維他命K能否改善透析患者血管疾病

德仁醫院腎臟科

臺北醫學大學醫學博士

林瑞祥醫師

透析中凝血徵兆

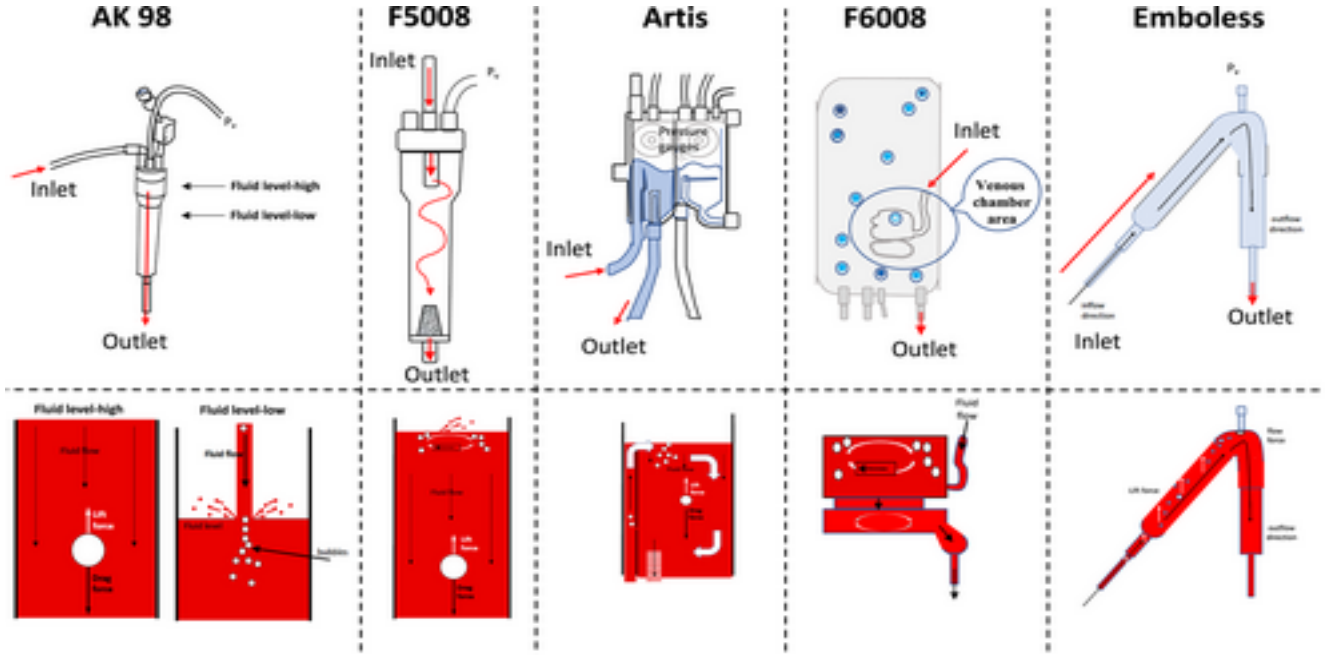
1. 體外循環血液顏色暗沈
2. 透析器出現暗紅血絲

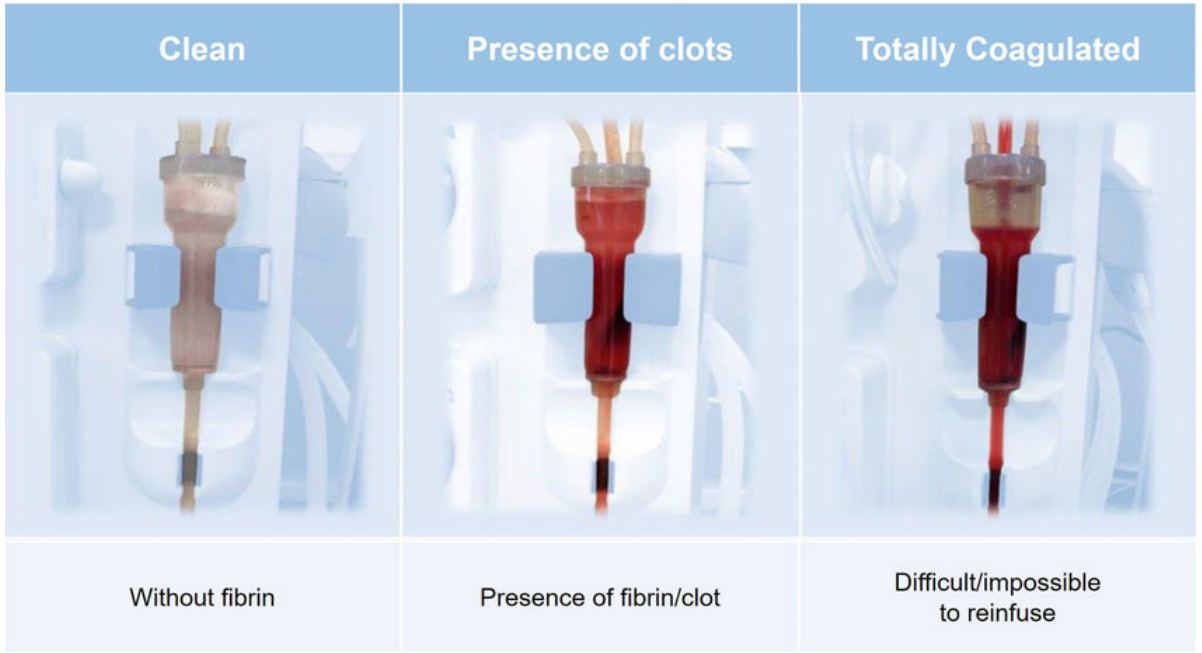
- **第一級凝血：< 10%**
- **第二級凝血：10-50%**
- **第三級凝血：> 50%**

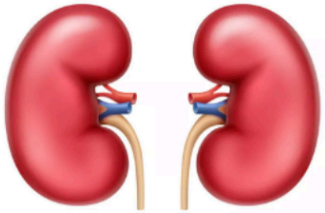
Clean	Light pink	Some coagulated fibers	Many coagulated fibers	Totally coagulated
				
No coagulated fibers	> Than 100 coagulated fibers	> 1000 (±10%) coagulated fibers	> 30% of coagulated fibers	Difficult/ Impossible to reinfuse

透析中凝血徵兆

- 動脈端管路血塊
- 靜脈滴室 (venous chamber) 血塊







CKD

impaired endogenous recycling of vitamin K

維他命K體內循環不良

drugs

藥物影響

dietary restriction

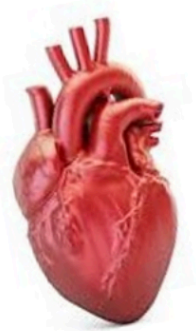
飲食控制

VITAMIN K DEFICIENCY

維他命K不足

Decreased activation of VKDPs (BGP, MGP, GRP)

維他命K蛋白質缺乏



VC and CVD

血管鈣化疾病

Progression of kidney damage

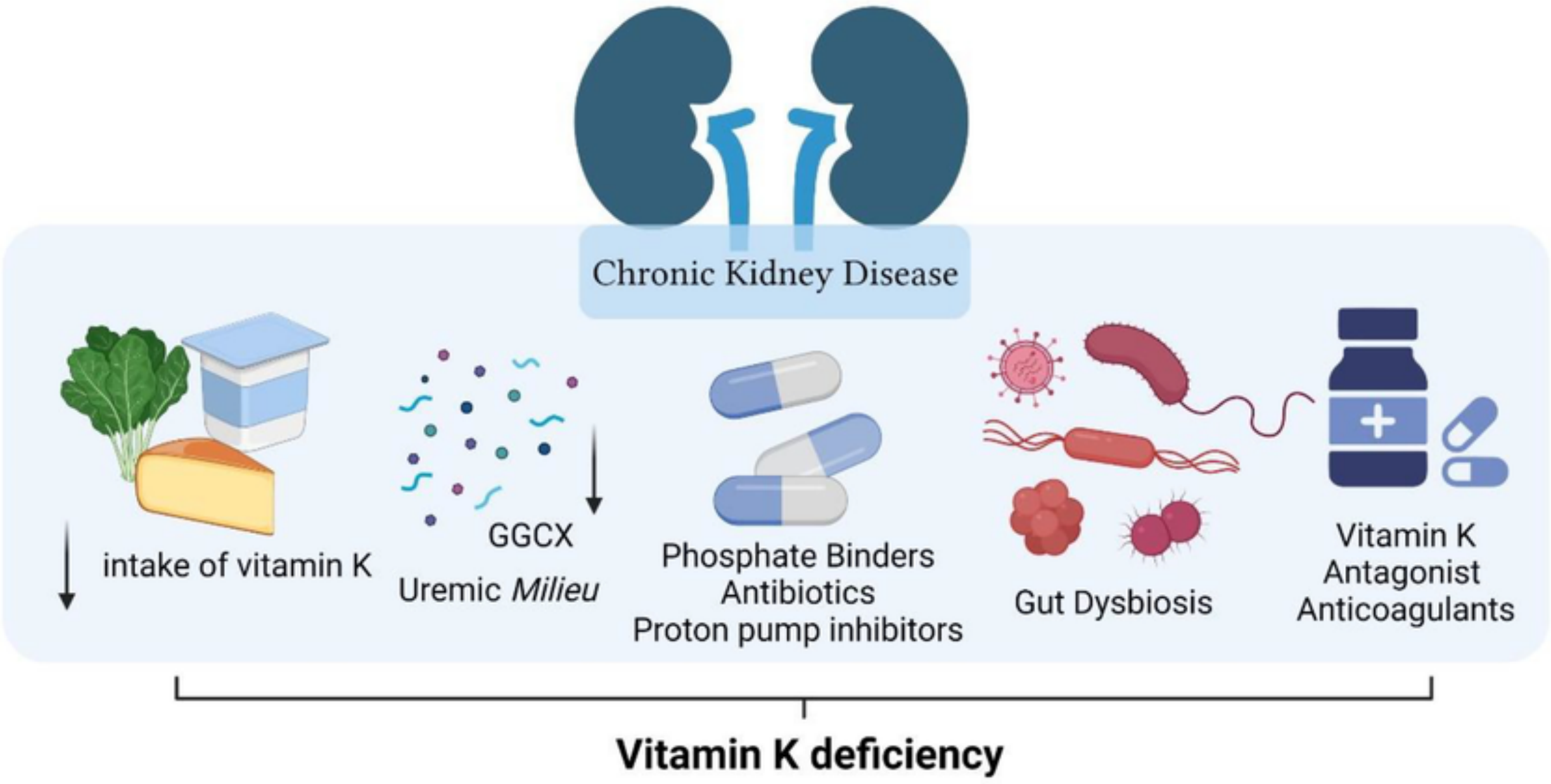
加速腎臟惡化

Bone disease

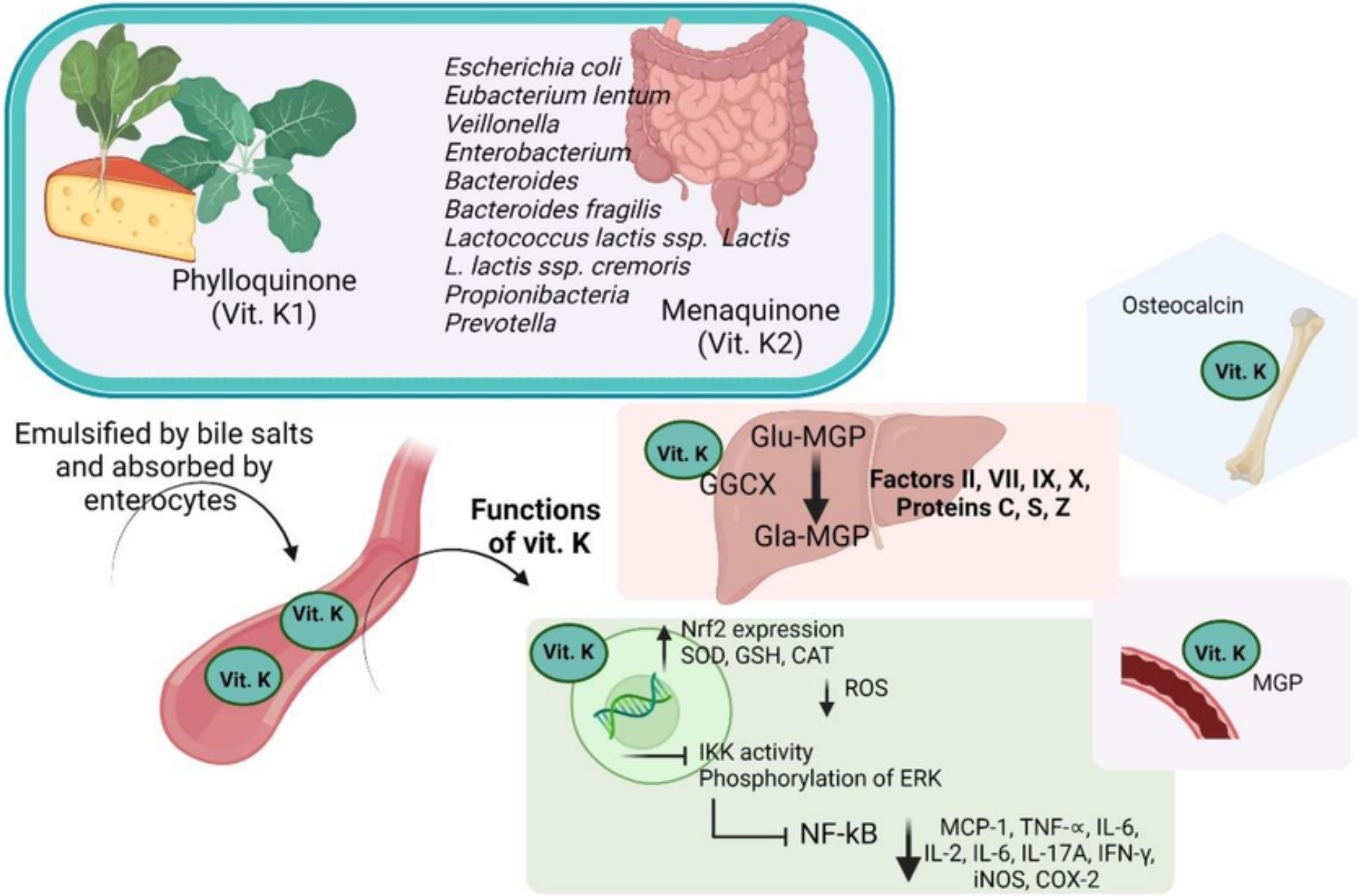
骨骼疾病

Int J Mol Sci. 2022 May; 23(9):

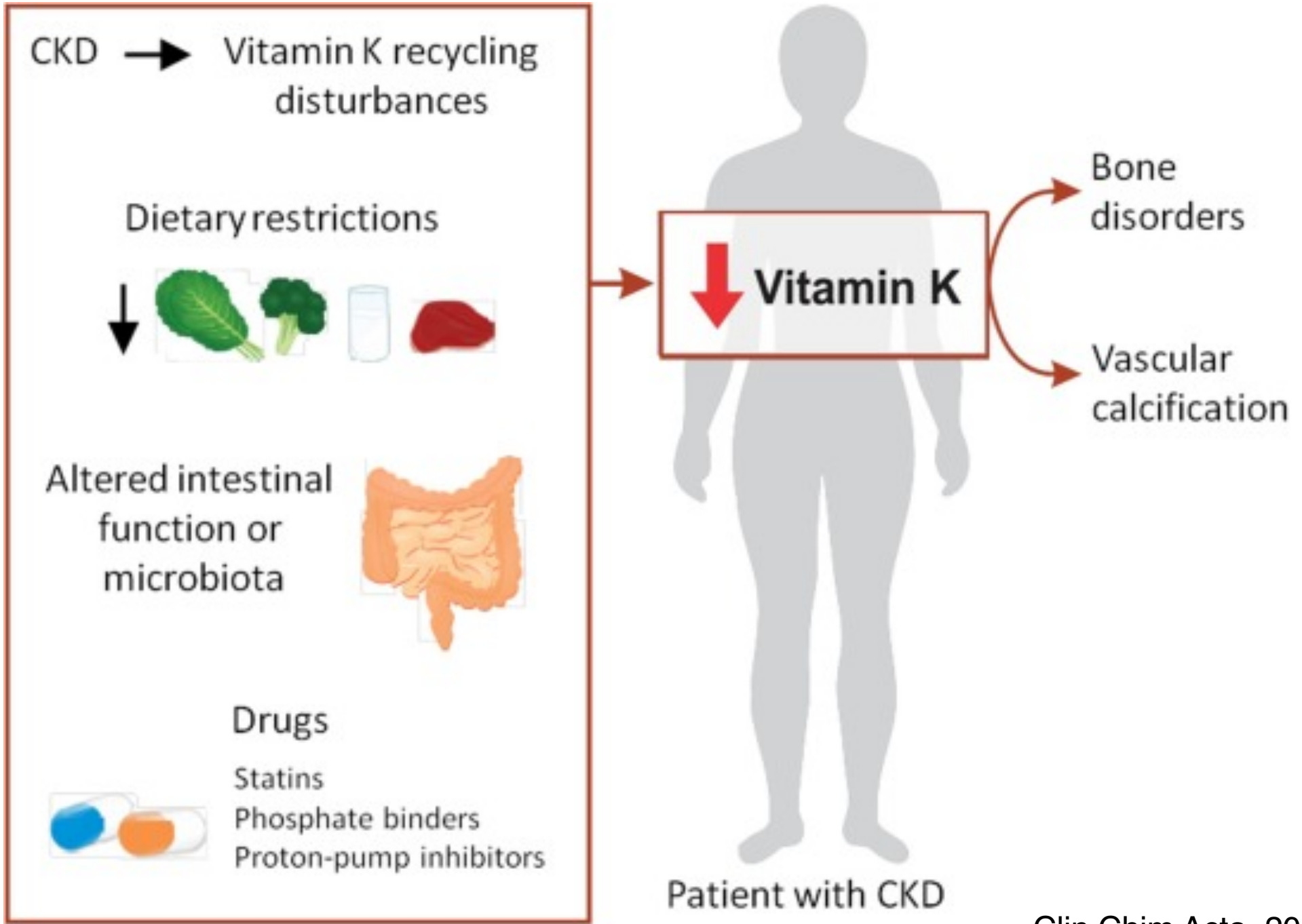
Study	Sample Size and Type of Patients	Study Type	Vitamin K Assessment and/or Supplementation	Cardiovascular Outcome
Brandenburg et al. [123]	*n* = 72 patients with asymptomatic or mildly symptomatic AVC	12-month prospective, single-center, open-label, randomized interventional trial	VK1 2 mg/d *n* = 38 PL *n* = 34 for 12 months	Lower progression of AVC by 12% ($p = 0.03$) after VK1 vs. PL plasma dp-ucMGP by 45% ($p < 0.001$) in the VK1 group;
Geleijnse et al. [99]	*n* = 4807 Women and men aged ≥55 years without MI	prospective, population-based study (7–10 years)	diet rich in VK1 mean intake of VK1: <200 µg/d, 200–278 µg/d and >278 µg/d diet rich in VK2 mean intake of VK1: <21.6 µg/d, 21.6–32.7 µg/d and >32.7 µg/d	VK1—no association with incidents of CHD mortality, all-cause mortality and aortic calcification VK2—reduction of CHD mortality and inverse relation to all-cause mortality and severe aortic calcification
Braam et al. [96]	*n* = 181 Healthy postmenopausal Caucasians between 50 and 60 years of age (only female)	double-blind RCT	vitamin K_1 (1 mg) + D_3 (8 µg) supplementation	Distensibility (+8.8%, $p < 0.05$) Compliance (+8.6%, $p < 0.05$) Pulse pressure (−6.3%, $p < 0.05$) CCA elasticity (−13.2%, $p < 0.01$)
Shea et al. [36]	*n* = 489 hypertension patients under drug treatment	prospective longitudinal cohort study	K1 K2	Low k1 (<0.2 nmol/die) is risk factor for incident CVD in older men and women treated for hypertension but was not associated with CVD in those not treated for hypertension
Beulens et al. [126]	*n* = 564 postmenopausal women between 62 and 72 years of age (only female)	cross-sectional study	Dietary menaquinone intake (31.6 ± 12.3 mcg/d)	High dietary VK2 intake is associated with decreased coronary calcification
Knapen et al. [127]	*n* = 244 postmenopausal women (age 59.5 ± 3.3)	RCT	Menaquinone-7 supplementation (180 mcg/d)	Menaquinone-7 supplementation improved arterial stiffness in people with higher baseline stiffness index.
Vaccaro et al. [97]	*n* = 5296; age >50	cross-sectional study	Dietary phylloquinone intake (women, 90 mcg/d; men, and 120 mcg/d)	Inadequate dietary phylloquinone intake was a strong and significant predictor of higher arterial pulse pressure.



Curr Nutr Rep. 2022

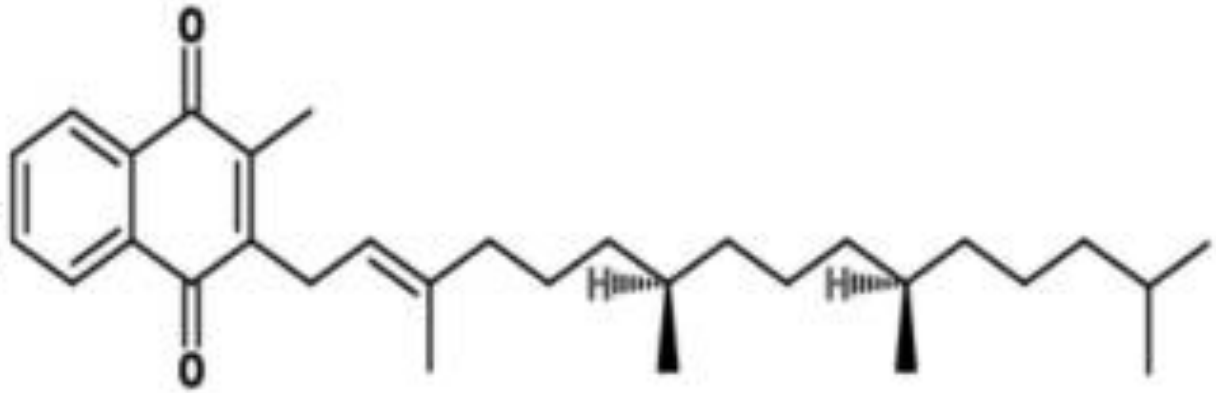


Curr Nutr Rep. 2022

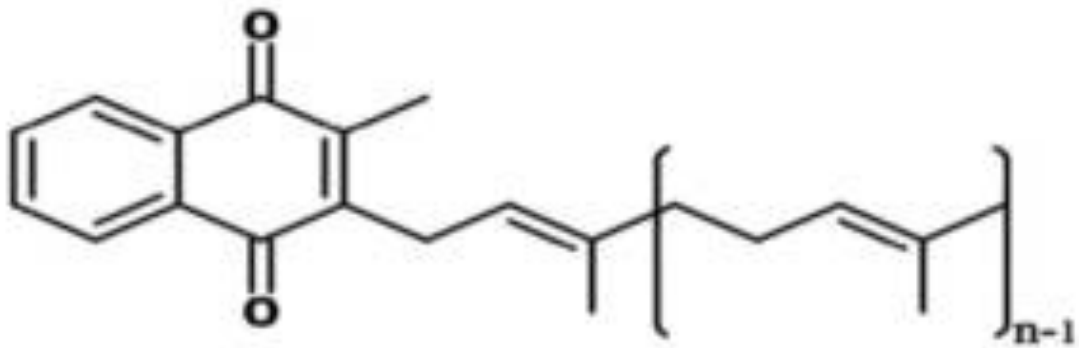


Clin Chim Acta. 2020

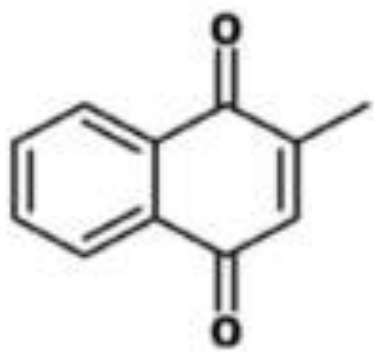
Vitamin K1
(phylloquinone)



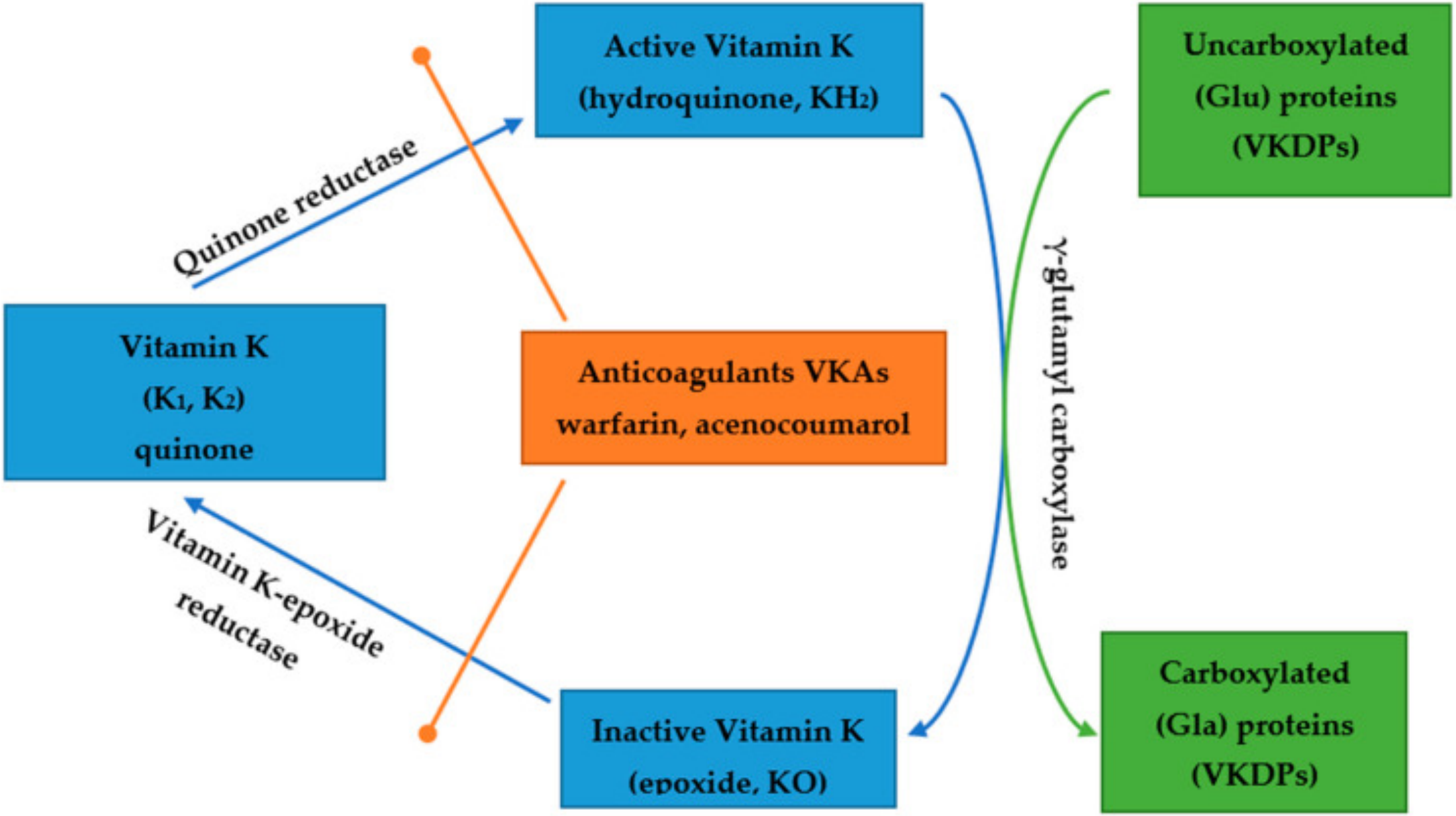
Vitamin K2
(menaquinone)



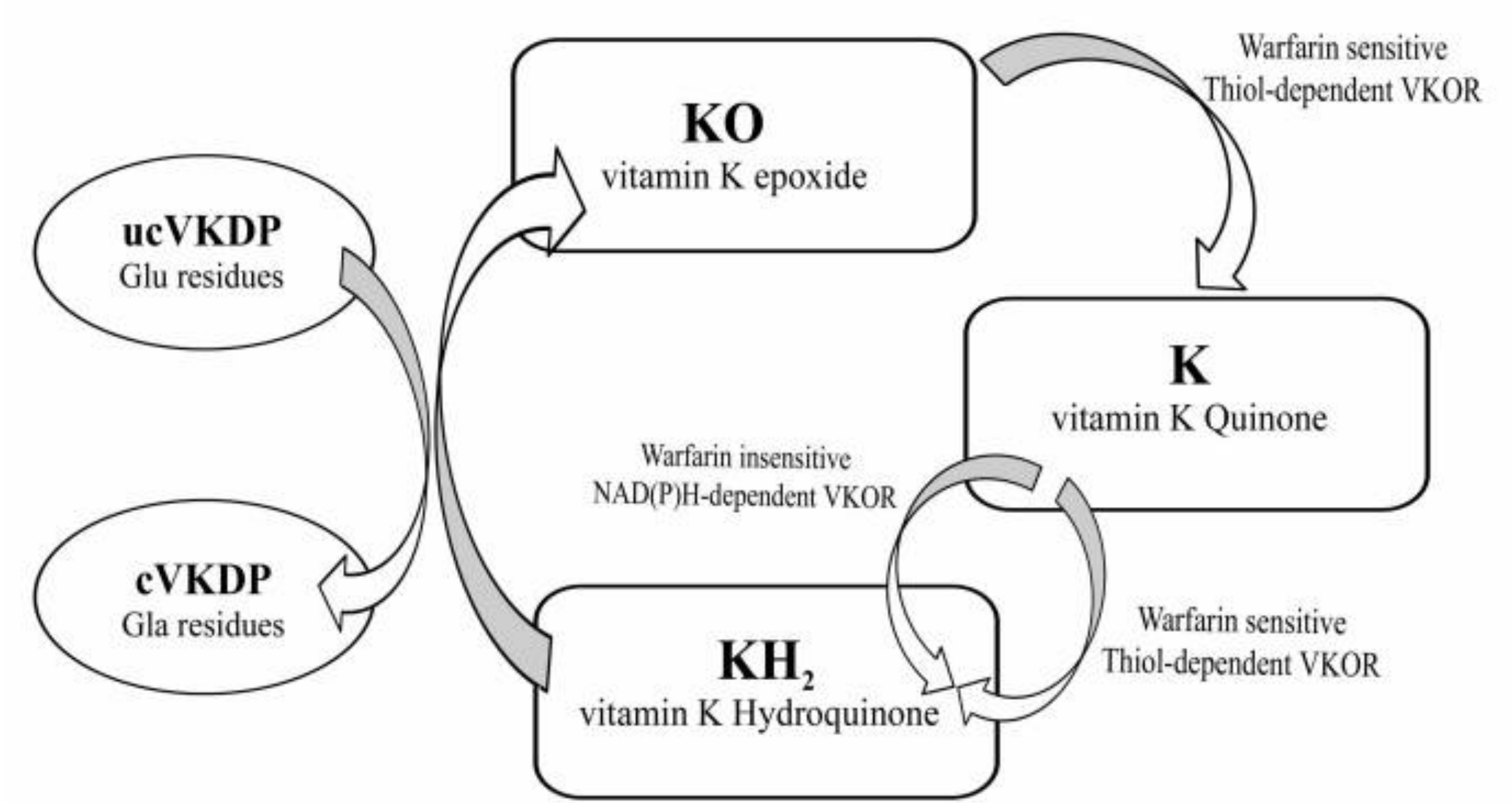
Vitamin K3
(menadione)



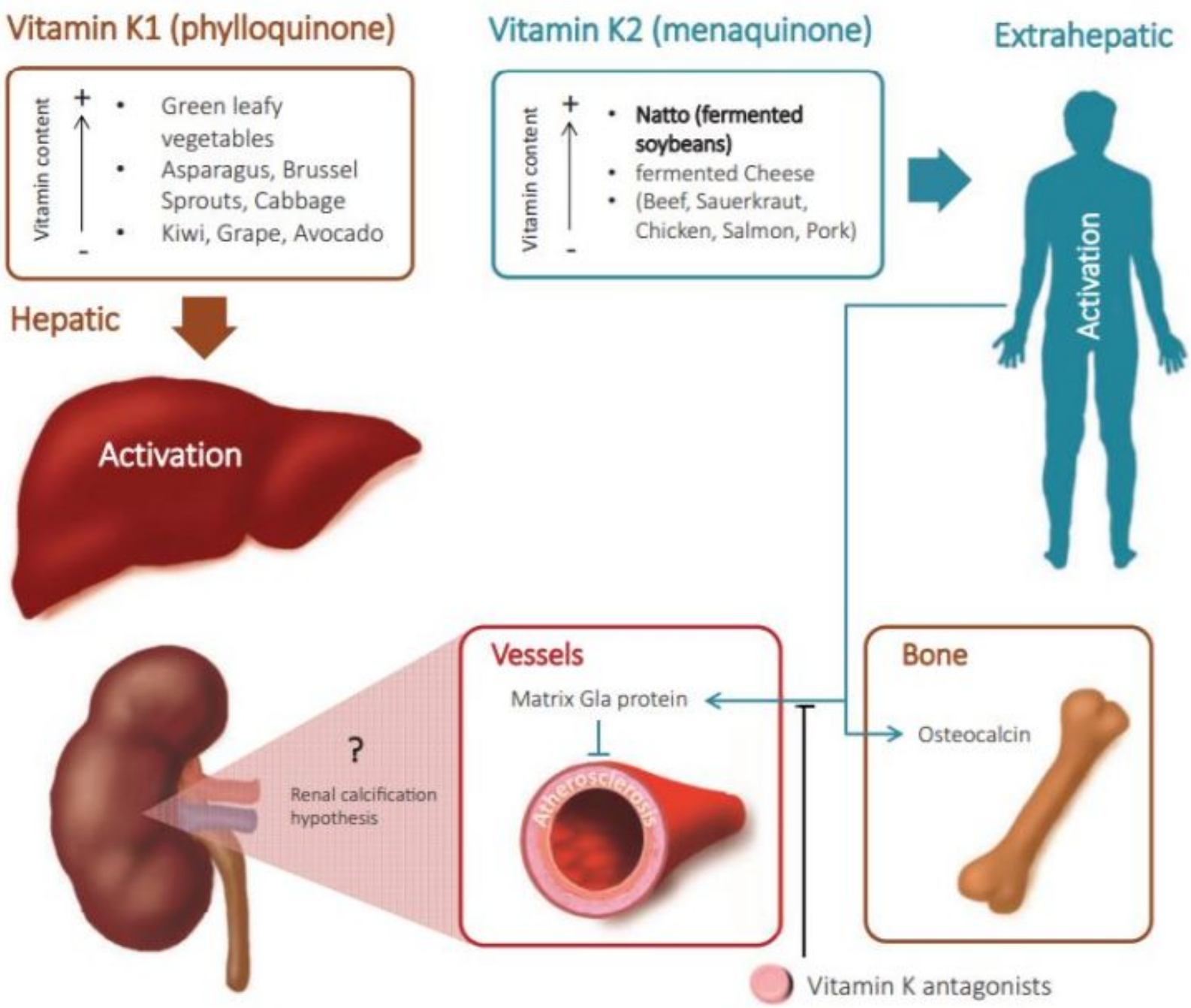
Oman Med J. 2014 May; 29(3): 172–



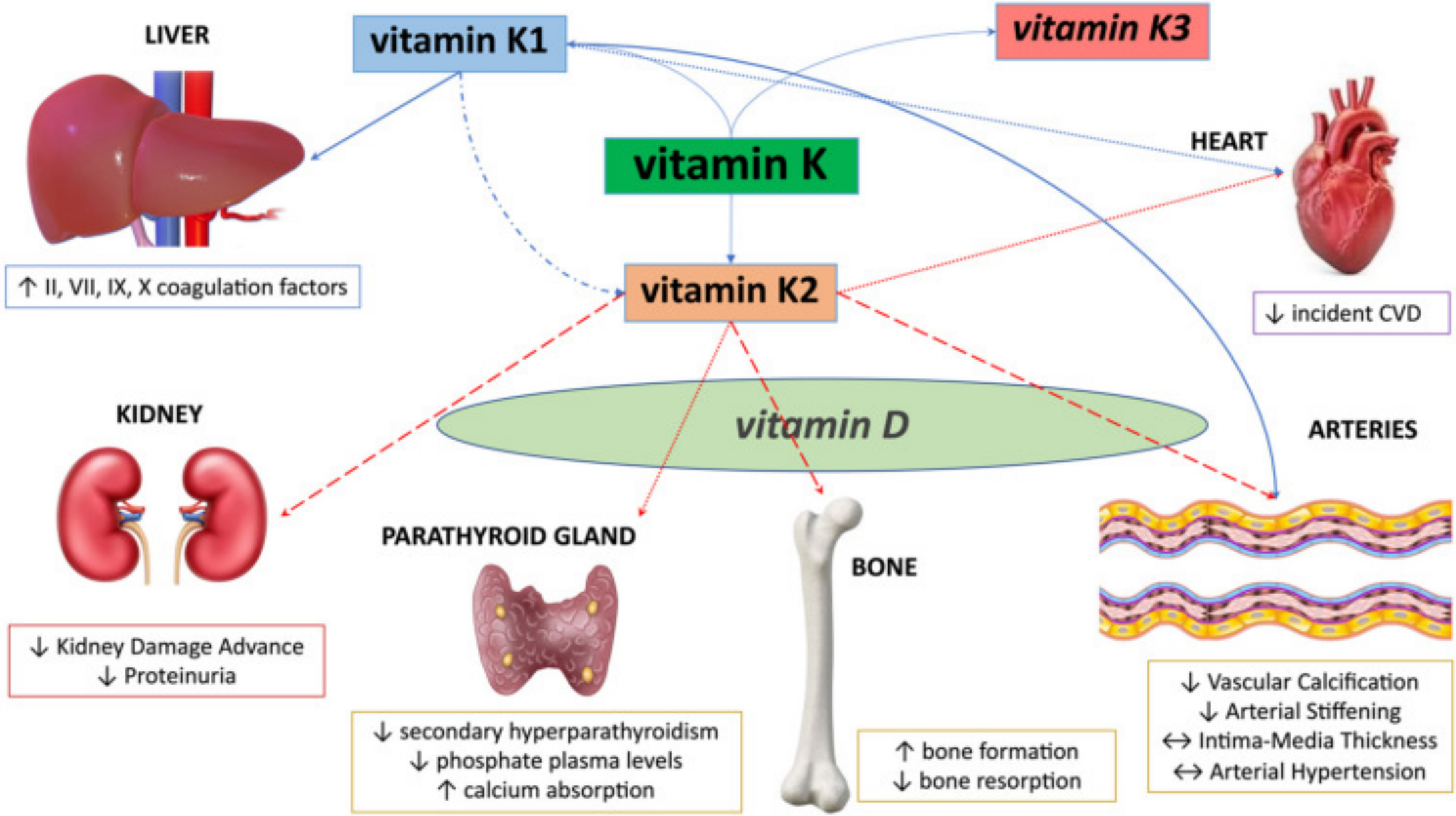
Nutrients. 2022 Jan; 14(2):



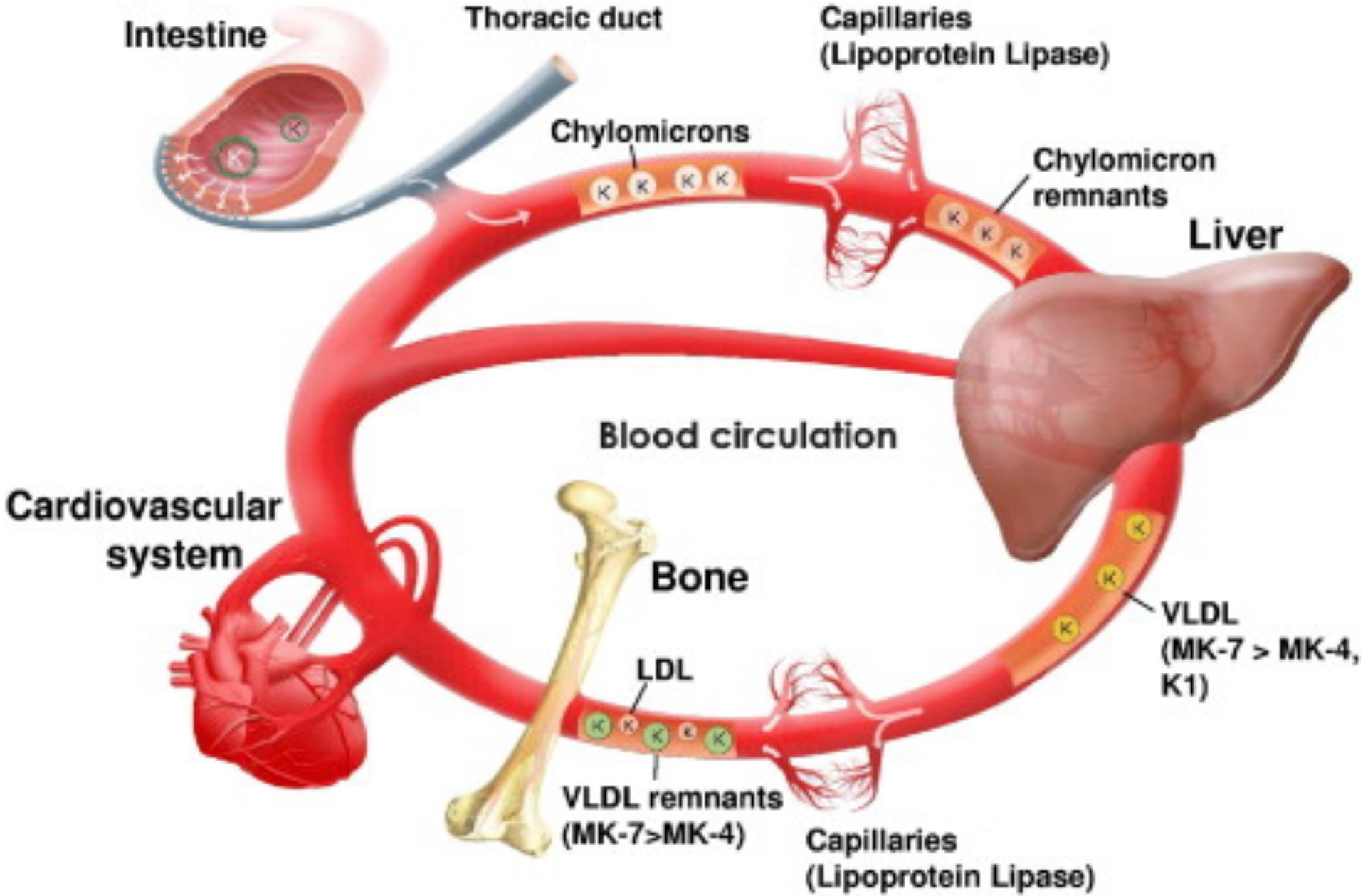
Oman Med J. 2014 May; 29(3): 172–



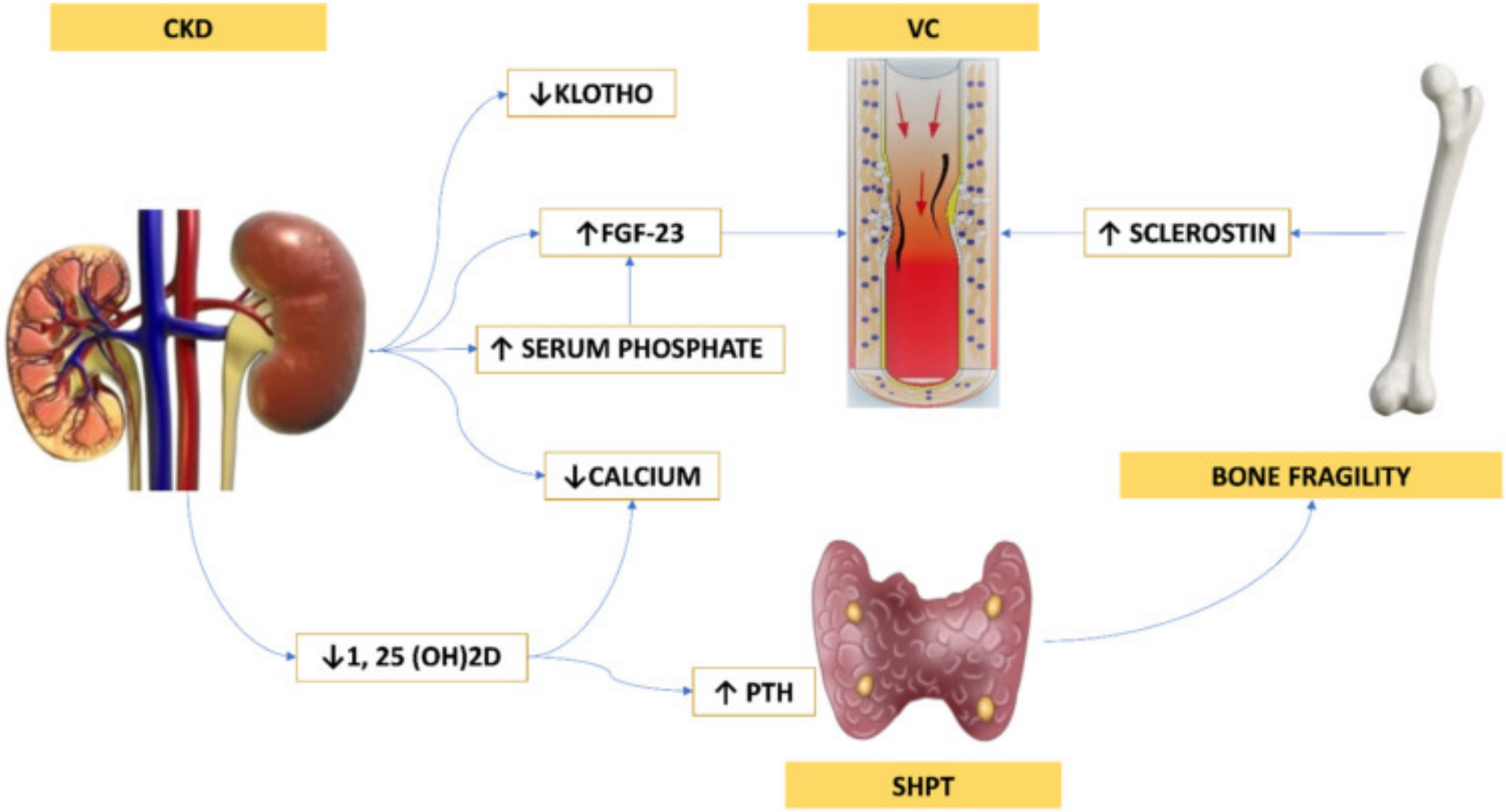
phrol Dial Transplant. 2021 Dec



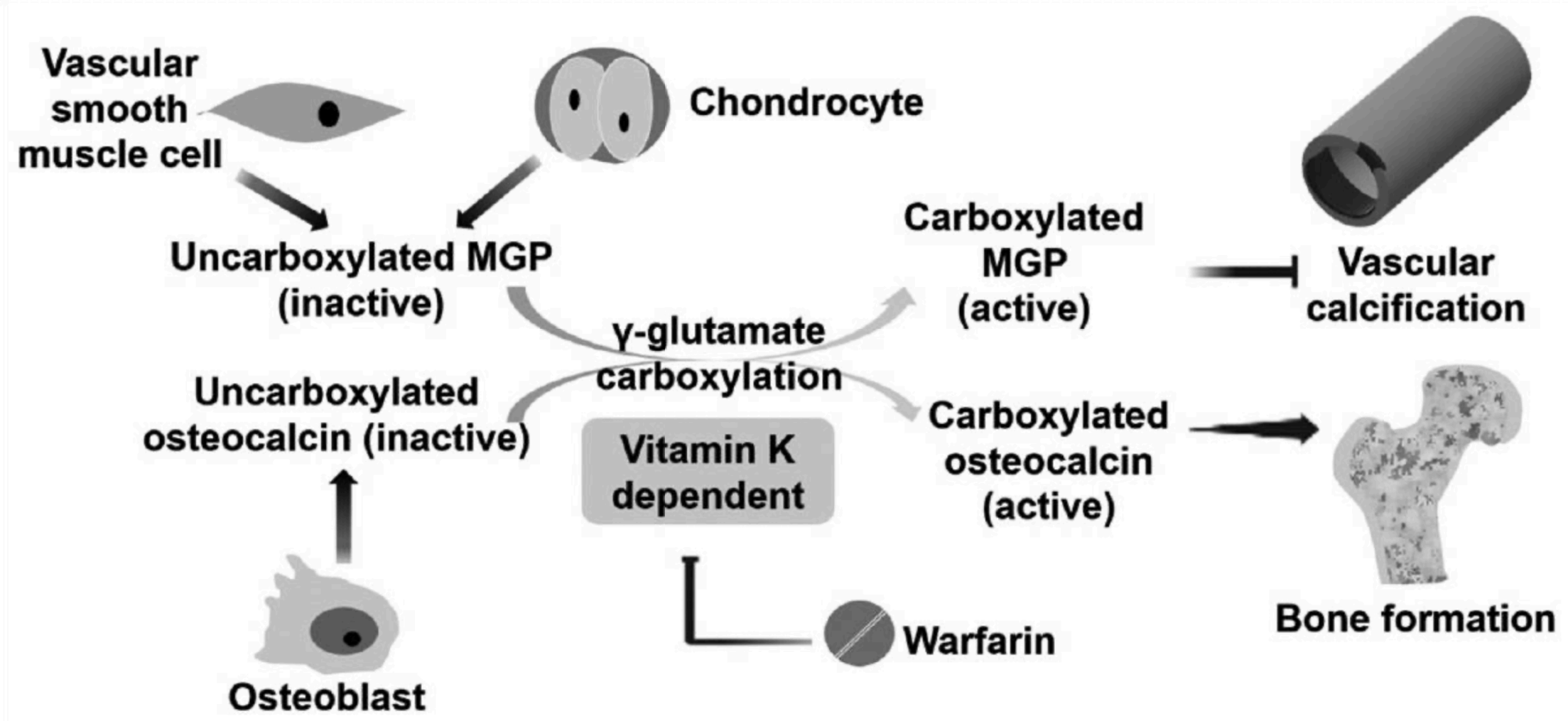
Int J Mol Sci. 2022 May; 23(9):



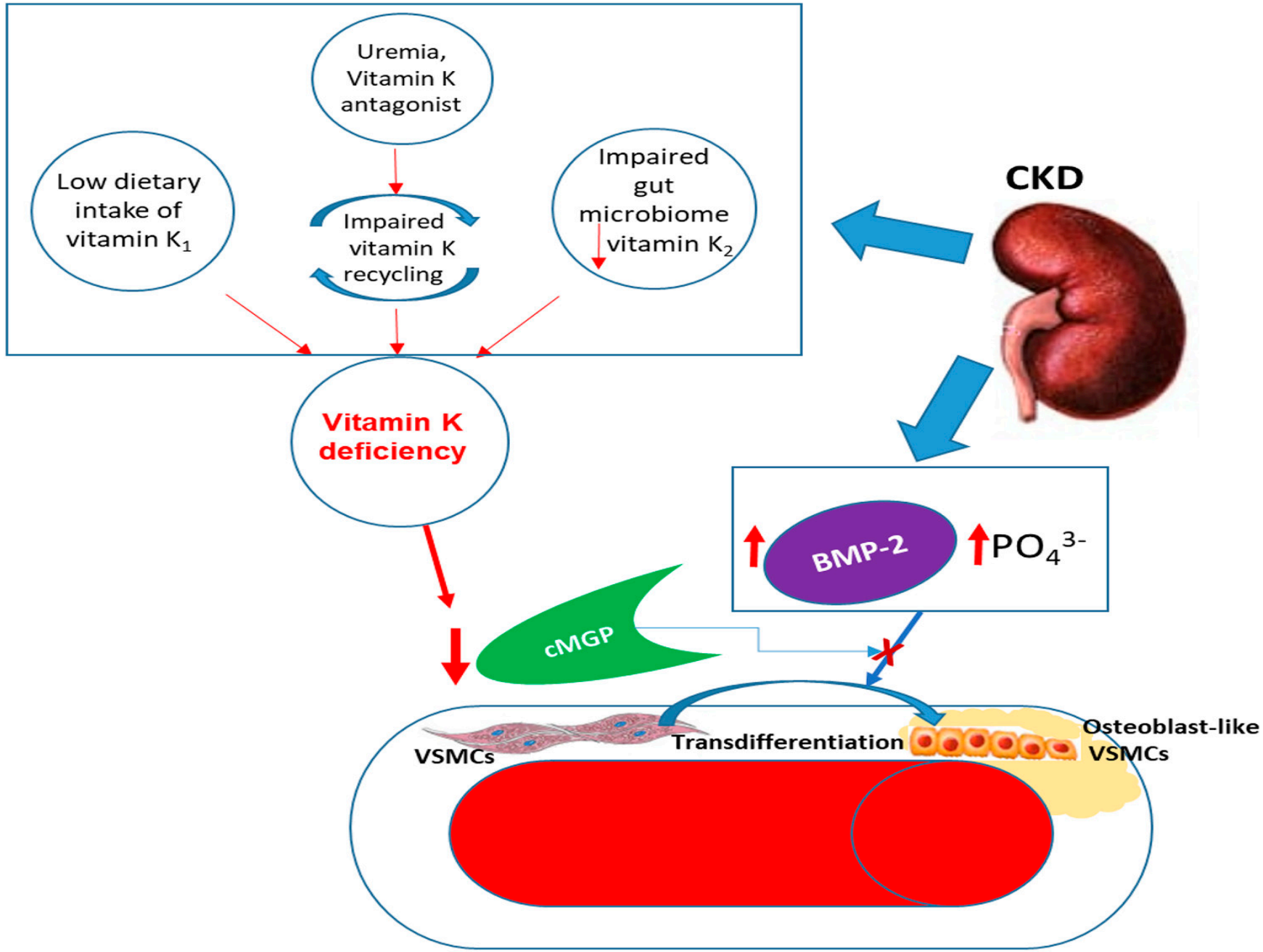
Am J Kidney Dis. 2012

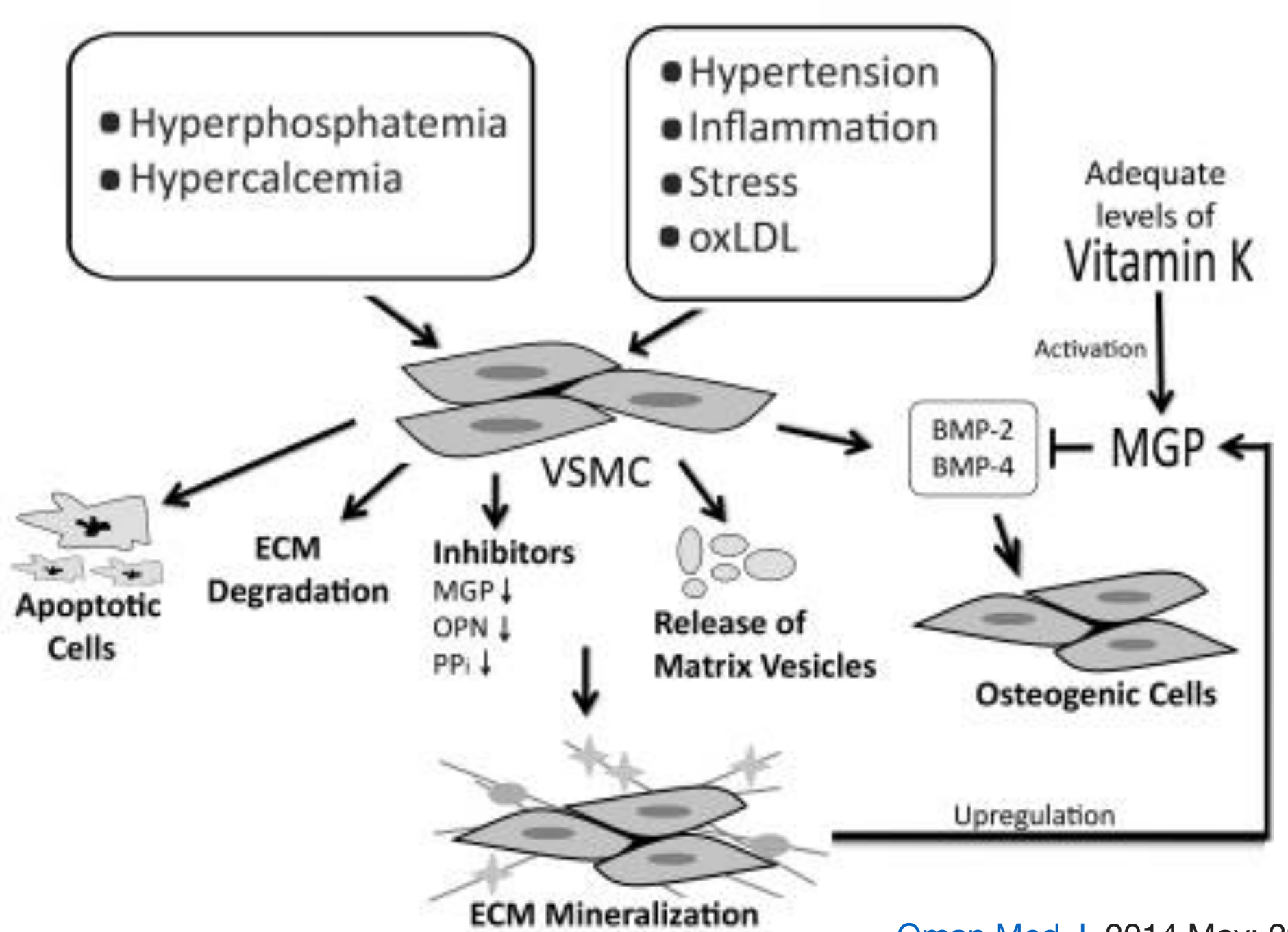


Int J Mol Sci. 2022 May; 23(9):

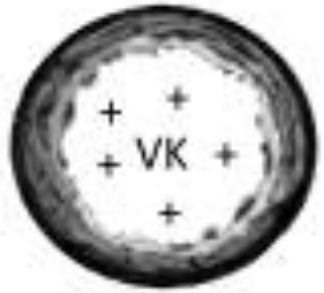


Tzu Chi Med J. 2023 Jan-Mar; 35(1): 44–


Uremia, Vitamin K antagonist
Low dietary intake of vitamin K_1
Impaired vitamin K recycling
Impaired gut microbiome vitamin K_2
CKD
Vitamin K deficiency
BMP-2
PO_4^{3-}
cMGP
VSMCs
Transdifferentiation
Osteoblast-like VSMCs



Oman Med J. 2014 May; 29(3): 172–



Adequate VK Intake

Vitamin K Sufficiency

Active MGP ↑**dp-cMGP**
↑**p-cMGP**

↑**Phagocytosis** ↓**Calcification**

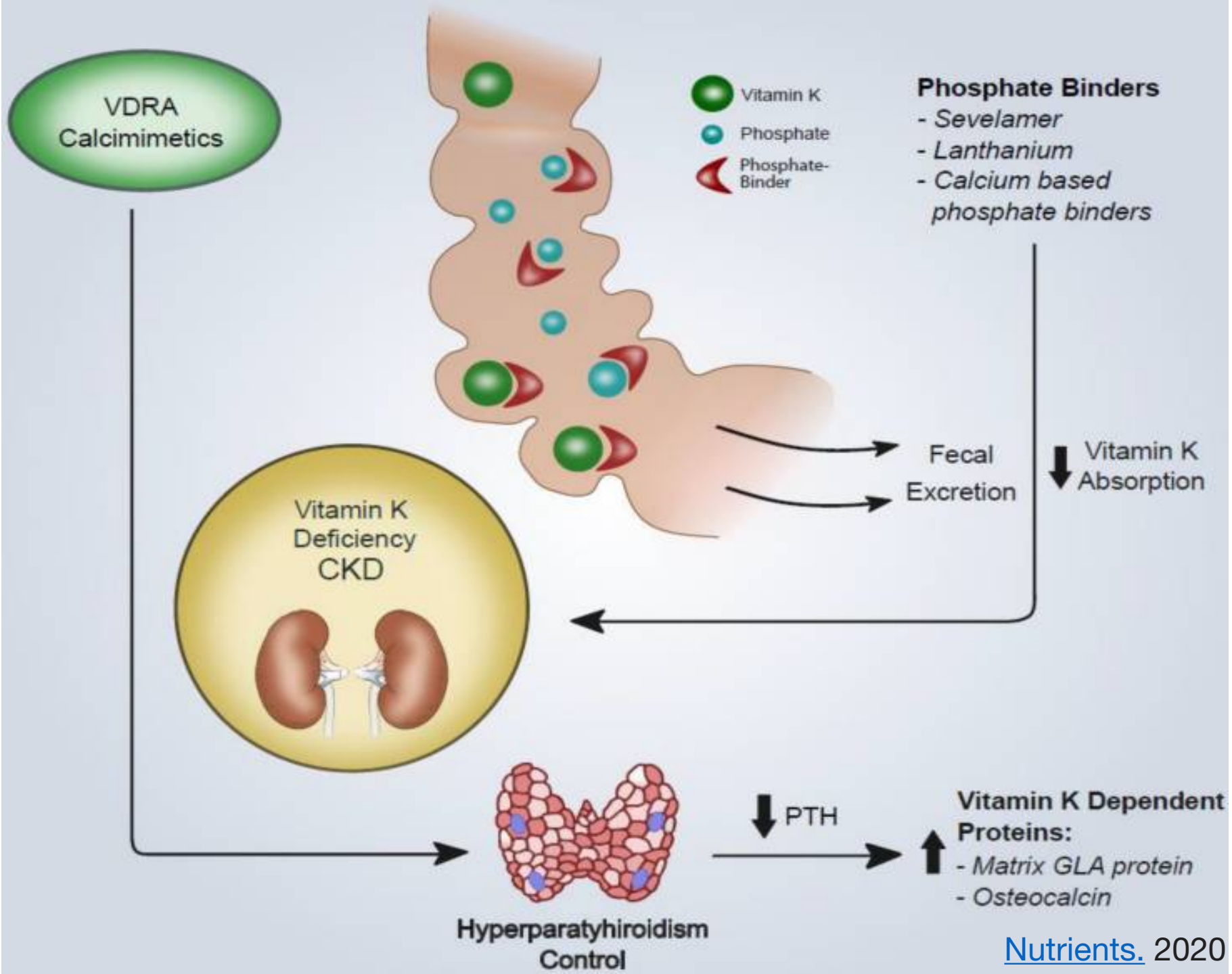
Inadequate VK Intake VKA Treatment

Vitamin K Insufficiency

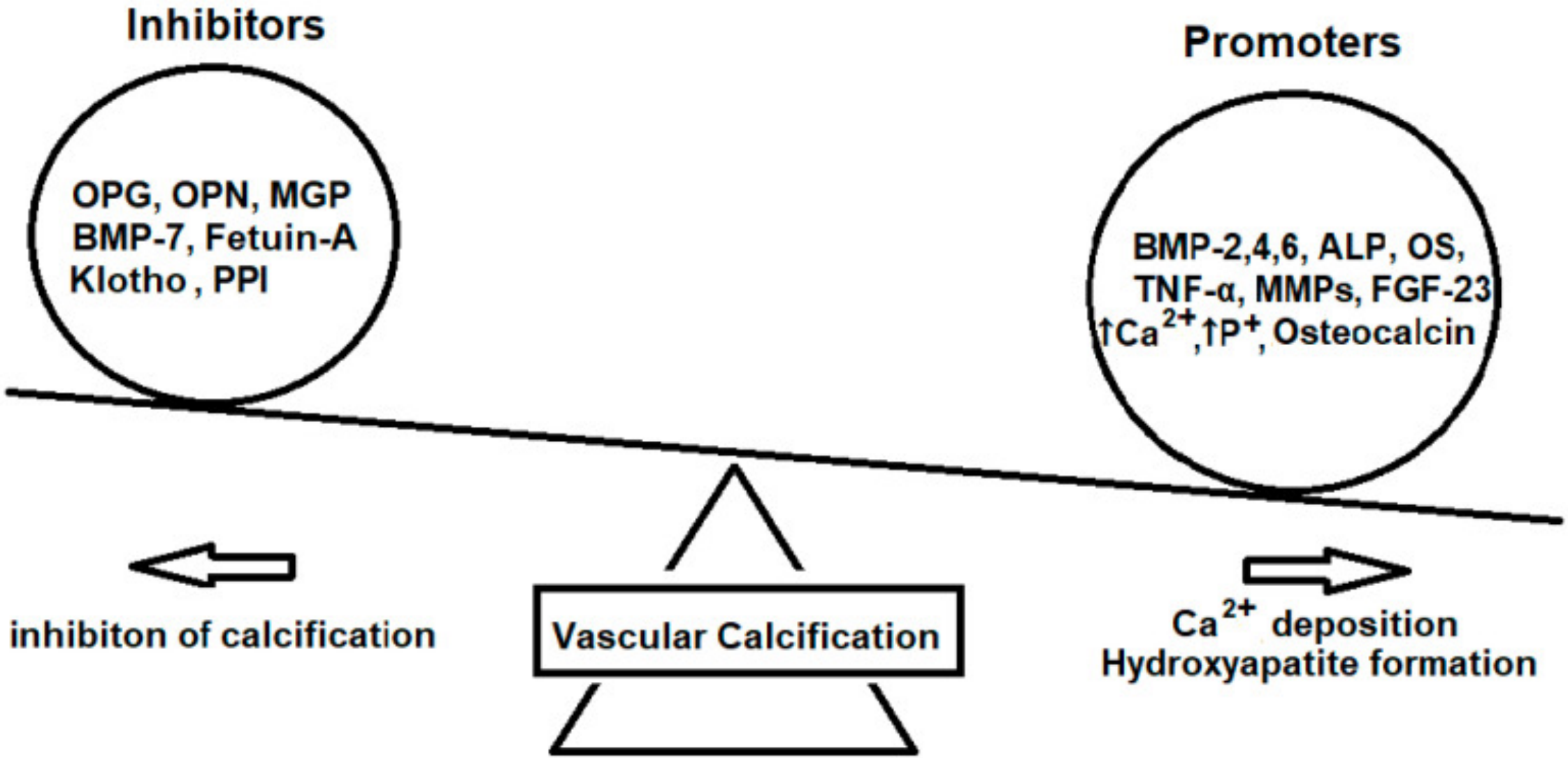
Inactive MGP ↓**p-ucMGP**
↑**dp-ucMGP**

↓**Phagocytosis** ↑**Calcification**

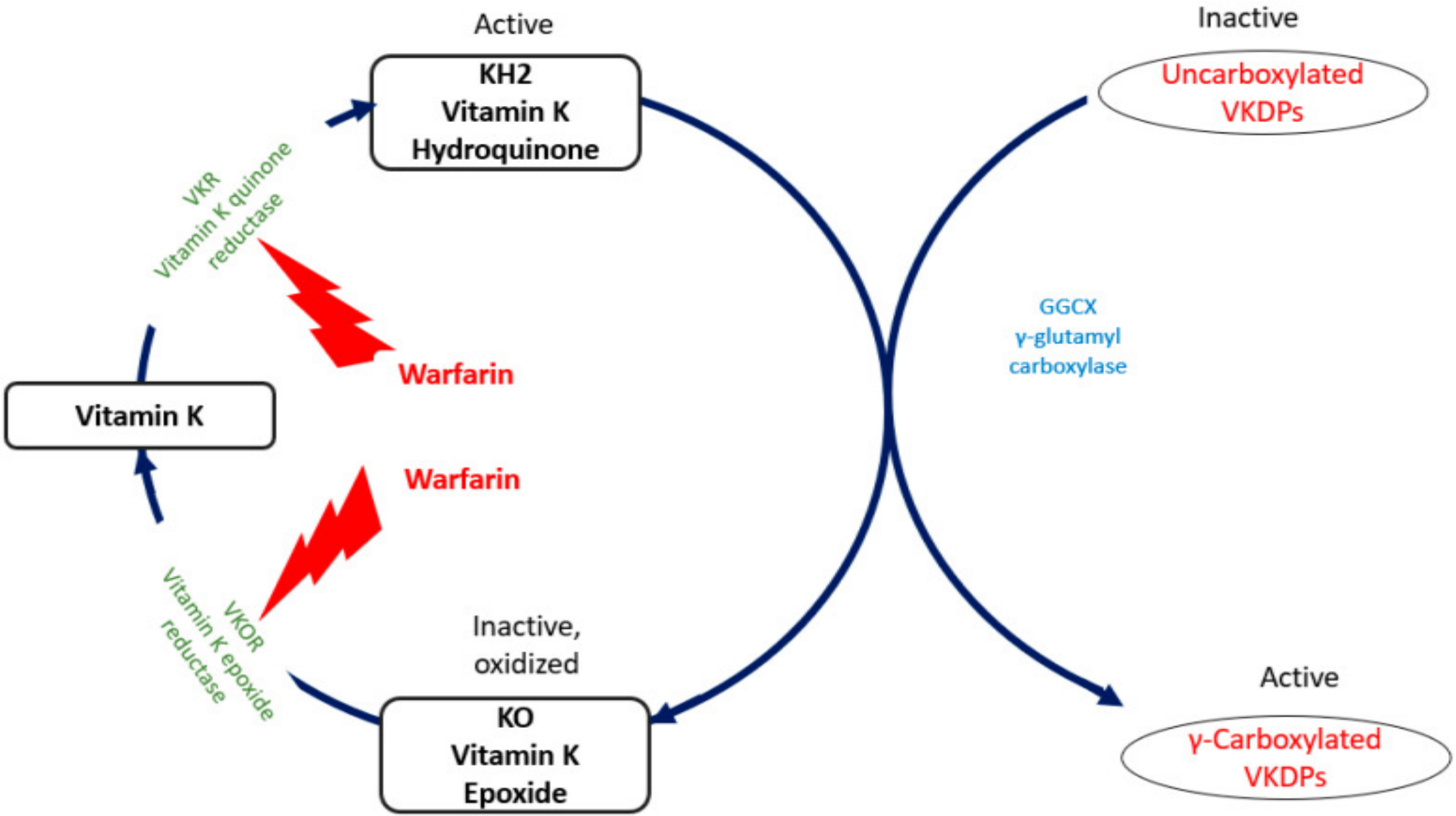
Oman Med J. 2014 May; 29(3): 172–



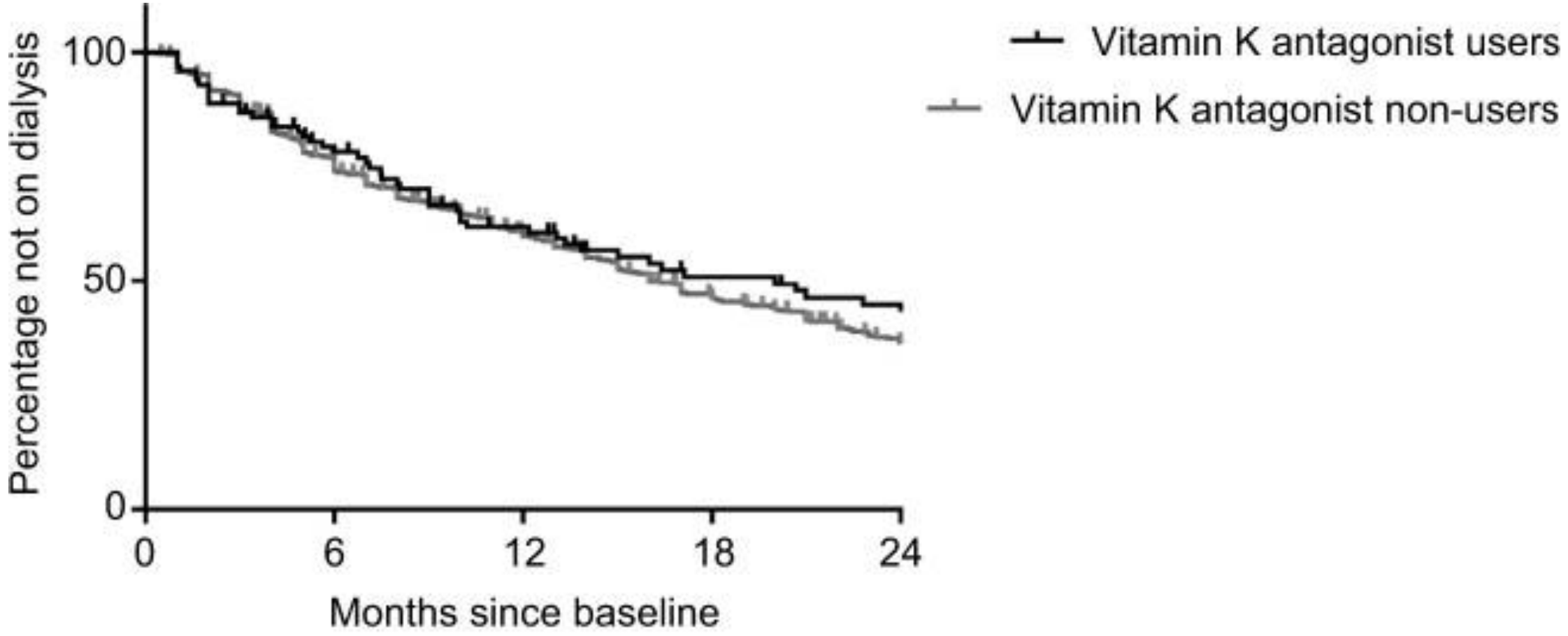
Nutrients. 2020 Jun; 12(6): 1609



Nutrients. 2024 Jun; 16(12): 1798

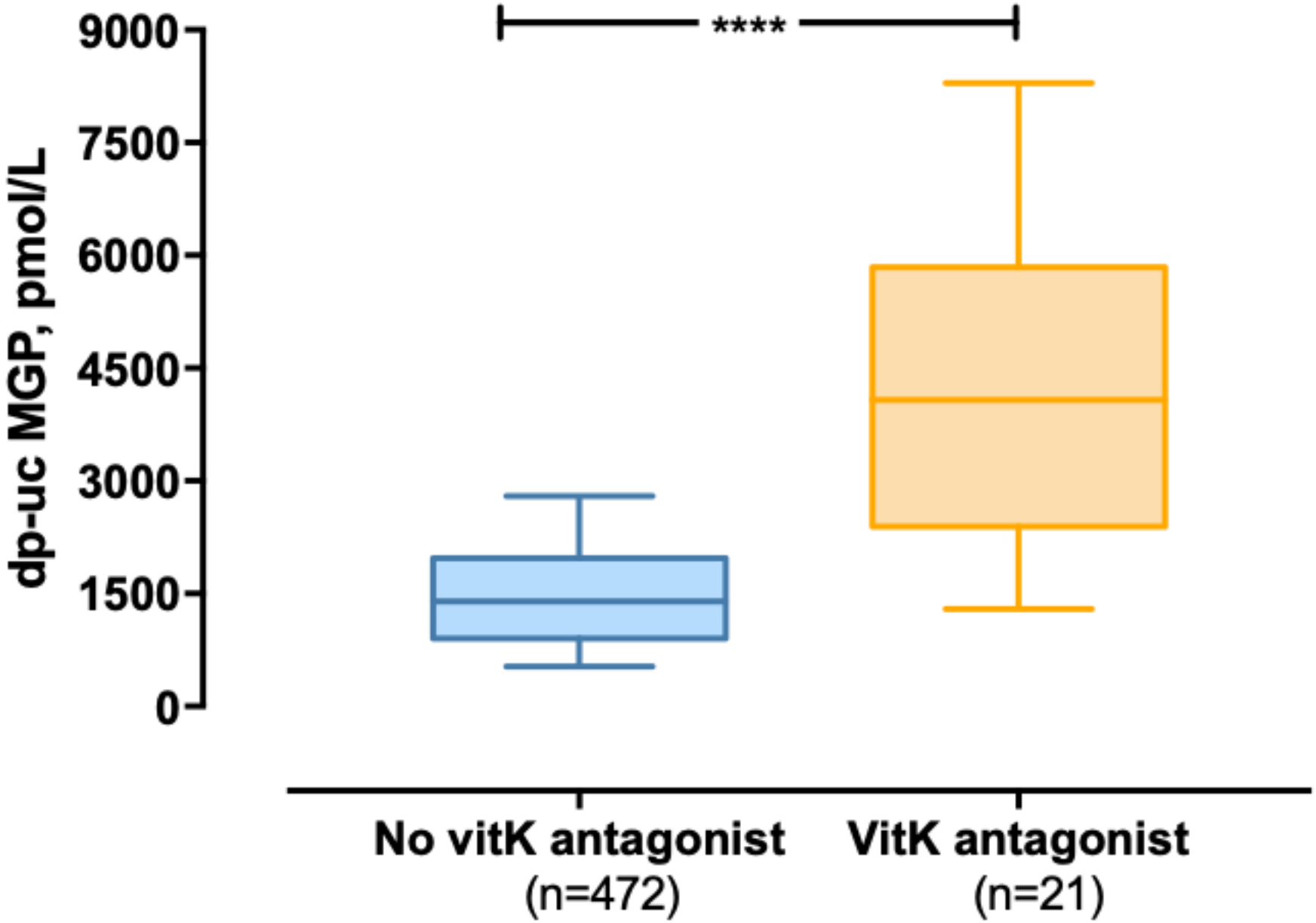


Nutrients. 2024 Jun; 16(12): 1798

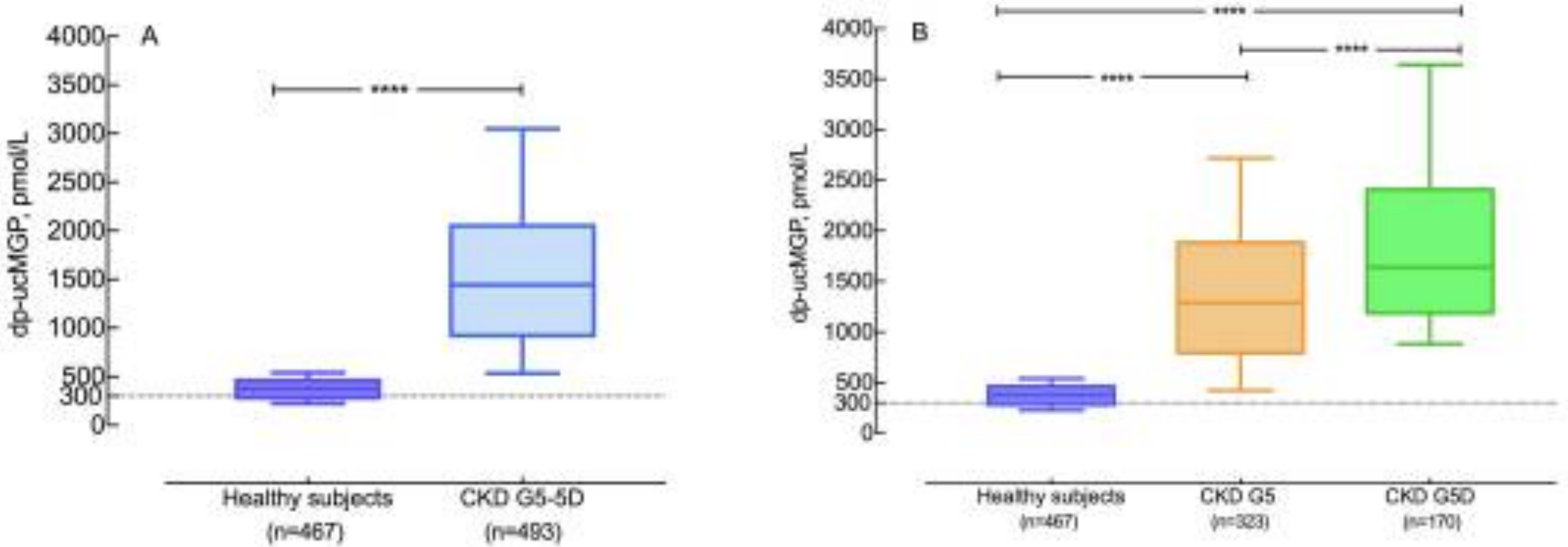


Month	0	6	12	18	24
Number at risk Vitamin K antagonist users	101	70	50	34	29
Number at risk Vitamin K antagonist non-users	883	632	470	336	248

Clin Epidemiol. 2018; 10: 623–



PLoS One. 2021; 16(2): e0247623



PLoS One. 2021; 16(2): e0247623

Multicenter RCT of vitamin K antagonist replacement by rivaroxaban with or without vitamin K2 in hemodialysis patients with atrial fibrillation: the Valkyrie study

METHODS

N=132

VKA INR 2-3

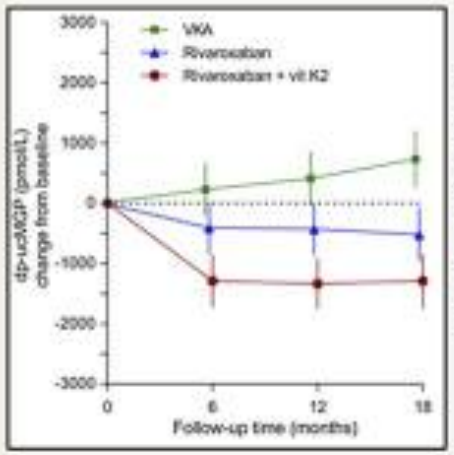
Rivaroxaban 10 mg od

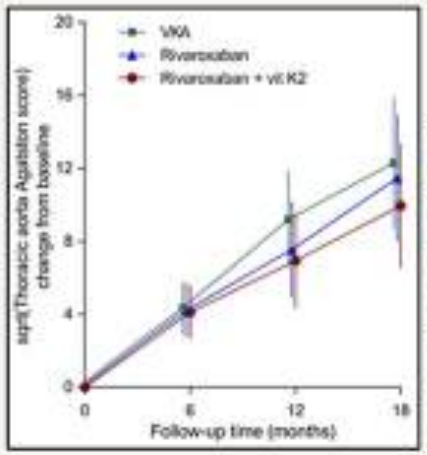
Rivaroxaban + Vit K2

0m* 6m* 12m* 18m*

*VitK status, PWV and CAC score

OUTCOME





Bleeding type	Rate per 100 person-years (number)		
	VKA (n=44)	Rivaroxaban (n=46)	Rivaroxaban + VitK2 (n=42)
Life-threatening	13.3 (7)	3.5 (2)	9.5 (5)
Major	22.7 (12)	13.8 (8)	3.8 (2)
Life-threatening + major	36.0 (19)	17.3 (10)	13.2 (7)
Minor	28.5 (14)	31.1 (18)	30.3 (16)
Gastro-intestinal	22.7 (12)	17.3 (10)	24.6 (13)

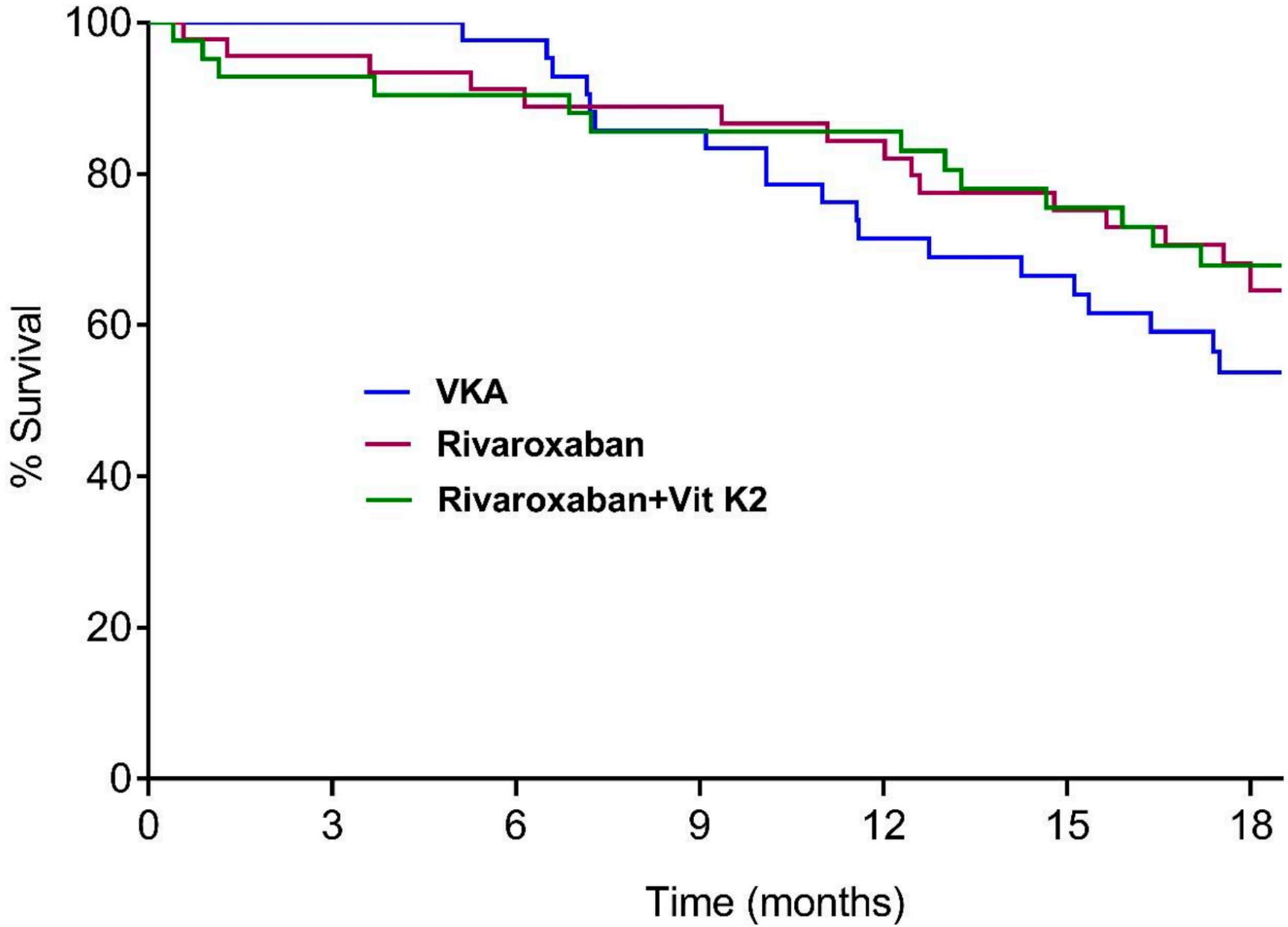
CONCLUSION

Withdrawal of VKA and high-dose Vitamin K2 improve Vitamin K status in hemodialysis patients, but have no significant favorable effect on VC progression. Severe bleeding complications may be lower with rivaroxaban than with VKA.

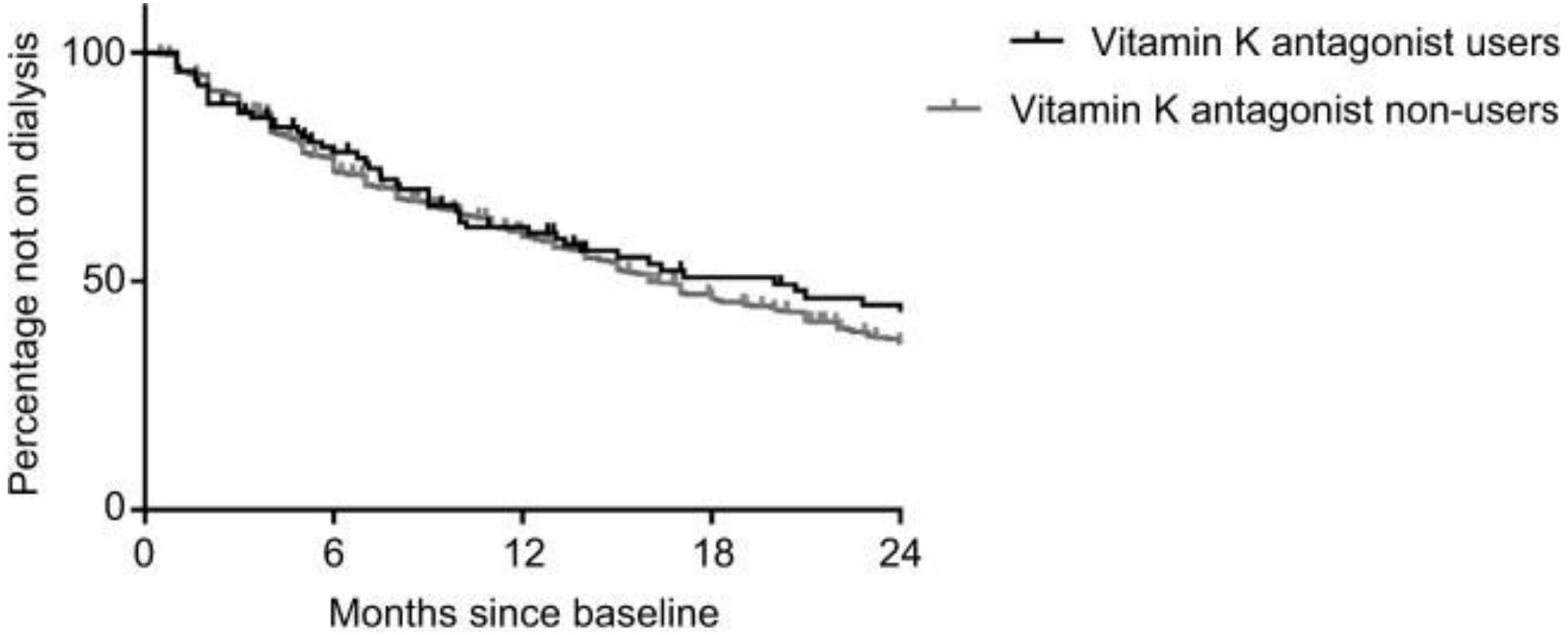
JASN

JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY

J Am Soc Nephrol. 2020 Jan; 31(1): 186–196



J Am Soc Nephrol. 2020 Jan; 31(1): 186–196



Month	0	6	12	18	24
Number at risk Vitamin K antagonist users	101	70	50	34	29
Number at risk Vitamin K antagonist non-users	883	632	470	336	248

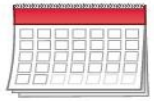
Clinical Kidney Journal

Vitamin K supplementation impact in dialysis patients: a systematic review and meta-analysis of randomized trials

Chronic kidney disease patients with optimal vitamin K status have better survival than patients with vitamin K deficiency. The present meta-analysis aimed to evaluate the impact of vitamin K supplementation in dialysis patients.

Methods

Multi-database search:
MEDLINE, EMBASE, Cochrane Library, Web of Science, ClinicalTrials.gov



Inception to September 2023

Primary outcome:
- Mortality

Secondary outcomes:
- Vitamin K biomarkers
- Vascular calcifications
- CKD-MBD parameters
- Safety

Results

11 studies with a total of 830 patients were included in this analysis

Vitamin K had **no significant impact on mortality in 7 studies**
OR 1.00 (95% CI 0.59–1.71)

- Vitamin K1 significantly lowers **MGP levels** and increases **vitamin K levels**
- Non-significant trend in lowering calcification score (OR −0.14 (95% CI −0.37–0.09))
- Vitamin K: non-significant impact on CKD-MBD parameters
- **No excess adverse events**

Conclusion: Vitamin K is a safe product in dialysis patients for improving vitamin K status but with no clear benefit in reducing vascular calcifications or improvement of mortality. Vitamin K1 had a higher impact on reducing calcification biomarkers.

Andrian, T.
Clinical Kidney Journal (2023)
accovic@gmail.com
@CKJsocial