



安心透析，

從『磷』開始

新光醫院 方昱偉 醫師

Let's Start from a REAL Case.....

A 68 year old woman with underlying

- 1.CKD stage 5 with impending dialysis
- 2.HTN
- 3.DM
- 4.Dyslipidemia
- 5.Old CVA

He suffered from general weakness and poor appetite for 2 weeks.

Laboratory investigation revealed advanced azotemia (BUN 148mg/dl, Cr 8.87 mg/dl) and hyperkalemia (K 7.5mg/dl).

Emergent hemodialysis was arranged through double lumen as vascular access.

Hospitalization Course

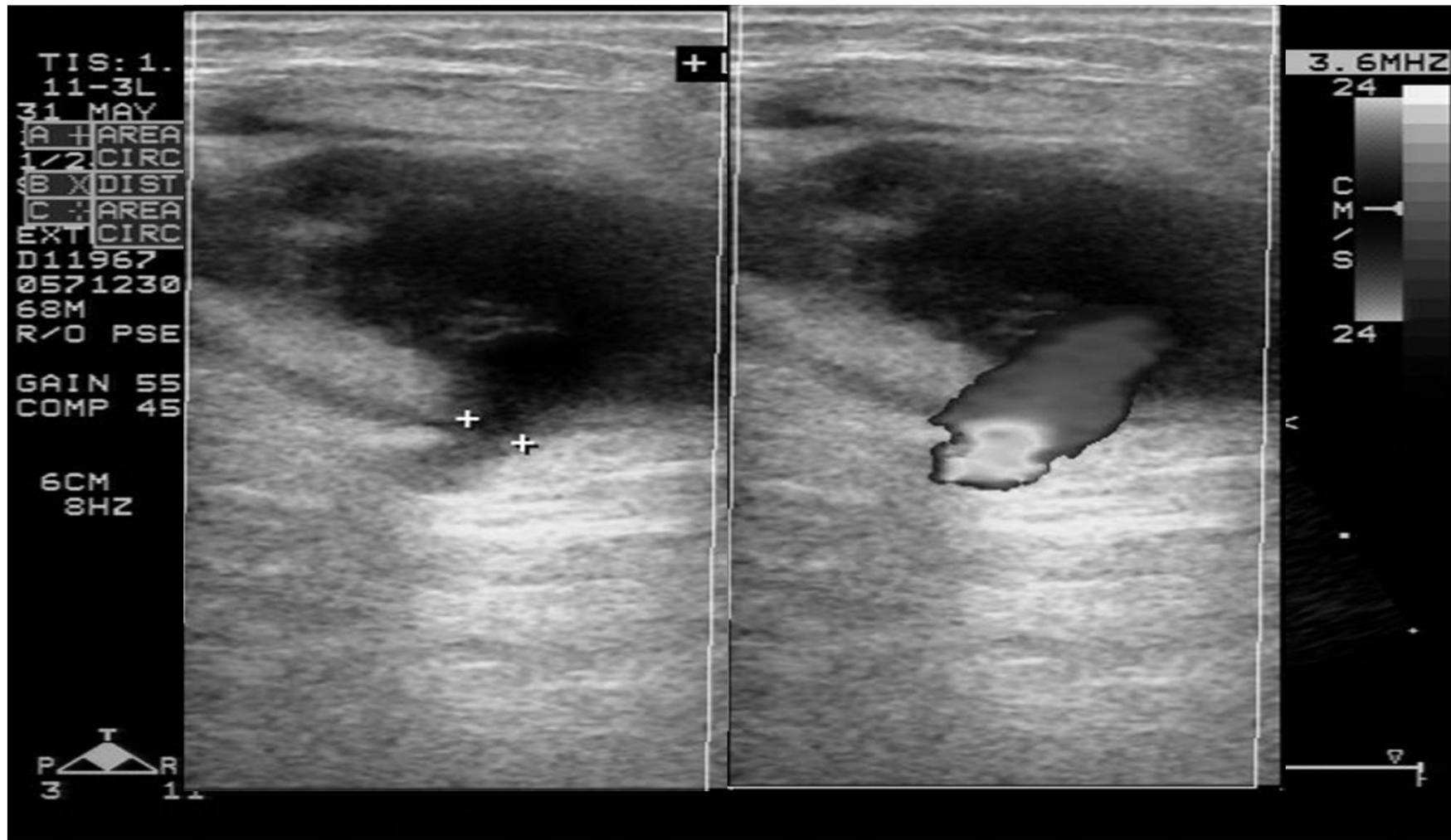
After hemodialysis, the symptoms subside.

However, progressive enlargement of double lumen inserting sites with local tenderness and painful sensation.

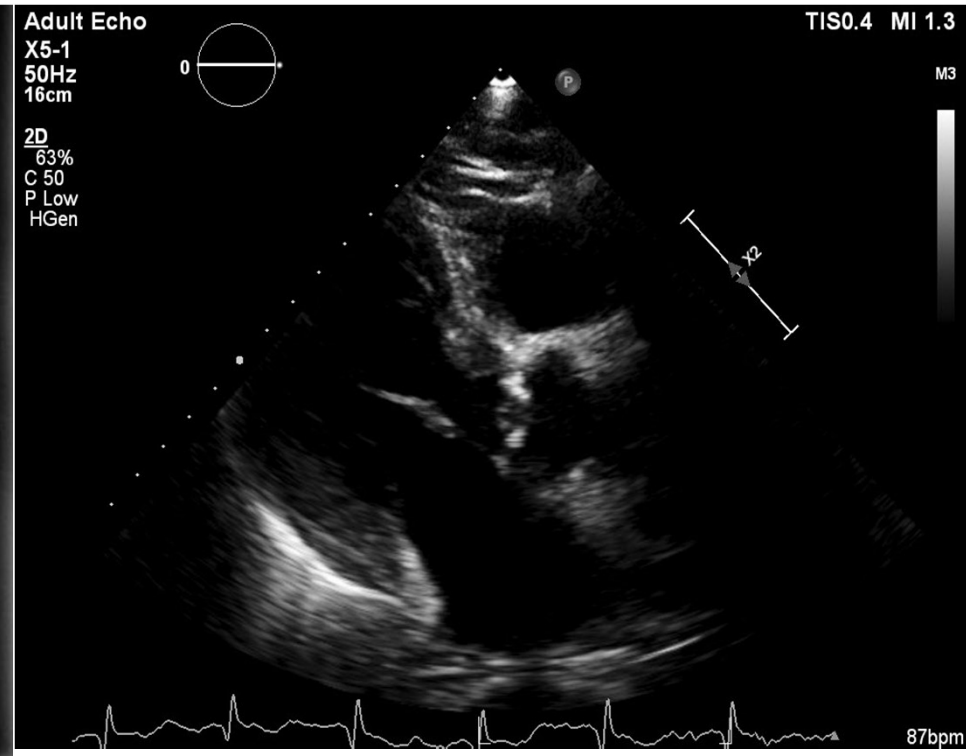
Cardiovascular surgeon was consulted



Leg Duplex



Tracing back Previous Film of this Patient

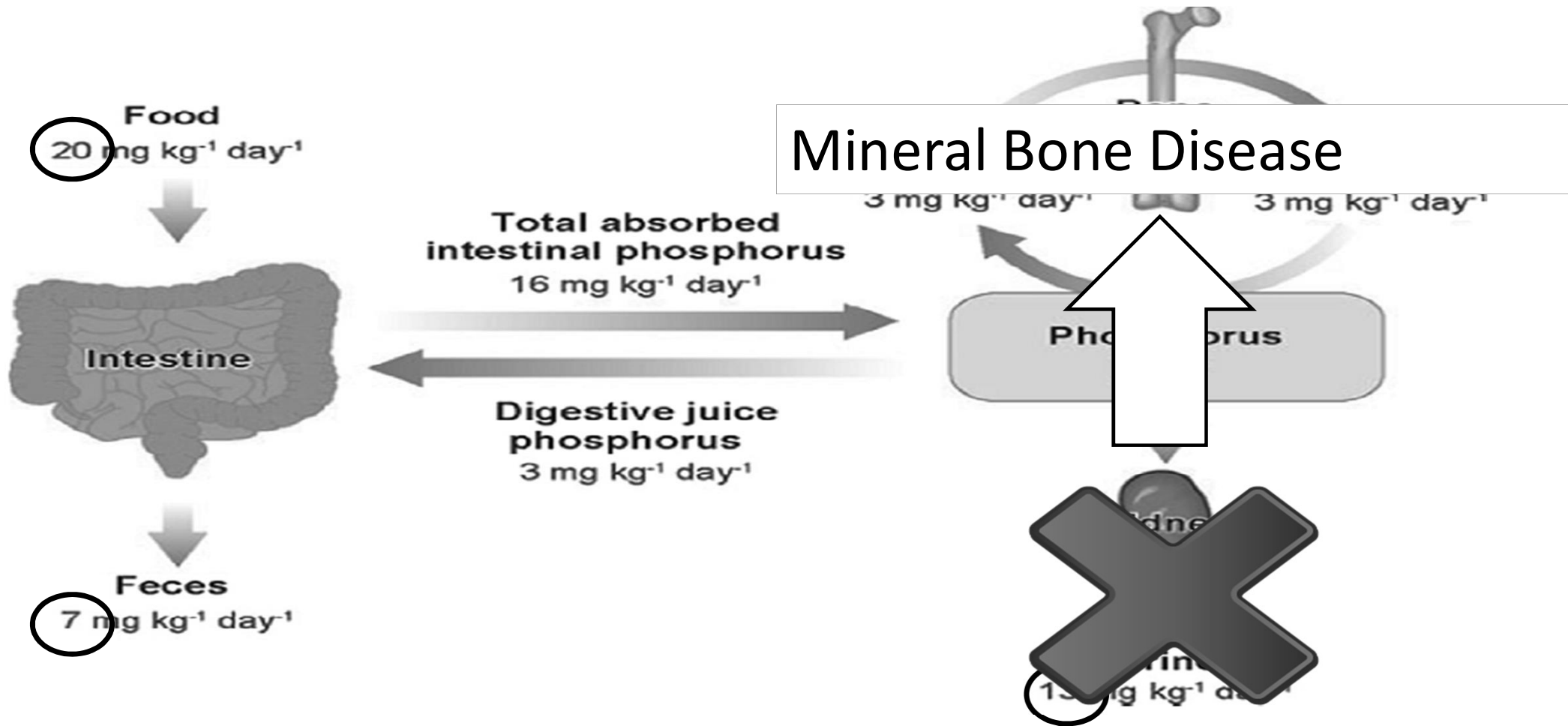


大綱

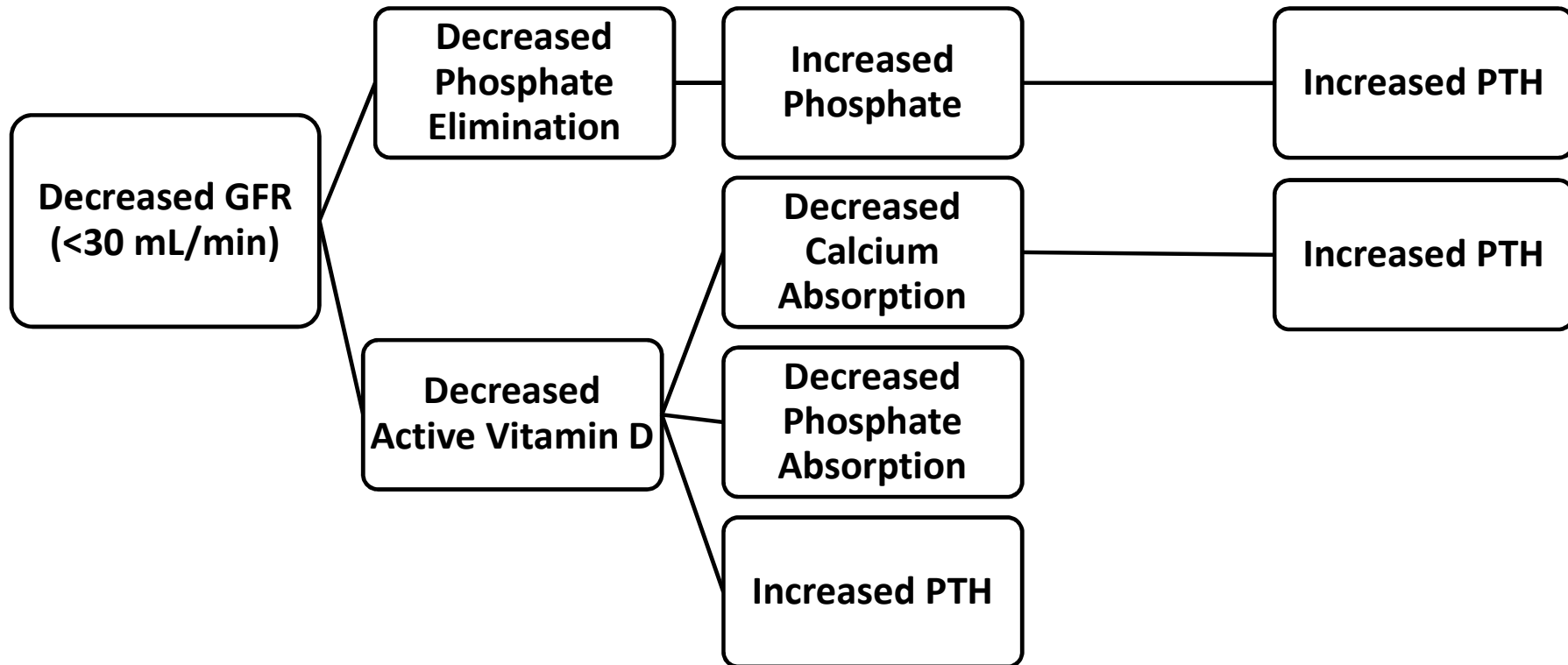


- 1 慢性腎病與鈣、磷異常
- 2 高血鈣磷的併發症
- 3 高血磷的解決方案
- 4 認識磷結合劑
- 5 臨床磷結合劑的使用

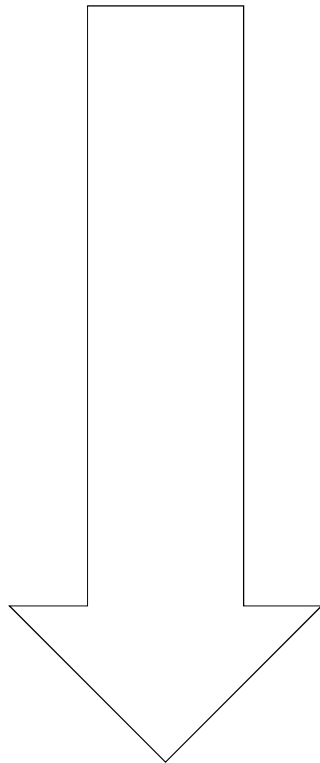
Phosphate Homoeostasis



Mineral and Bone Disorder Pathway



高血鈣產生的四部曲



1

腎臟排磷功能變差

2

血磷濃度升高

3

身體試著降低血磷濃度

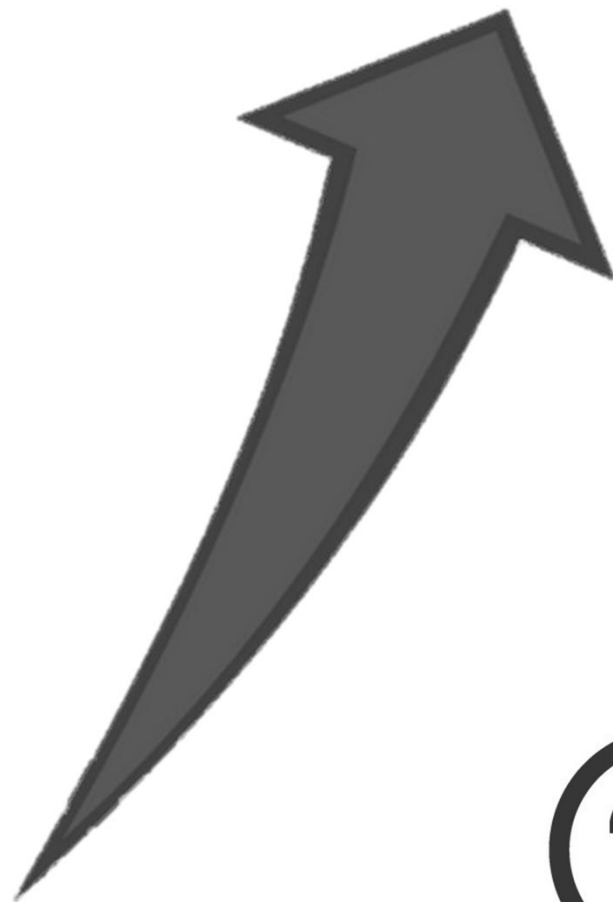
4

**異常的血磷濃度影響到
血鈣濃度**

第四部：異常的血磷濃度影響血鈣濃度



血鈣



大綱



- 1 慢性腎病與鈣、磷異常
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Hyperphosphatemia

The hidden killer in chronic kidney disease

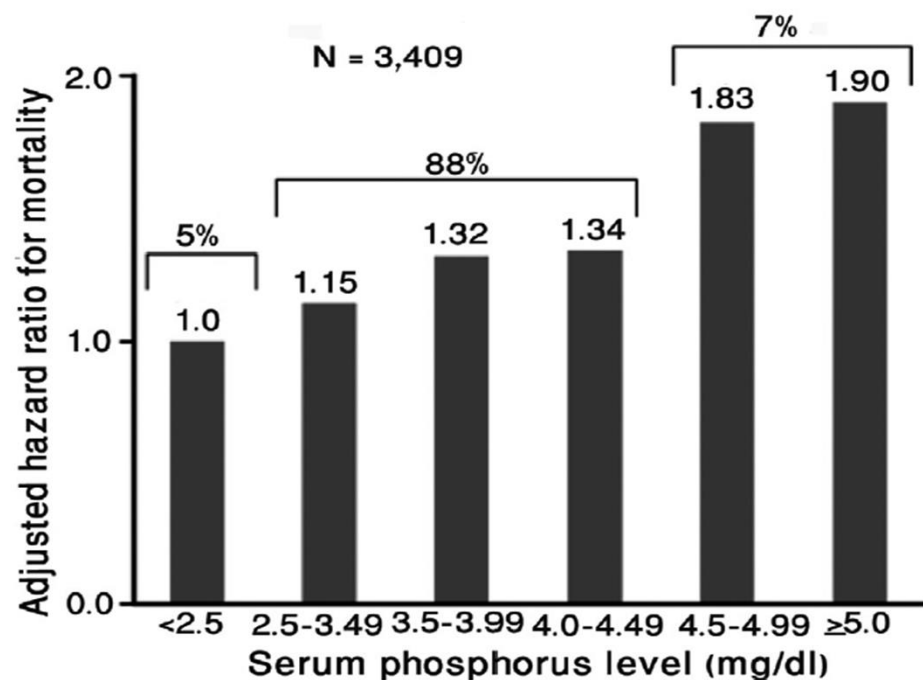


Figure 1 - Mortality risk increases with serum phosphorus in patients with chronic kidney disease-stage 3 not on dialysis. Republished with permission from the American Society of Nephrology. Kestenbaum B, Sampson JN, Rudser KD, Patterson DJ, Seliger SL, Young B, et al. Serum phosphate levels and mortality risk among people with chronic kidney disease. *J Am Soc Nephrol* 2005; 16: 520-528.

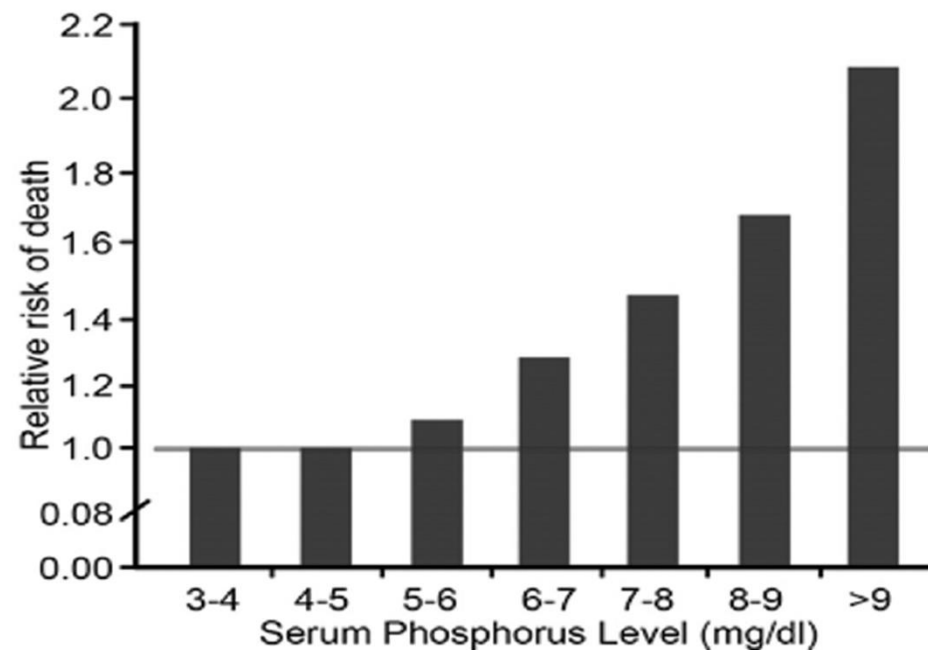
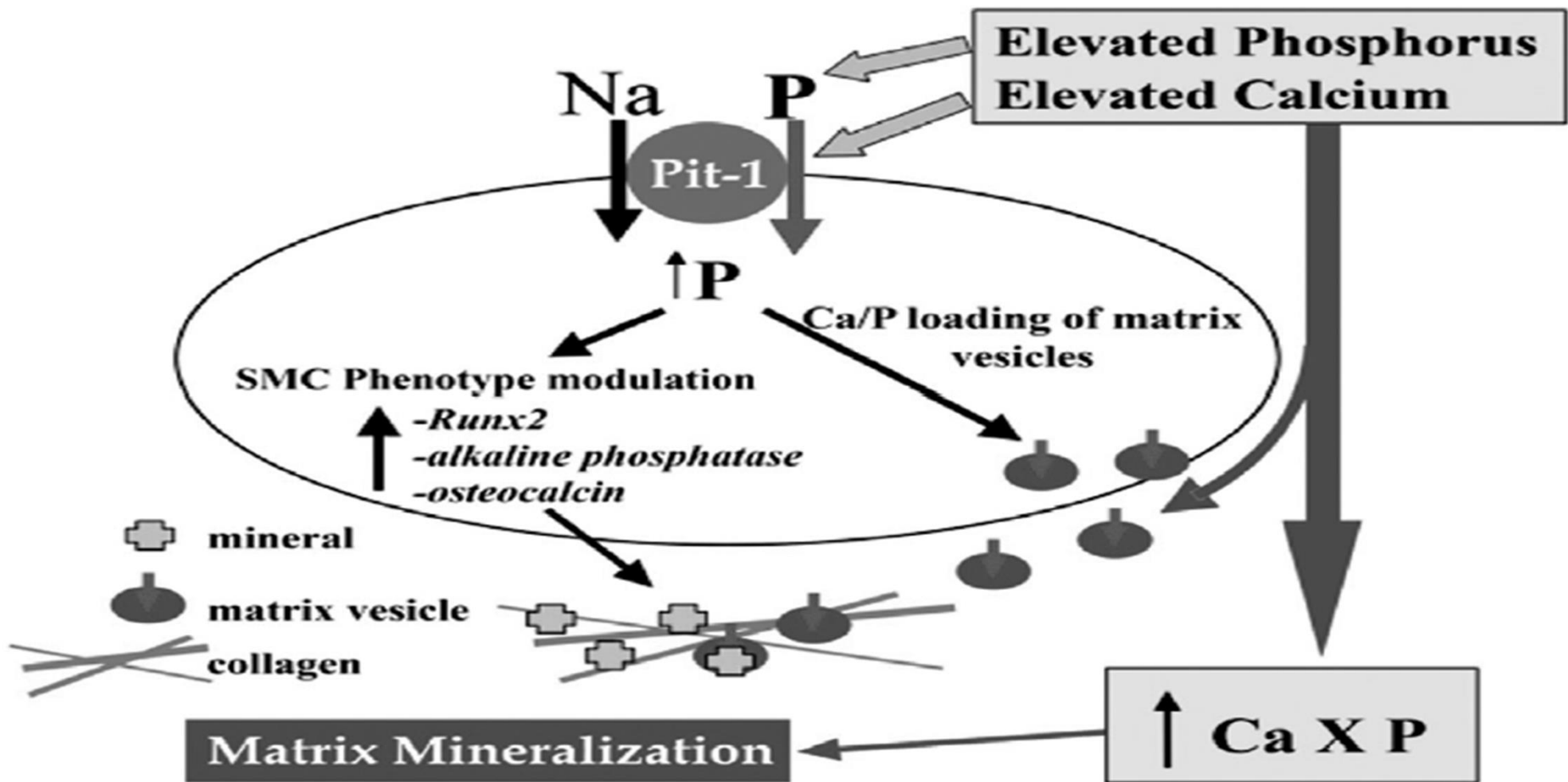


Figure 2 - Mortality risk increases with increased serum phosphorus in dialysis patients. Republished with permission from the American Society of Nephrology. Block GA, Klassen PS, Lazarus JM, Ofsthun N, Lowrie EG, Chertow GM. Mineral metabolism, mortality, and morbidity in maintenance hemodialysis. *J Am Soc Nephrol* 2004; 15: 2208-2218.

Consequences of of poorly controlled phosphorus

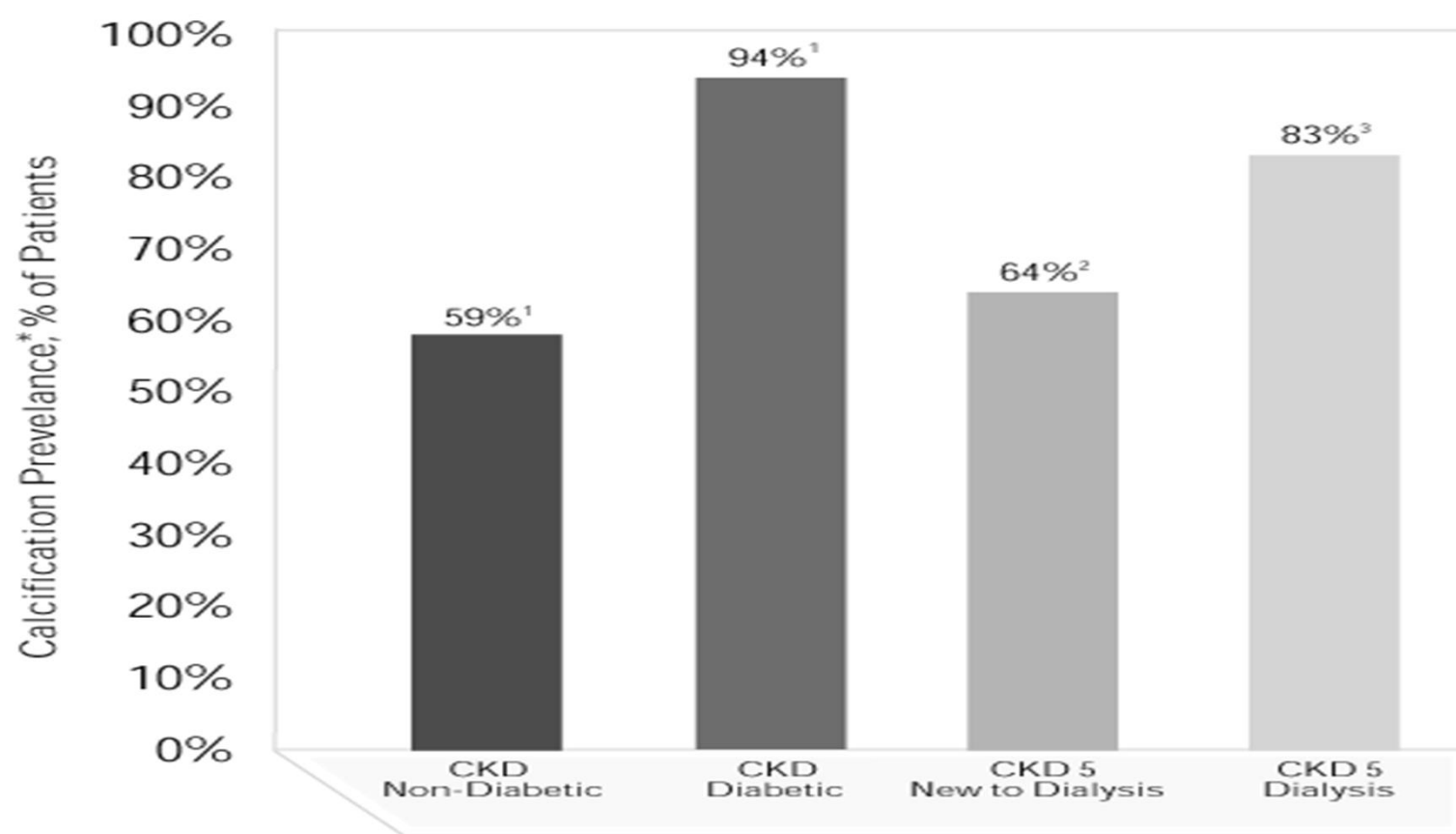
- **Each 1mg/dL increase in serum phosphorus was linked to a estimated 23% increased risk of mortality**
- **Serum phosphate concentrations greater than 6.5 mg/dL have been independently associated with an increased morbidity and mortality in patients on hemodialysis**
- **Dialysis-related itching**
- **Calcifications**

Kestenbaum B et a JASN 2005;16(2)



Proposed model for the effects of elevated calcium (Ca) and phosphorus (P) on vascular smooth muscle cell (SMC) matrix mineralization.

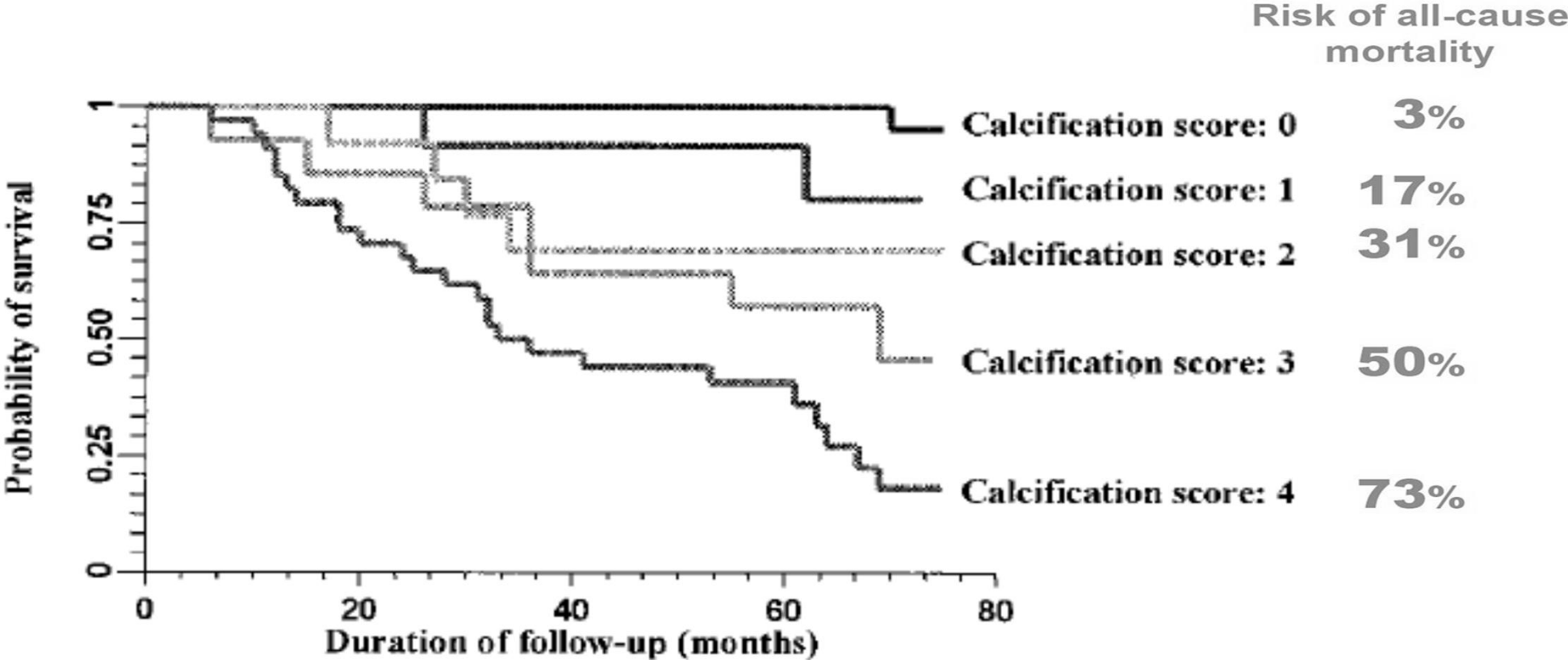
Calcification prevalence in CKD



1. Merjanian et al, *Kidney Int.* 2003; 64: 263 2. Spiegel et al, *Hemodialysis Int.* 2004; 8: 265

3. Raggi et al, *J Am Coll Cardiol.* 2002; 39: 695

Severity of Vascular Calcification Predicts Outcome

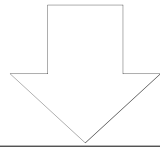


Blacher J, et al. Hypertension 2001;38:938-42.

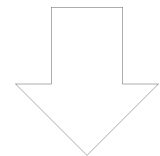
血管鈣化的影響



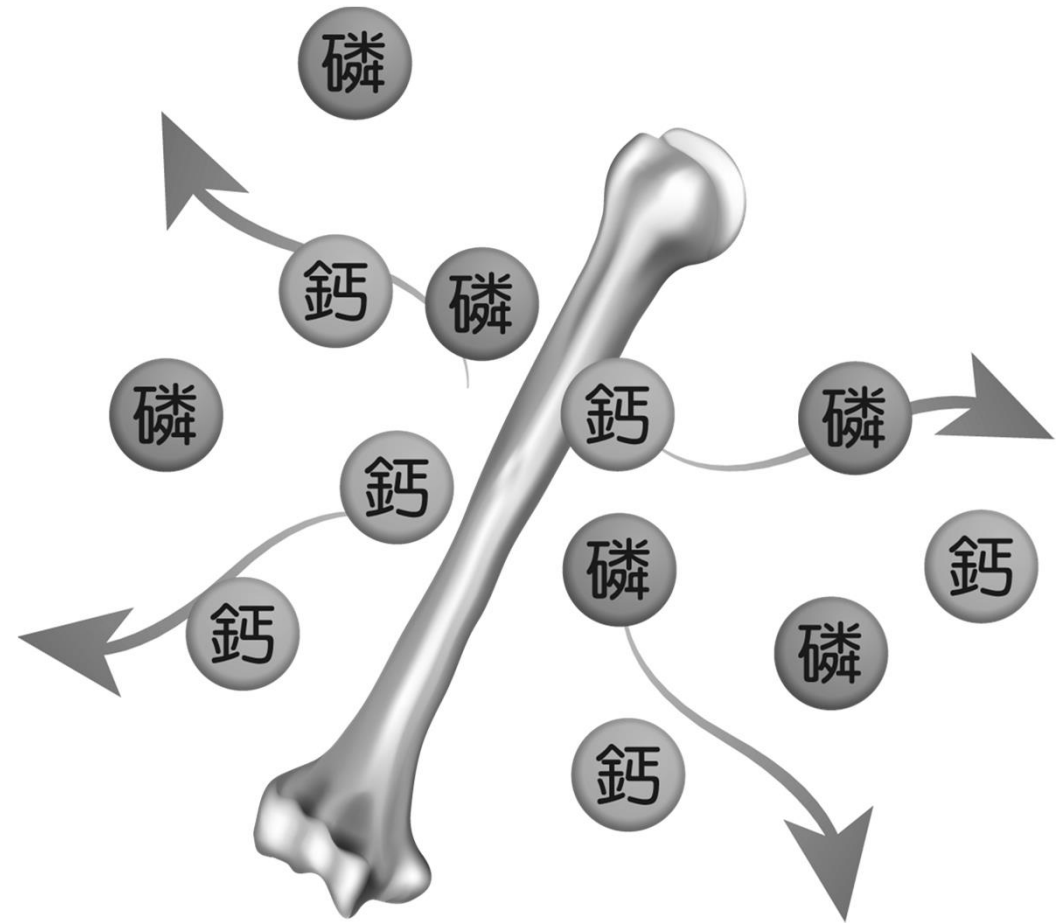
**高血磷使
血鈣濃度降低**



**骨骼會釋放鈣質
提高血鈣濃度**



**骨骼也會流失
支撐的鈣質**



Llach F & Forero FV. Am J Kidney Dis 2001; 38:20-33.

骨骼病變會有什麼影響？

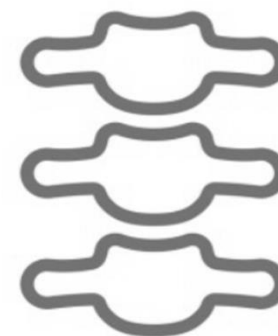
骨質疏鬆 常見骨折



前臂手腕



腕部

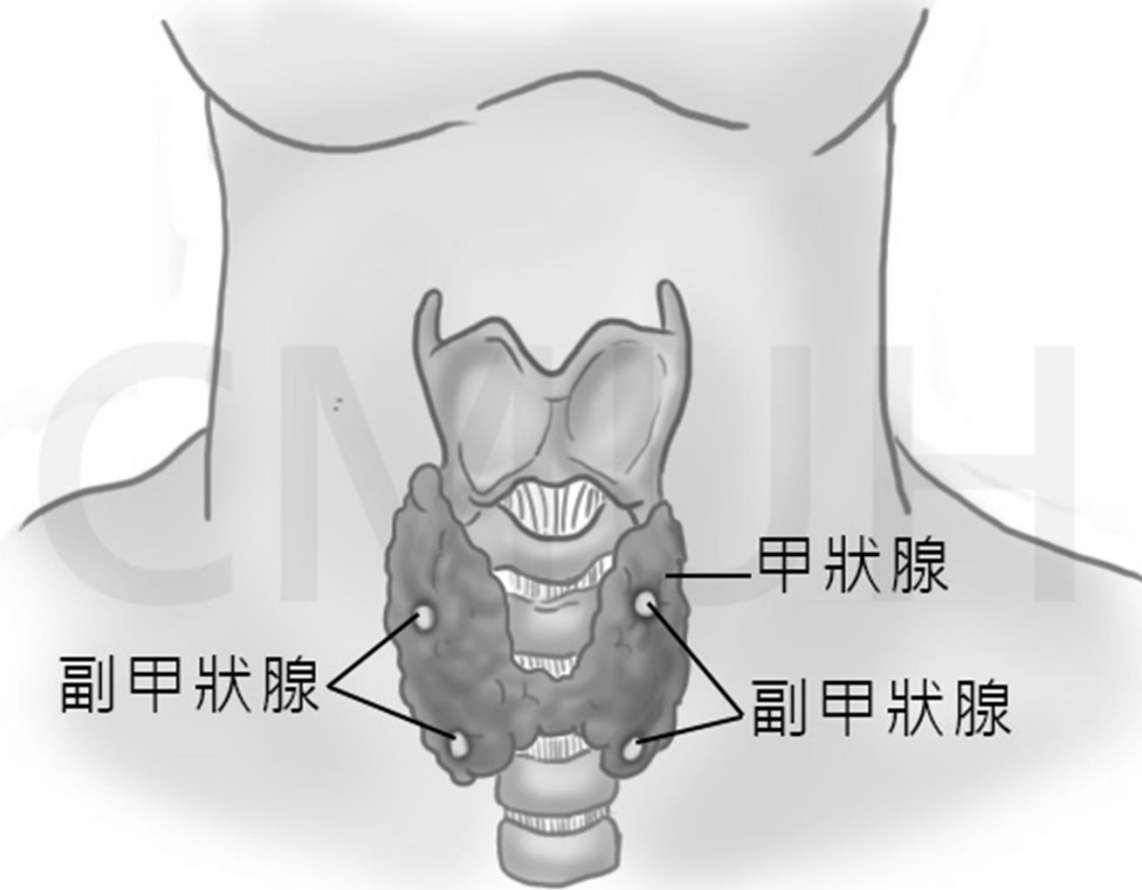


脊椎



高血磷與副甲狀腺亢進

高血磷與副甲狀腺異常



尿毒症

血磷濃度
增加

副甲狀腺素
上升

150–300

pg/ml

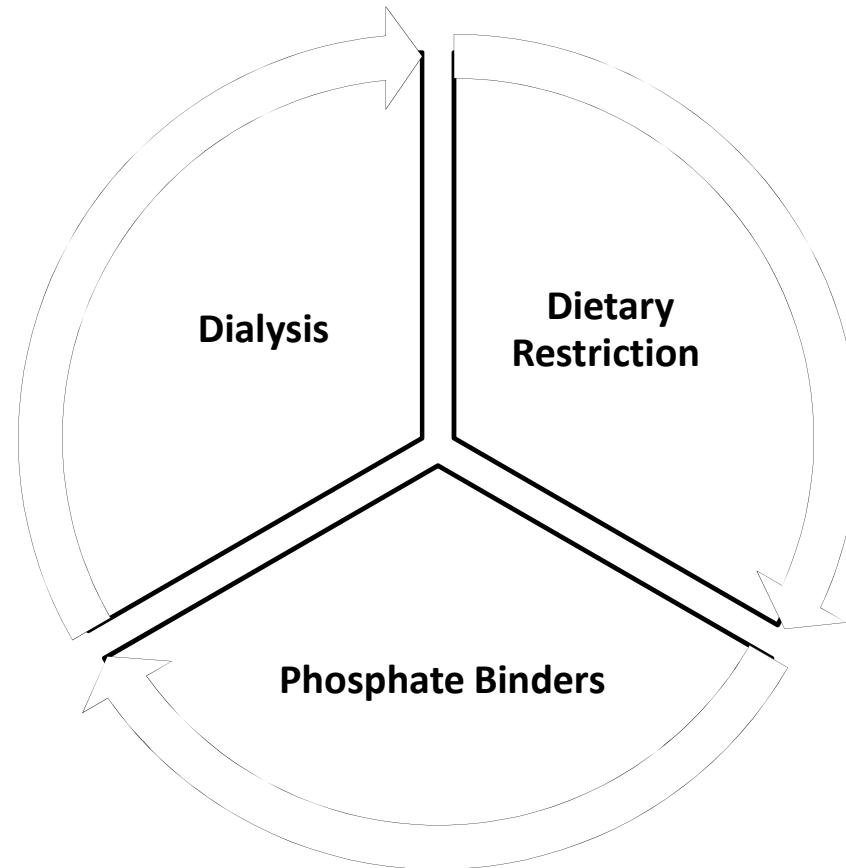
透析腎友副甲狀腺素的正常範圍

大綱

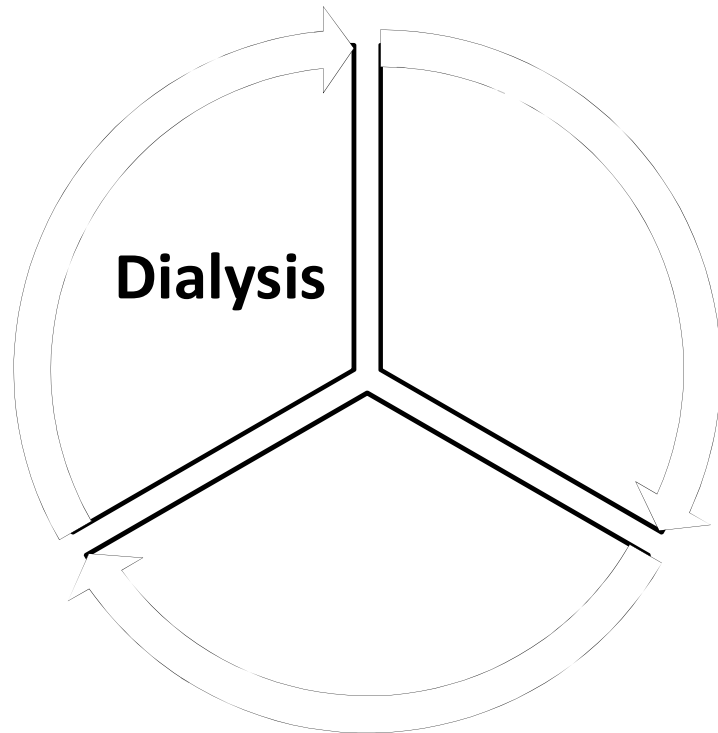
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Control Phosphorus in HD



Mechanisms to Control Phosphorus in HD



- The amount of P removal is 2.3-2.6g/wk in HD (4hr TIW) & 2.0-2.2g/wk in PD (2L 4 cycle per day)
- Insufficient on its own to maintain phosphorus levels

Other Hemodialysis Modulation

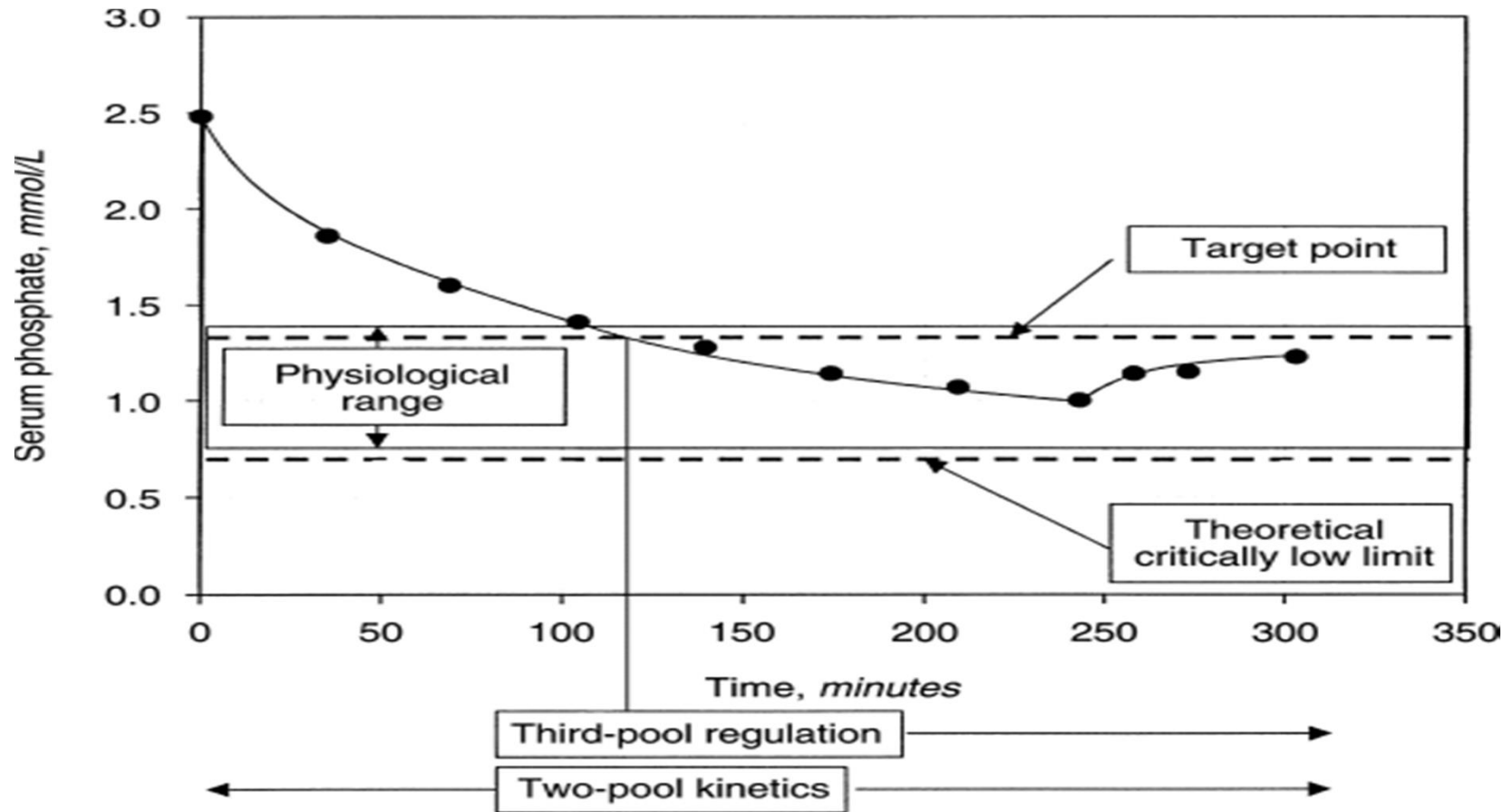
- Extended HD : 5hr per session → 3.0-3.6 g /wk
- Nocturnal HD : 8hr/day → 4.5-4.9 g/wk
- Post-dilutional HDF → 3.0-3.3 g per session

- *What is Post-dialysis P means to you ?*

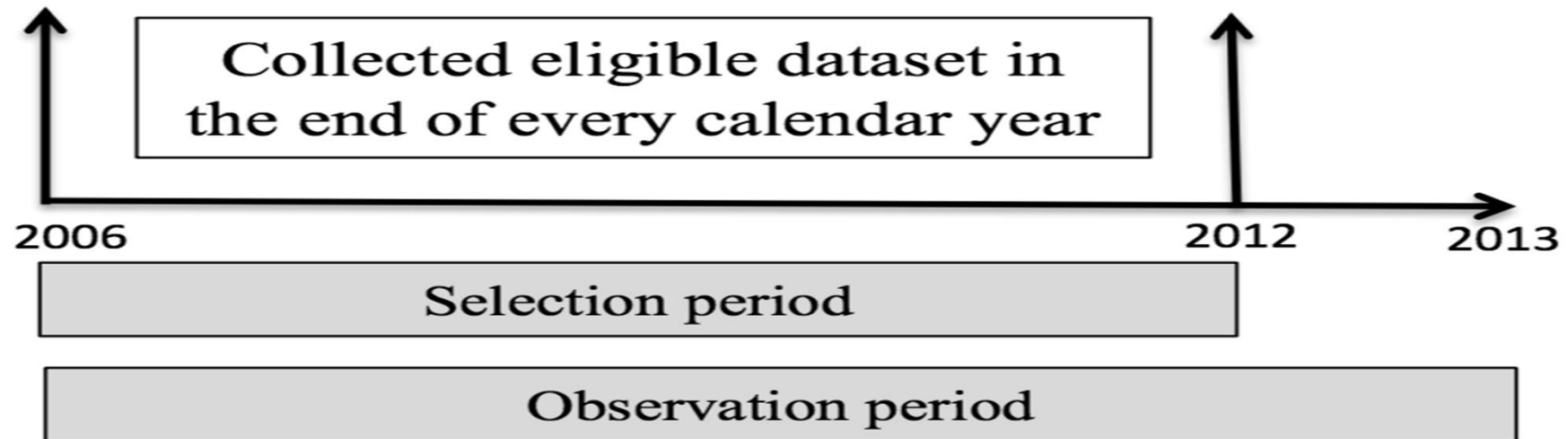
Semin Dial. 2015 Nov-Dec;28(6):620-3

Int J Nephrol Renovasc Dis 6:193–205, 2013

Phosphate Kinetics during HD



Investigate Clinical Significance of ΔP during HD in CHD

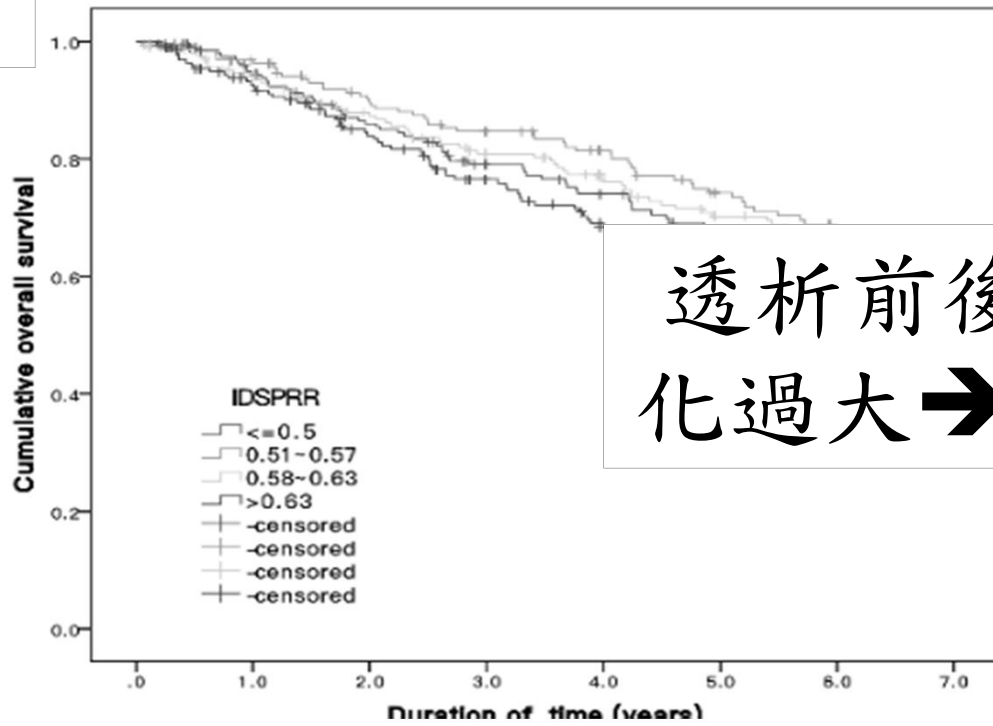


IDSPPR=

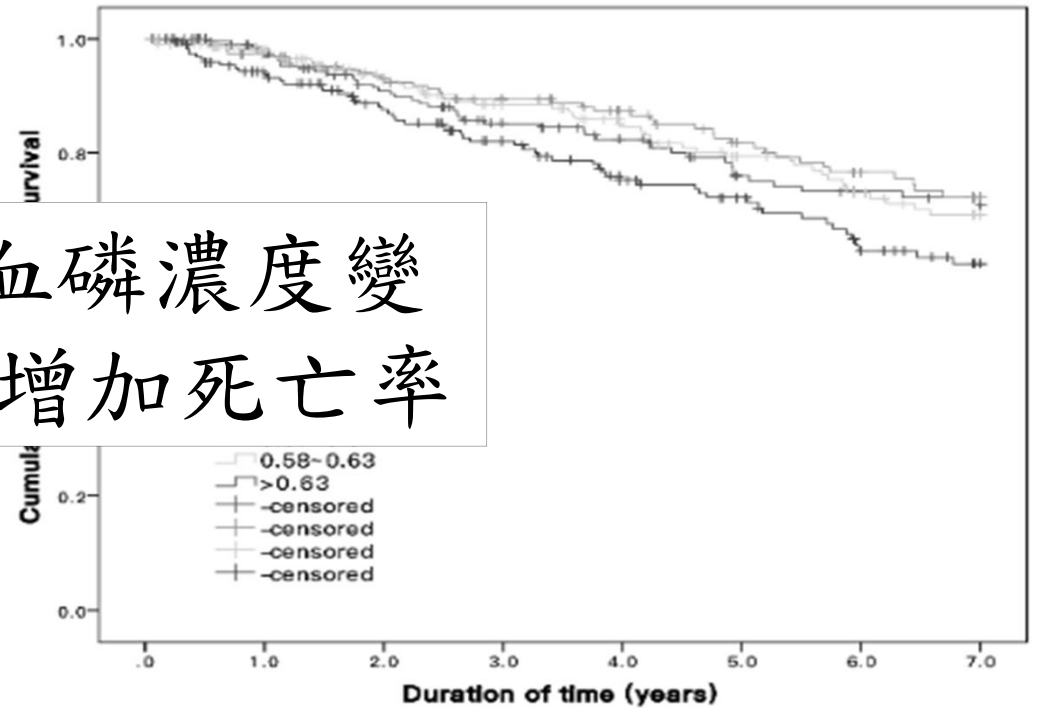
Serum phosphorus level before dialysis – Serum phosphorus level after dialysis

Serum phosphorus level before dialysis

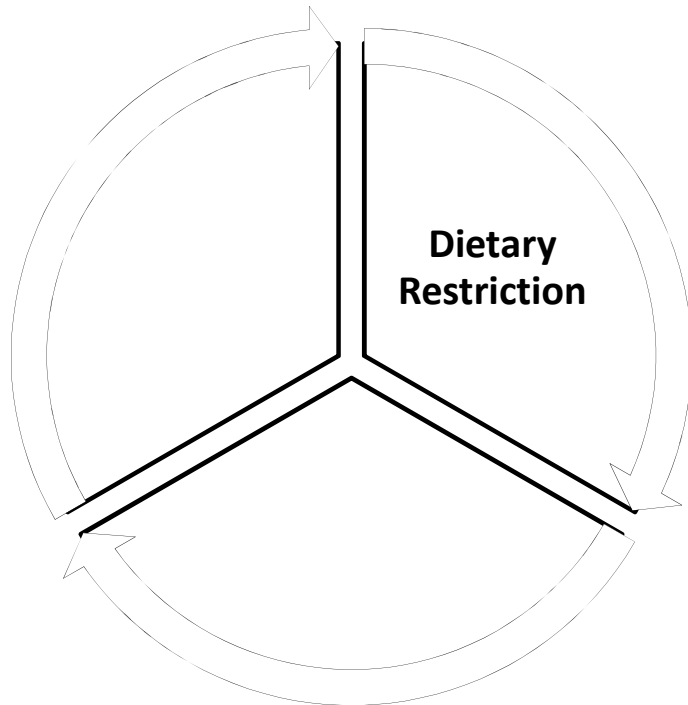
IDPSRR Has Impact on Survival



透析前後血磷濃度變化過大 → 增加死亡率



Mechanisms to Control Phosphorus in HD



- **Difficult to determine phosphate content of food**
- **Protein Needs/Malnutrition**
- **Phosphate additives = highly bioavailable**
- **Low phosphorus-protein ratio (P-P ratio)**

減少每天吃下的磷

- 減少每天吃下的磷，就可以降低腎臟排磷的負擔
- 透析病人每天不可吃超過800-1,000毫克(mg)的磷



Peacock M. Clin J Am Soc Nephrol 2010; 5:S23-30.
Uribarri J. Semin Dialysis 2007; 20:295-301.

以下這些食物含有很高的磷，應該盡量不要吃或少吃

高磷食物

堅果類

紅豆
綠豆
豌豆
花生米
黃豆
豆皮
蠶豆
芝麻
瓜子



肉類

豬肉鬆
牛肉乾
豬肝



漁產類

吻仔魚

奶蛋類

硬質乳酪
雞蛋黃



飲料

綠茶
健素汁

其他

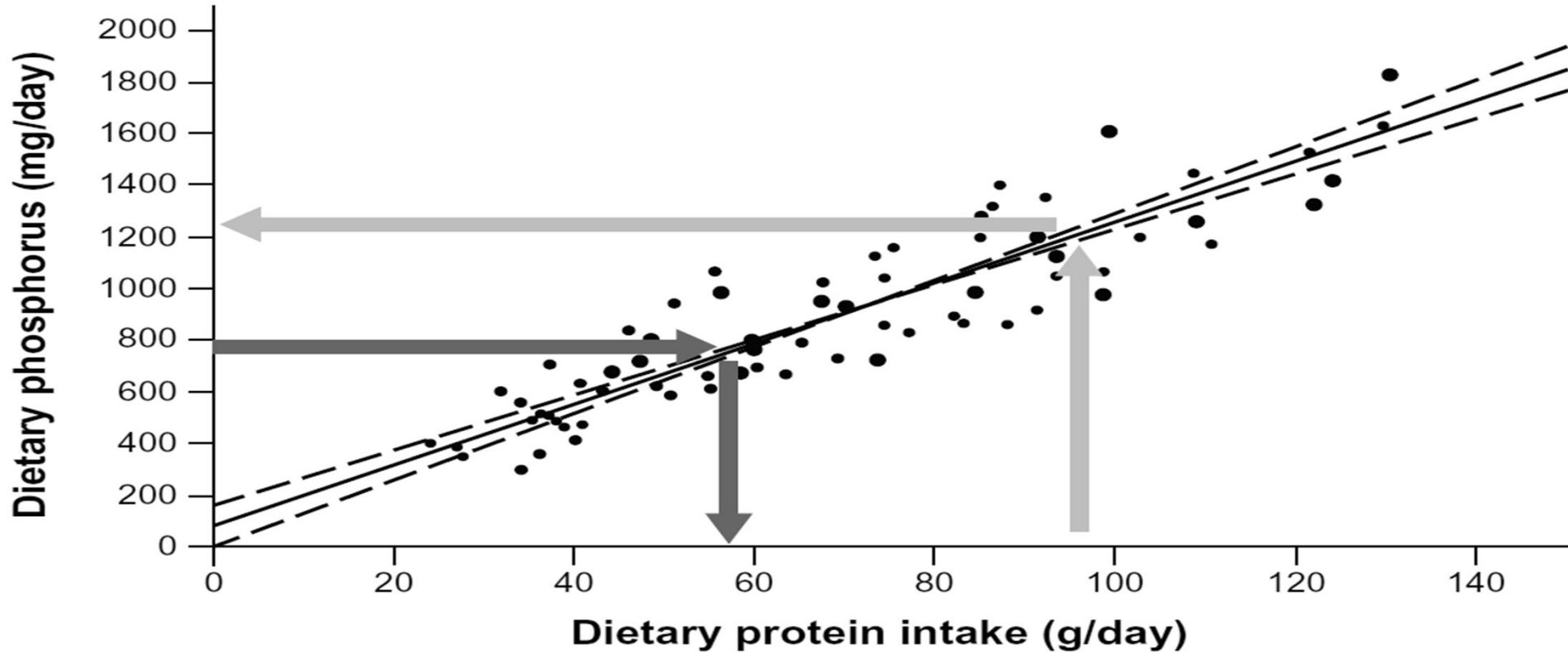
酵母粉

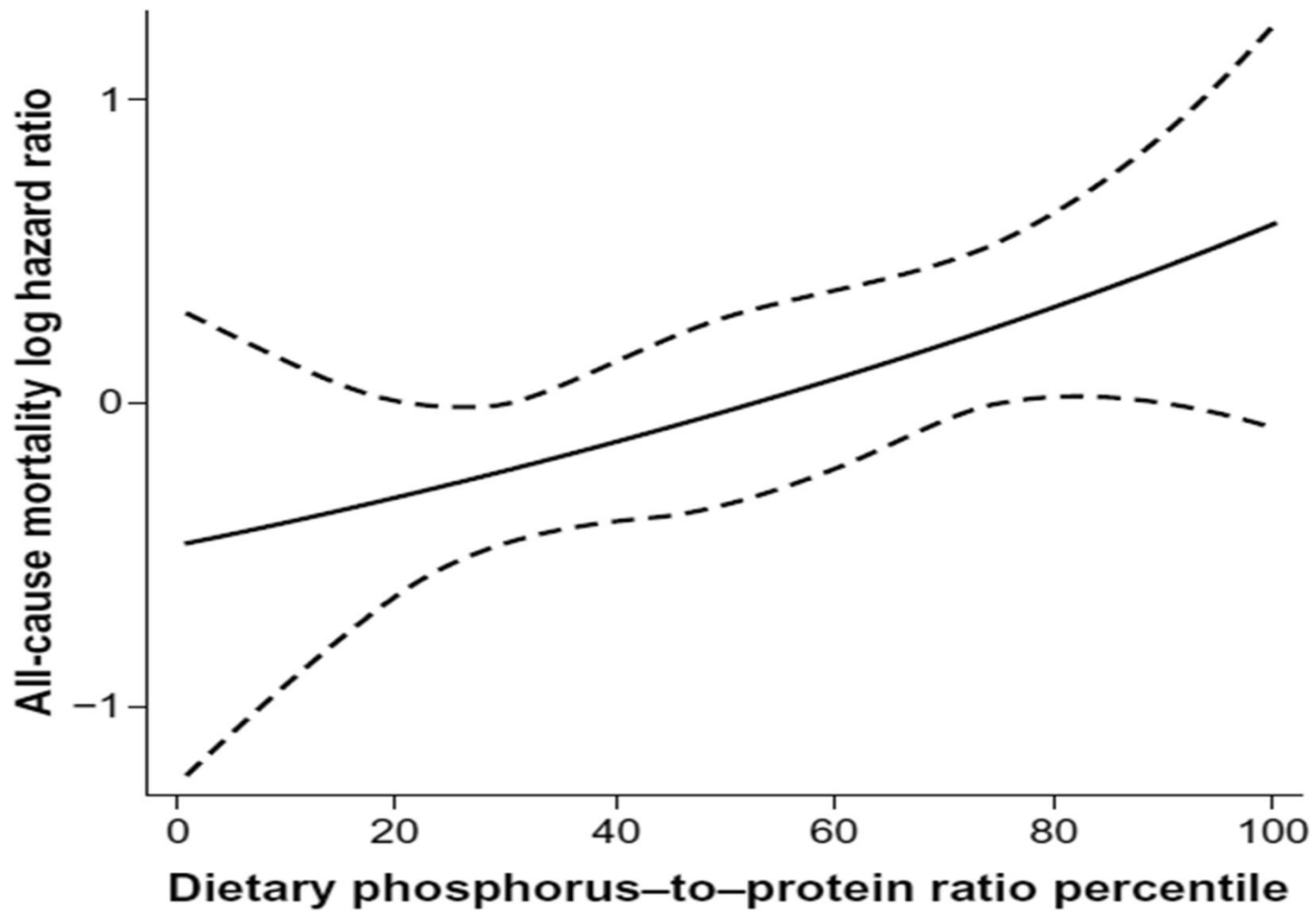
五穀類

小麥
燕麥
營養米



Dietary phosphorus (mg) = $11.8 \times (\text{protein intake [g]}) + 78$ ($R^2 = 0.83$)

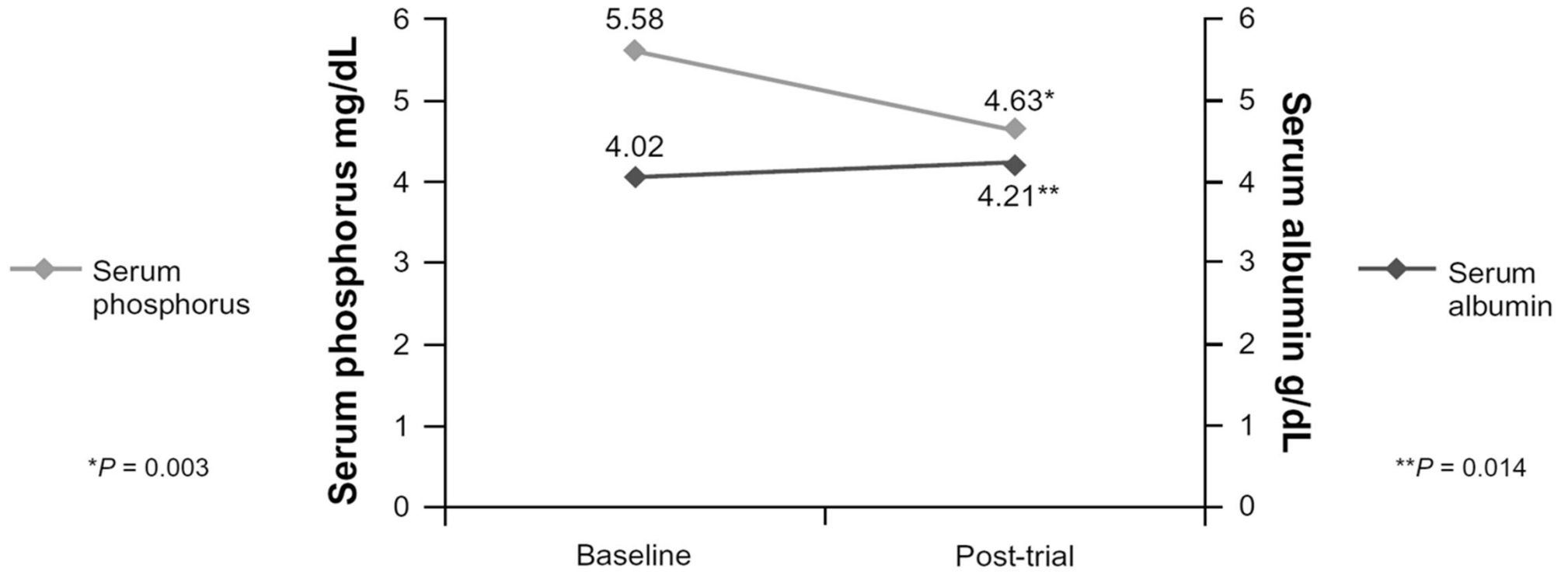




Clin J Am Soc Nephrol. 2010;5(4):683–692

Table 2 Summary of phosphorus and protein content of selected foods according to US Department of Agriculture national nutrient database²¹

Food	Common measure	Phosphorus content (mg)	Protein content (g)	Phosphorus (mg)/protein (g) ratio
Veal (leg)	85 g	212	31	6.8
Chicken (broiled)	140 g	259	35	7.4
Lamb (leg)	85 g	162	22	7.4
Beef (roasted)	85 g	200	26.4	7.6
Turkey (roasted)	85 g	208	24	8.7
Fish (cod, canned)	85 g	221	19.4	11.4
Pork	85 g	224	18	12.4
Crab	85 g	238	16.5	14.4
Salmon	85 g	280	17	16.5
Bread (white)	1 slice	25	3.4	7.3
Bagel (plain)	3 1/2"	68	7.5	9.0
Bread (mixed grain)	1 slice	46	2.6	17.7
Almonds	28 g	134	6.0	22.3
Pistachio	28 g	137	6.0	22.8
Walnuts	28 g	98	4.3	22.8
Biscuits	2 1/2	98	4.2	23.3
Cereals (Kellogg's® Raisin Bran)	250 mL	259	5.2	49.8
Cereals (General Mills)	250 mL	232	4.4	52.7
Egg, white raw	1 large	5	3.64	1.4
Egg, whole, fried	1 large	96	6.27	15.3
Cheese (Muenster)	28 g	133	6.64	20.0
Egg, yolk, raw	1 large	65	2.63	24.7
Cheese (American)	28 g	124	4.65	26.6
Yogurt (plain, low-fat)	236 mL	327	11.9	27.5
Milk (whole)	250 mL	222	7.86	28.2
Milk shake	312 mL	378	9.15	41.3



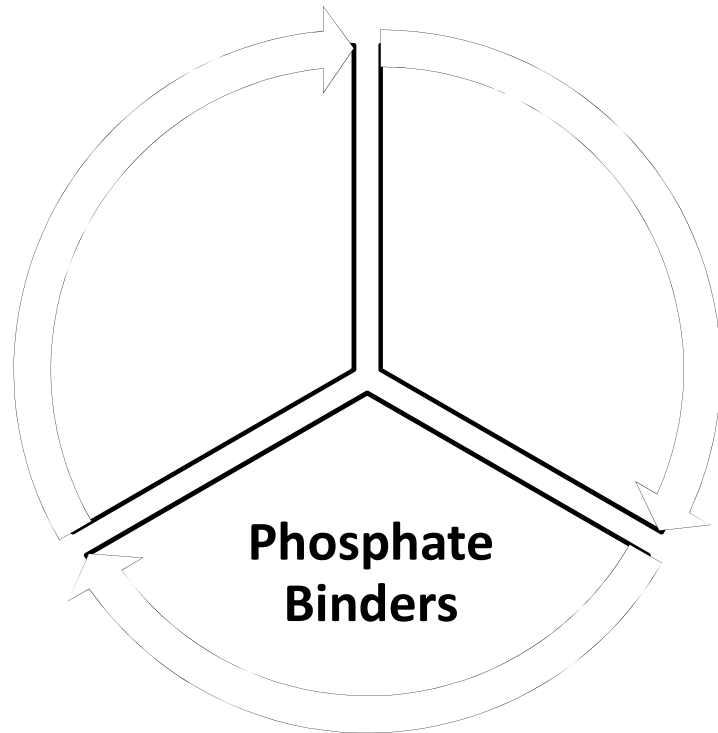
Dietary egg whites for phosphorus control in maintenance haemodialysis patients: a pilot study. J Ren Care. 2011;37(1):16–24.

含磷的合法食品添加物

種類	用途	品項
品質改良用、釀造用及食品製造用劑	為改良加工食品之品質、釀造或食品製造加工必需時使用之物質	三偏磷酸鈉、多磷酸鉀等25項 舉例：磷酸二氫鈣、磷酸氫鈣、磷酸鈣、酸性焦磷酸鈣、甘油醇磷酸鈣、偏磷酸鈉、磷酸氫二鈉、偏磷酸鉀…等
結著劑	增加肉類及魚肉類製品結合性之物質	磷酸鹽類等16項 舉例：焦磷酸鉀、焦磷酸鈉、多磷酸鉀、多磷酸鈉、磷酸二氫鉀、磷酸二氫鈉…等

(資料來源：衛生福利部食品添加物手冊)

Mechanisms to Control Phosphorus in HD



- **Medications- Phosphate Binders**
 - Calcium-based phosphate binders
 - Non-Calcium based phosphate binders
 - Iron-based phosphate binders

大綱

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常見的磷結合劑

非金屬類

樹脂類

金屬類

含鋁

含鋁

含鈣

含鐵

含鎂

常見的磷結合劑

含鋁

降磷效果佳，但會堆積於體內造成腦病變、骨骼軟化、肌肉病變、以及小球性貧血

含鐵

效果較不好，可改善貧血，但會增加鋁的吸收。

含鎂

效果較不好，且可能造成高血鎂、高血鉀、以及腹瀉等副作用

含鈣

效果佳，但長期使用可能引起高血鈣、便秘、甚至是骨病變等副作用

含鋁

效果佳，但動物研究發現鋁會堆積於體內。但長期追蹤沒發現異常。

樹脂

成份是一種不會被身體吸收的交換樹脂，可替換出鉀離子。

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Treatment Strategy to Reduce Vascular Calcification



KDIGO Recommendation

- 4.1.1. In patients with CKD stages 3–5, we suggest maintaining serum phosphorus in the normal range (2C). In patients with CKD stage 5D, we suggest lowering elevated phosphorus level toward the normal range (2C).

Not to let it happen

- 4.1.2. In patients with CKD stages 3–5D, we suggest maintaining serum calcium in the normal range (2D).

Calcium restrictions and Calcification Detection in High Risk Group

In patients with CKD stages 3-5D and hyperphosphatemia, KDIGO recommends restricting the dose of calcium-based phosphate binders and/or the dose of calcitriol or vitamin in the presence of:

**Persistent/
recurrent
hypercalcemia**

Arterial calcification

**Persistently
low PTH**

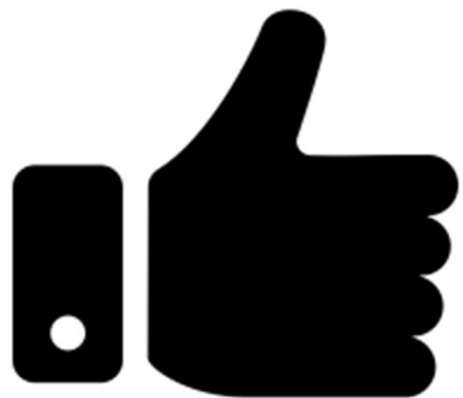
**Adynamic bone
disease**

非鈣磷結合劑，預後較佳

相對磷結合能力 Relative Phosphate-Binding Capacity

磷結合量 (mg)	Calcium Acetate (元素鈣) (克) ¹	(顆)	Sevelamer HCl/CO ₃ (克) ²	(顆/包)	Lanthanum Carbonate (克) ³	(顆)
100	2.5 (0.64)	5顆	2.35	3顆	0.73	1顆
150	3.8 (0.96)	7.6顆	3.55	4.4顆	1.05	1.4顆
200	5.0 (1.27)	10顆	5.34	6.7顆	1.52	2顆
250	6.3 (1.58)	12.6顆	8.00	10顆	2.20	3顆
300	7.5 (1.90)	15顆	12.2	15.3顆	3.15	4.2顆
350	8.7 (2.21)	17.4顆	18.4	23顆	4.58	6.1顆
400	10.0 (2.52)	20顆	27.9	34顆	6.60	8.8顆

說明: 以結合250mg磷為目標，需6.3克的醋酸鈣(=1.58克元素鈣，已>1.5克上限)
需8克sevelamer(=10顆) 或 2.2克lanthanum carbonate (3顆)



• 福斯利諾

• 磷解樂

• 檸檬酸鐵

貴

Take Home Message

- Hyperphosphatemia in CHD:
 - Multifactorial control – Diet, Dialysis, Binder
 - Reducing vascular calcification & CV risk
- Non-calcium phosphate binder had superior in efficacy and safety

The End

Thanks for your attention !

Jaymie's Eyes