13:403–409

Lanthanum vs Calcium - 301: Design



Hutchison AJ. *Nephron Clin Pract* 2005;100:c8–19

Mean (± SD) serum phosphate levels



Hutchison AJ. *Nephron Clin Pract* 2005;100:c8–19

Costo-efectividad de los quelantes del fósforo

Medicación	N.º Pastillas/día	Coste € mes	Coste € año
AL OH	6	4,28	51
Carbonato cálcico	3	5,07	61
Acetato cálcico	6	18	219
Sevelamer	8	209	2.512
Carbonato de lantano	3	181	2.178

Nefrología (2008) **2,** 129-134

A. L. Martín de Francisco

Salivary Phosphate-Binding Chewing Gum Reduces Hyperphosphatemia in Dialysis Patients

Vincenzo Savica,*† Lorenzo A. Calò,‡ Paolo Monardo,† Paul A. Davis,§ Antonio Granata,‖ Domenico Santoro,* Rodolfo Savica,¶ Rosa Musolino,¶ Maria Cristina Comelli,** and Guido Bellinghieri*

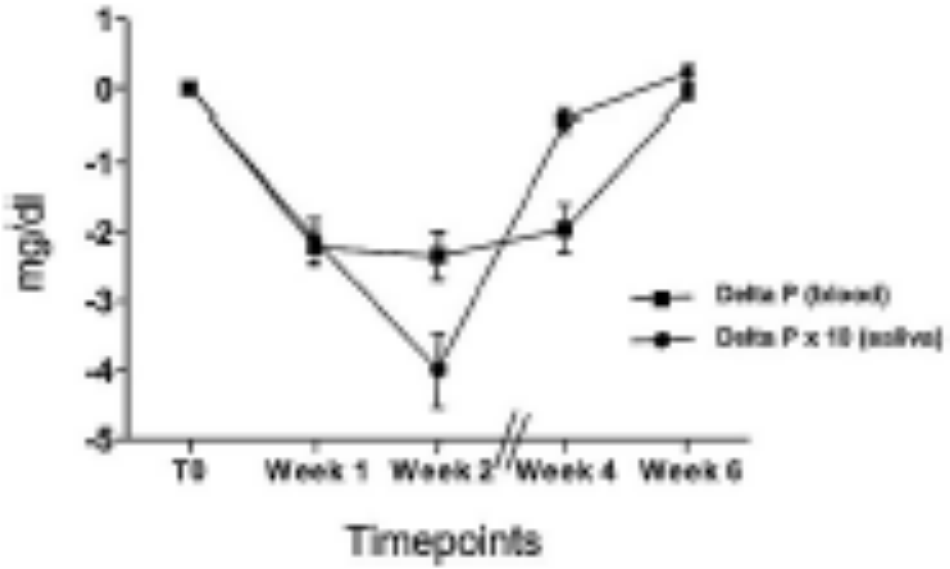
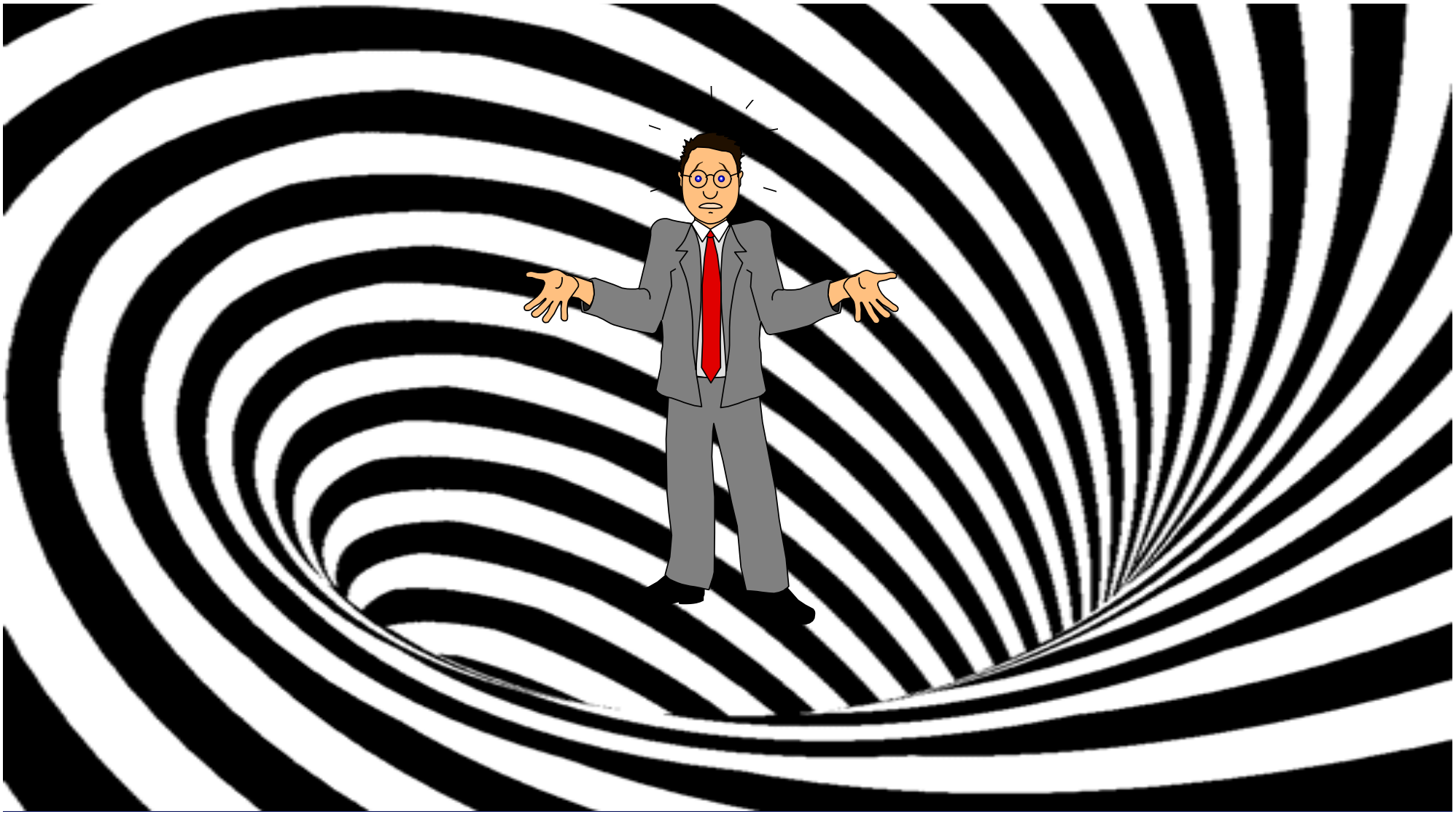


Figure 1. Serum and salivary PO_4 levels (mg/dl) at baseline (T0), at 7 d (week 1) and 14 d (week 2) of chewing gum use, and at 14 d (week 4) and 30 d (week 6) after chewing gum discontinuation.

J Am Soc Nephrol 20: 639–644, 2009

Quelantes calcicos o no calcicos ???




QUERIDO... ¿QUÉ ES PEOR?
¿LA IGNORANCIA O LA INDIFERENCIA?
NO SÉ
NI ME IMPORTA
Nik

4.1.4. En pacientes con ERC estadios 3-5 (2D) y 5D (2B) sugerimos utilizar quelantes de fósforo en el tratamiento de la hiperfosfatemia.

Es razonable que la elección del tipo de quelante de fósforo tome en consideración el estadio de ERC, la presencia de otros componentes de CKD–MBD, los tratamientos concomitantes y los efectos adversos que estos quelantes puedan tener (sin grado).

Kidney International

VOLUME 76 | SUPPLEMENT 113 | AUGUST 2009

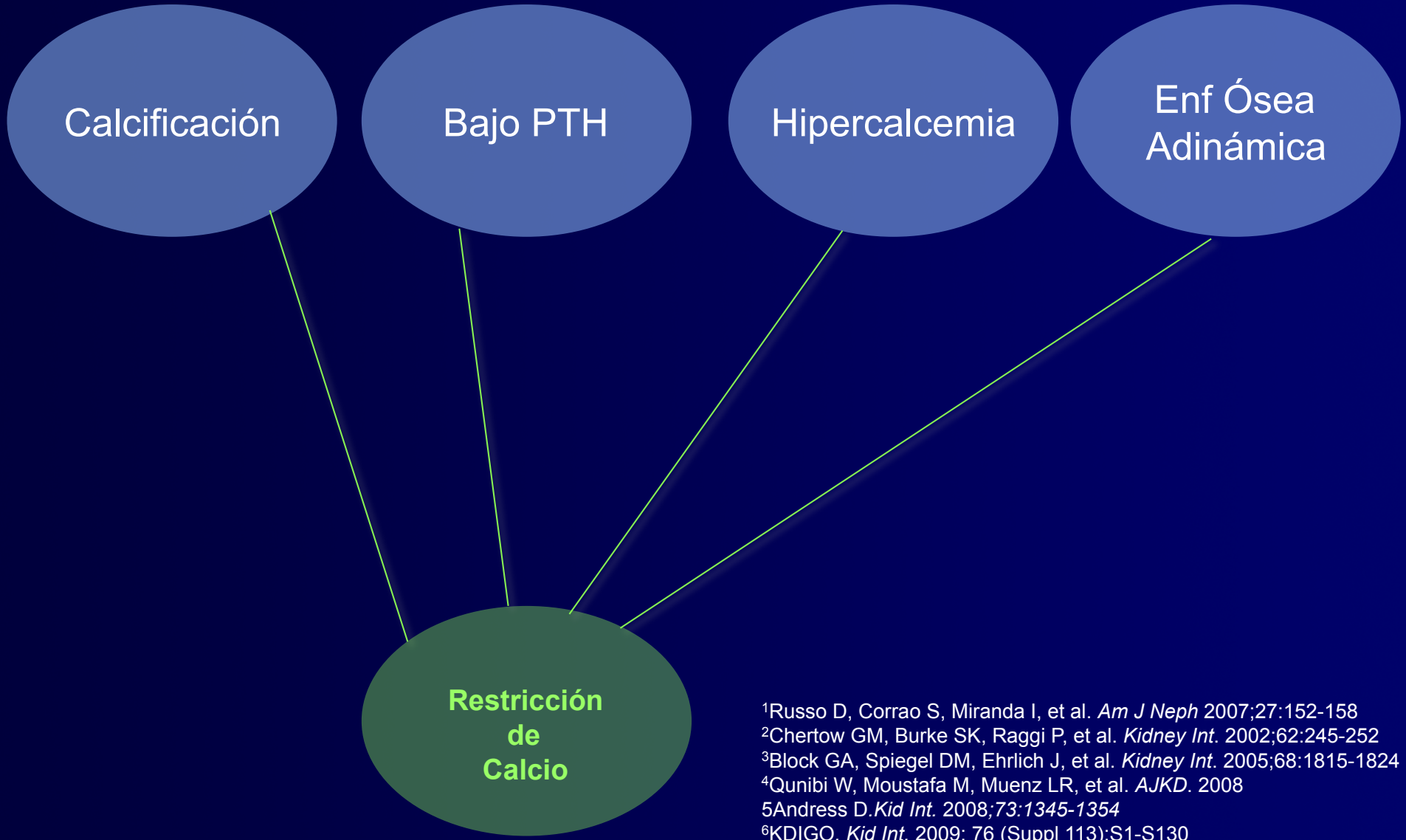
- **4.1.5.** En pacientes con ERC estadios 3-5D e hiperfosfatemia recomendamos restringir las dosis de quelantes de fósforo a base de calcio y/o las dosis de calcitriol o análogos de la vitamina D cuando exista hipercalcemia persistente o recurrente (1B).

- En pacientes con ERC estadios 3-5D e hiperfosfatemia sugerimos restringir las dosis de quelantes de fósforo que contengan calcio cuando existan calcificaciones arteriales (2C) y/o enfermedad ósea adinámica (2C) y/o valores de PTH persistentemente bajos (2C).

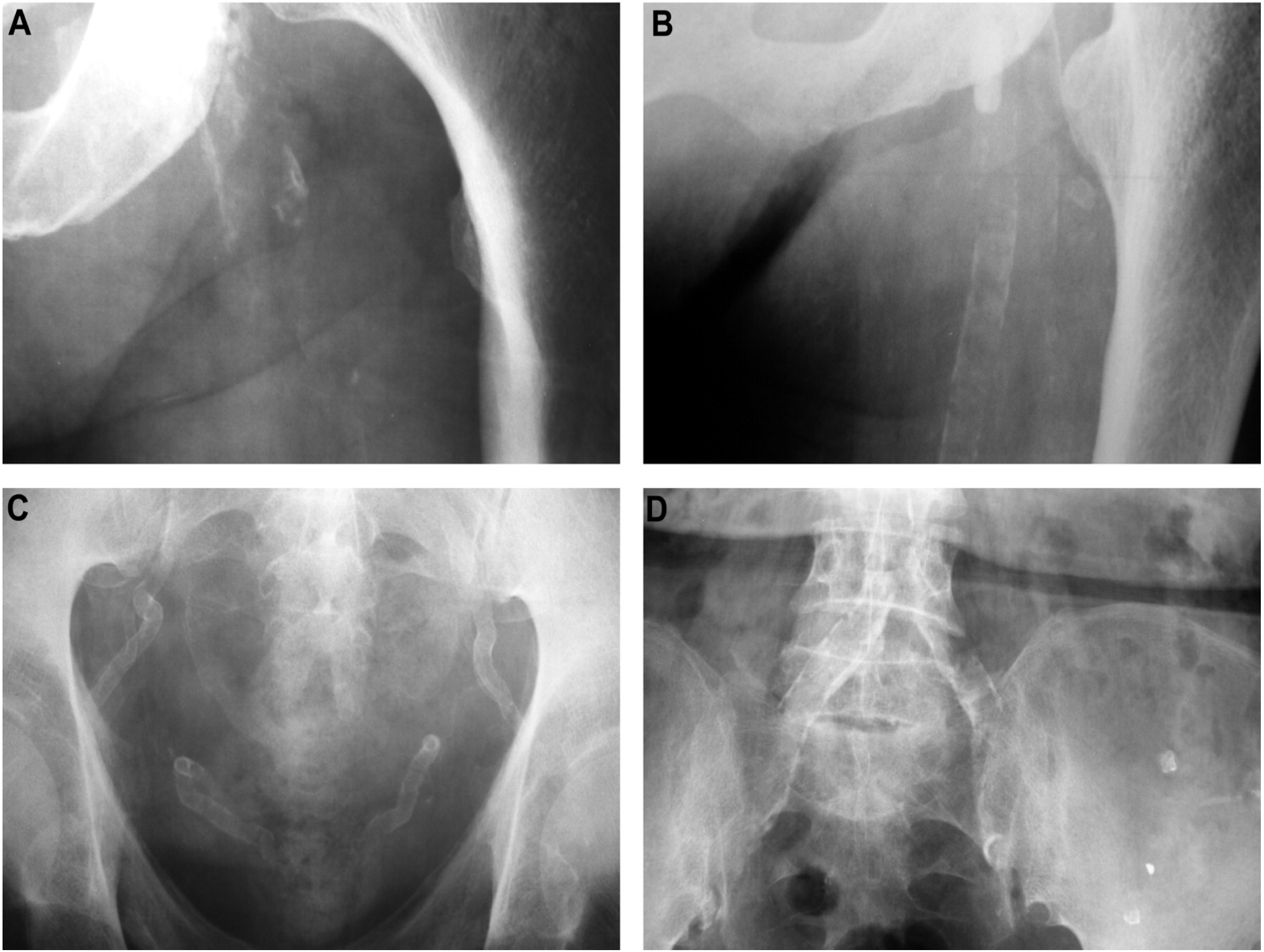
Kidney International

VOLUME 76 | SUPPLEMENT 113 | AUGUST 2009

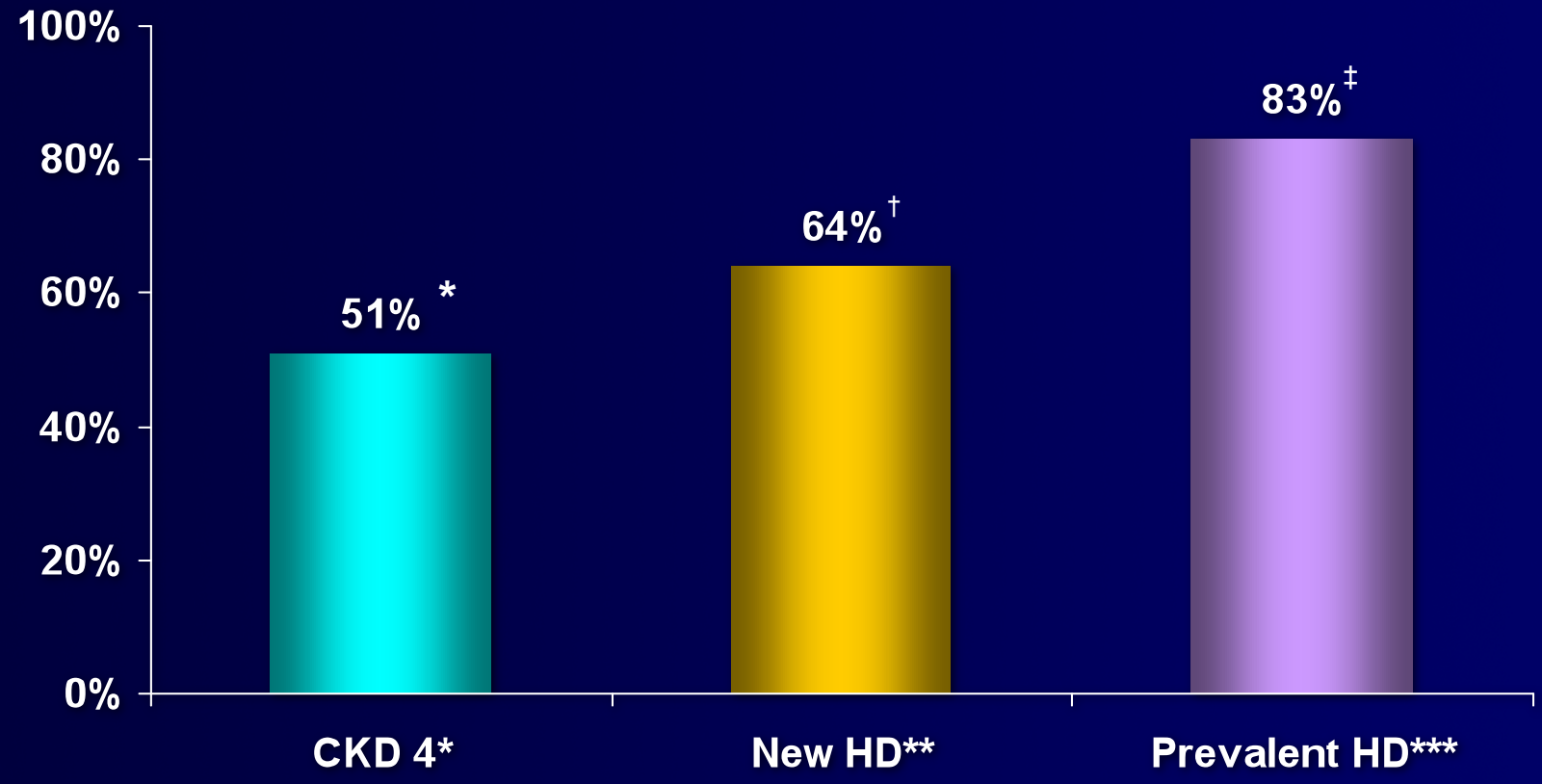
En que pacientes se recomienda restringir el calcio ?



[1]Russo D, Corrao S, Miranda I, et al. *Am J Neph* 2007;27:152-158
[2]Chertow GM, Burke SK, Raggi P, et al. *Kidney Int*. 2002;62:245-252
[3]Block GA, Spiegel DM, Ehrlich J, et al. *Kidney Int*. 2005;68:1815-1824
[4]Qunibi W, Moustafa M, Muenz LR, et al. *AJKD*. 2008
5Andress D.*Kid Int*. 2008;*73:1345-1354*
[6]KDIGO. *Kid Int*. 2009; 76 (Suppl 113):S1-S130


A
B
C
D

Prevalencia de calcificación vascular en la Insuficiencia renal



*Russo D, Corrao S, Miranda I, et al. Progression of coronary artery calcification in predialysis patients. *Am J Nephrol.* 2007;27:152-158.

†Spiegel DM, Raggi P, Mehta R, et al. Coronary and aortic calcifications in patients new to dialysis. *Hemodialysis Int.* 2004;8:265-272.

‡Chertow GM, Burke SK, Raggi P; for Treat to Goal Working Group. Sevelamer attenuates the progression of coronary and aortic calcification in hemodialysis patients. *Kidney Int.* 2002;62:245-252.

Gracias


NO LE VEO NADA RARO A SU MARIDO, SEÑORA.
EN ESTA RADIOGRAFÍA SE LO VE FENÓMENO
ÉSA ES UNA FOTO, DOCTOR.
LAB
NIK


UD. NO SE CUIDÓ NADA, MI AMIGO... LE SUBIÓ EL COLESTEROL, AUMENTÓ 15 KILOS...; Y MIRE LO QUE ES ESTA PANZA!
PARE, PARE, DOCTOR... QUE DUELE...
¿QUÉ ES LO QUE MÁS LE DUELE?
LA VERDAD
NIK