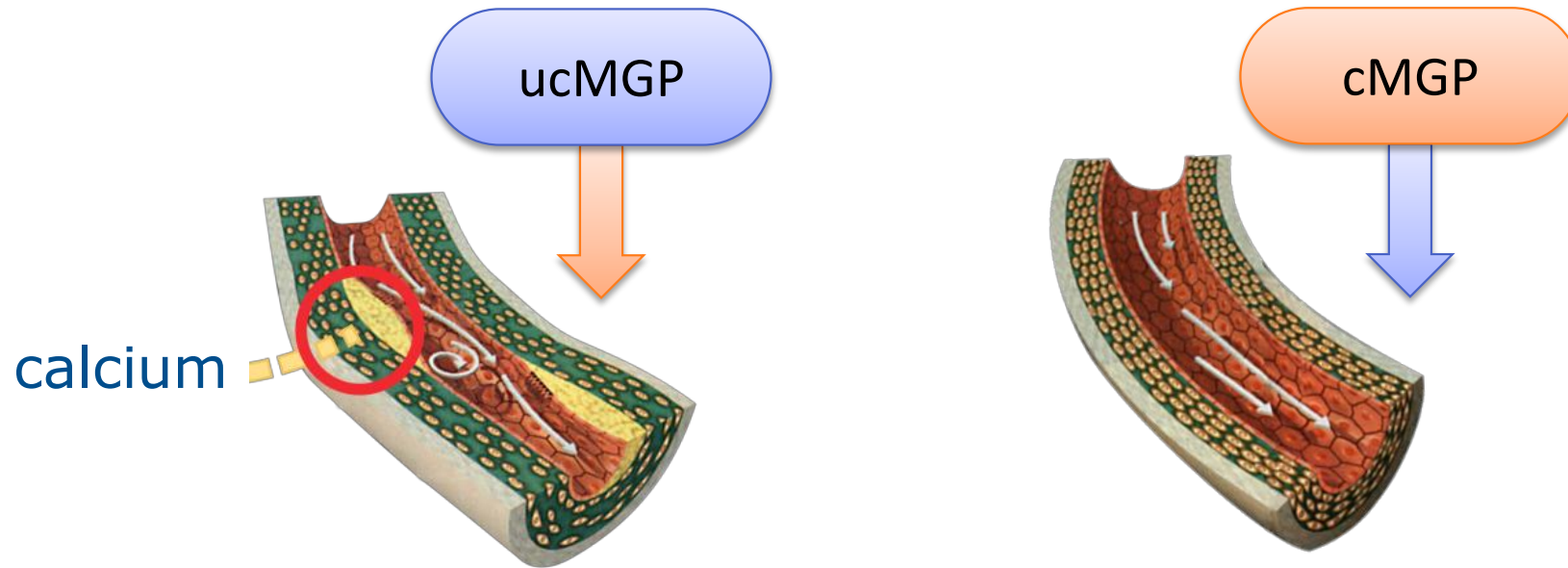


MenaQ7[®]
Natural Vitamin K2

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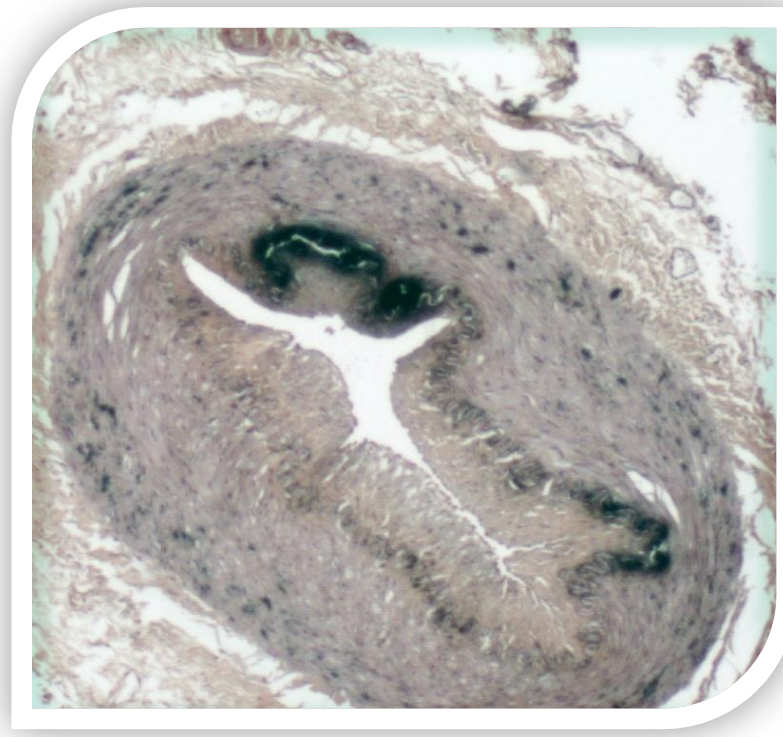
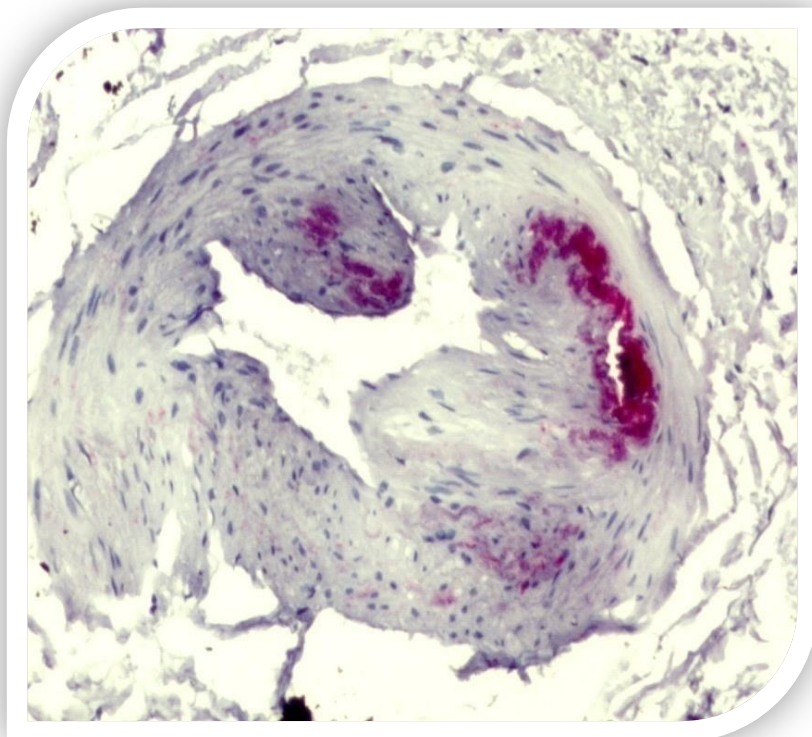
Cardiovascular Health

Calcification process



- Vitamin K deficiency results in undercarboxylation of MGP (ucMGP) that impairs its biological function
- A massive accumulation of ucMGP is present in atherosclerotic plaques
- Recently ucMGP was shown a biomarker for CVD

Inactive MGP "leads" to calcification



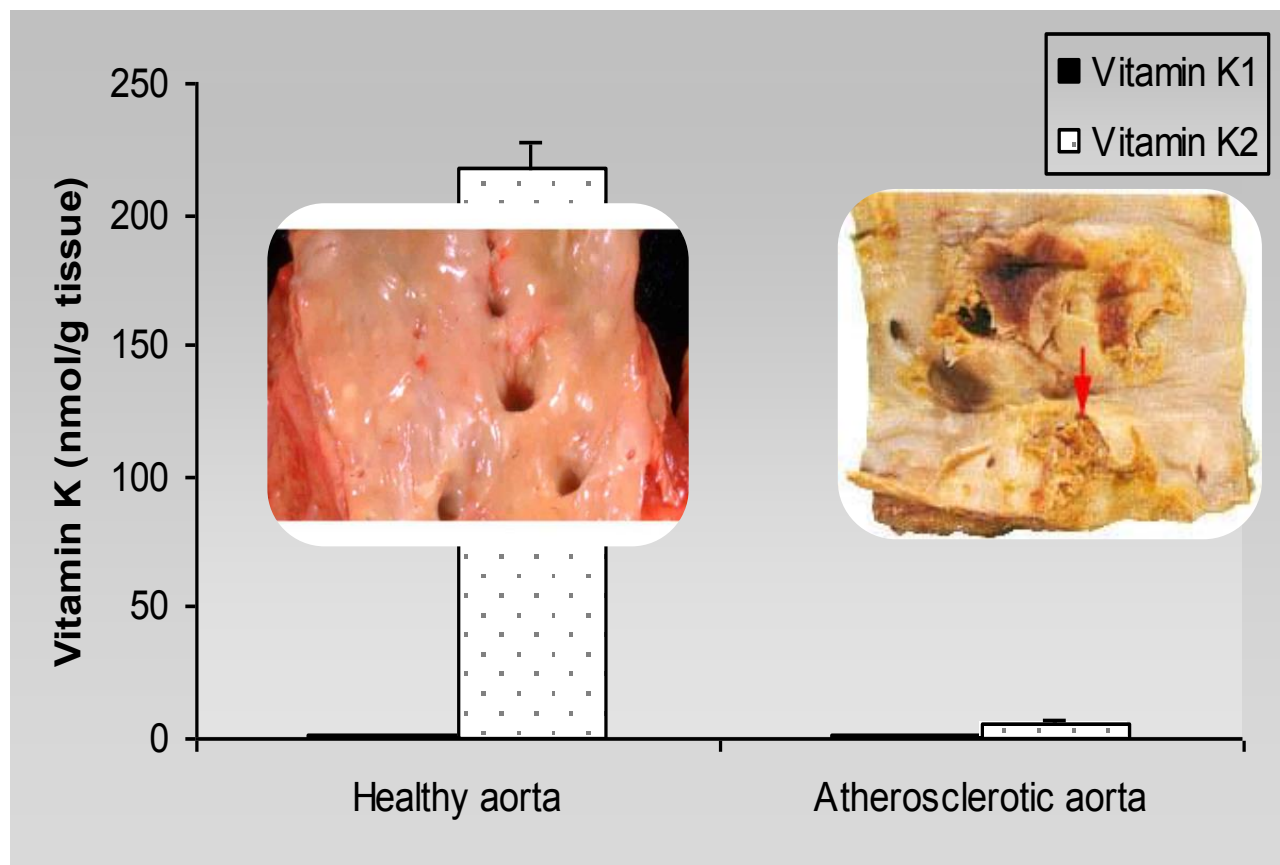
Immunohistochemistry staining

In red: localization
of the inactive MGP

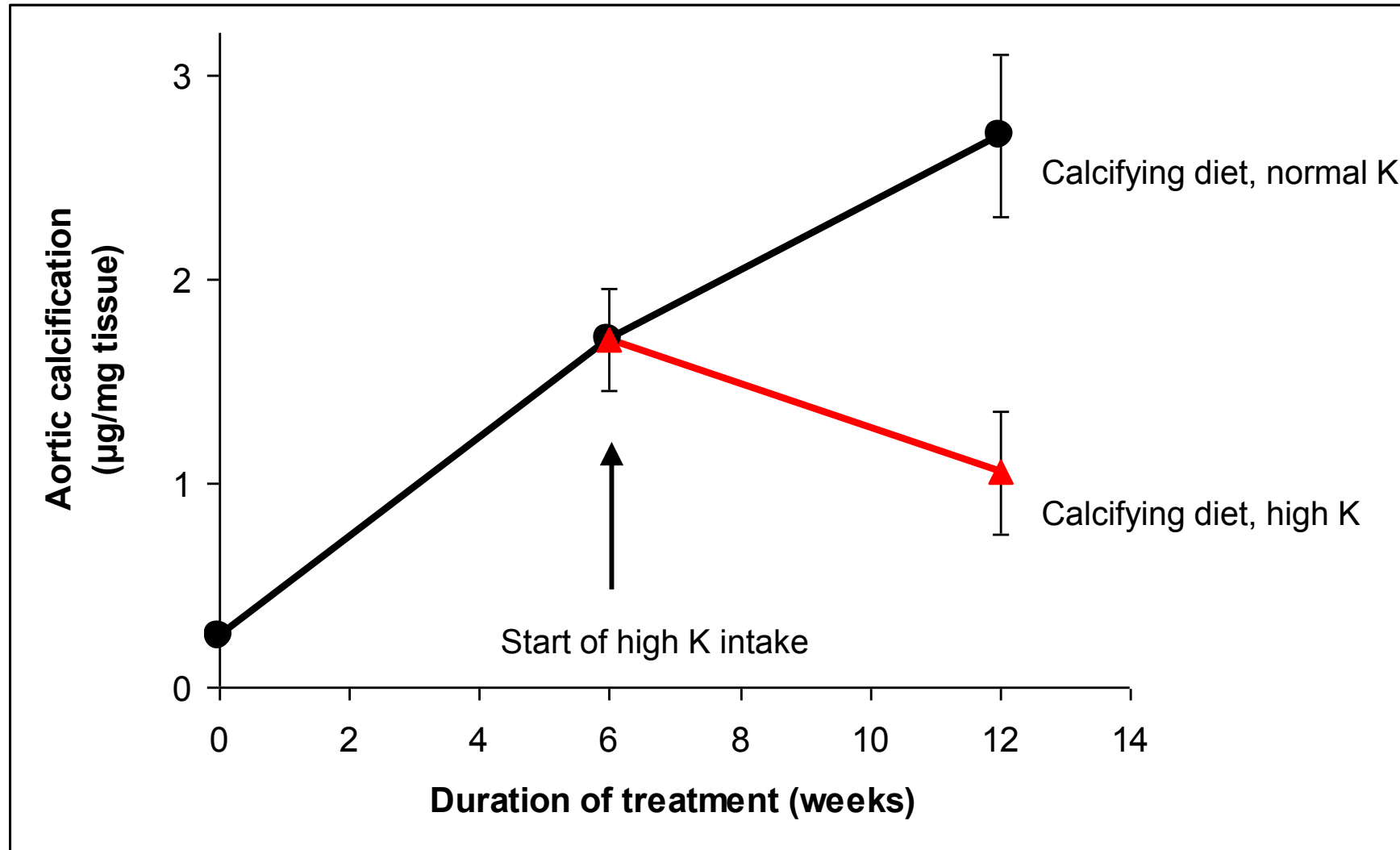
Von Kossa staining.
In black: calcification

Clinical results of vitamin K2 deficiency

K vitamins in healthy and atherosclerotic human aorta:
Biopsies from University Hospital Maastricht

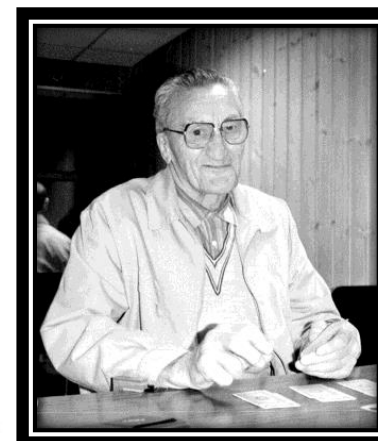
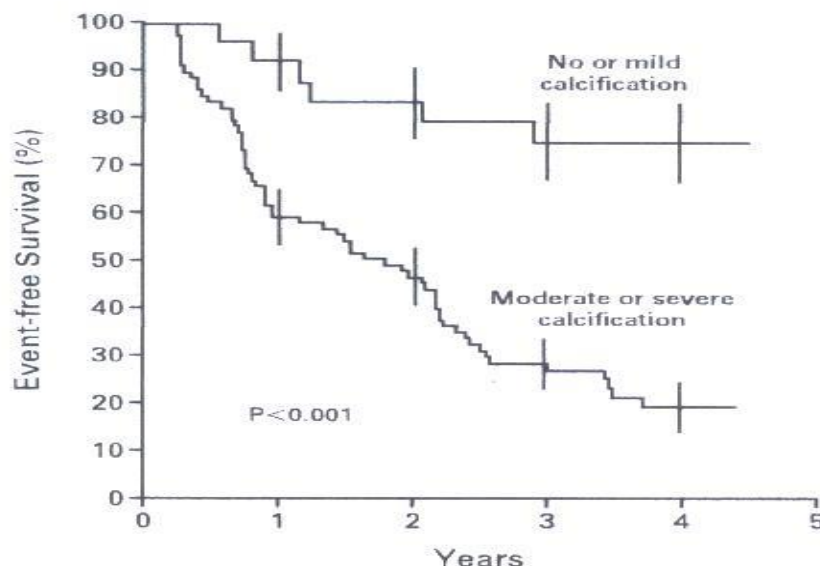
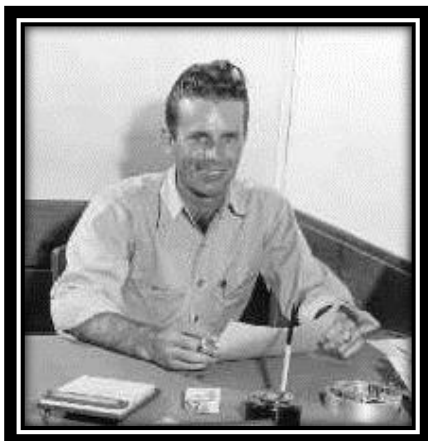


Regression of arterial calcification by vitamin K in rats



Calcification of arteries

Rosenhek, et al. *New England Journal of Medicine* 2000



Age < 40 years; calcification > 1000 units: Biological age 70 years!

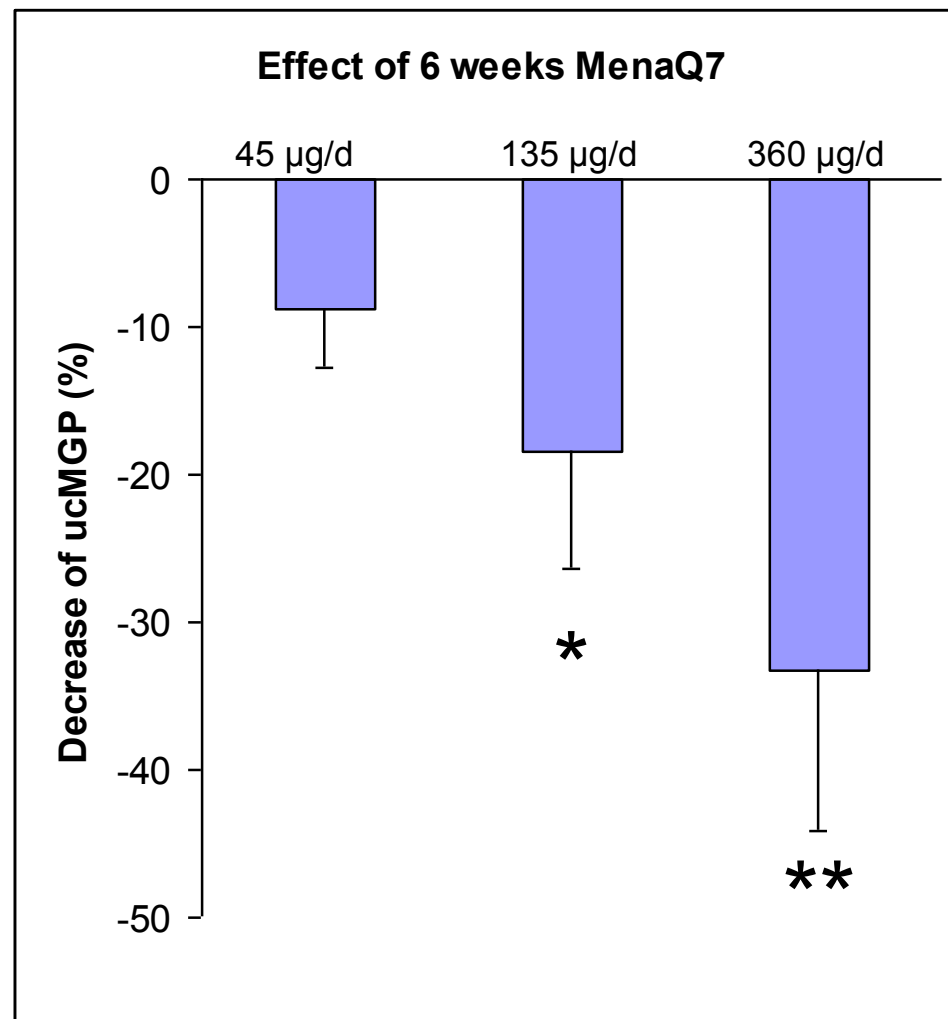
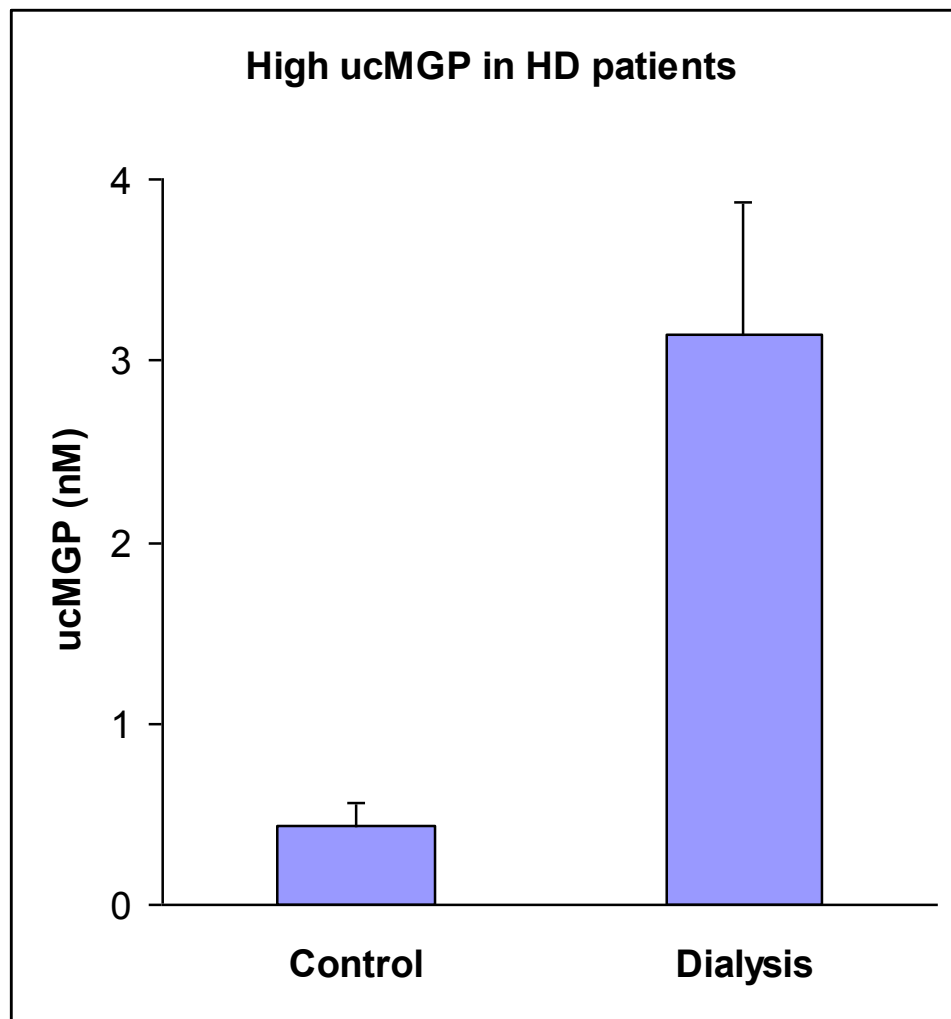
Scores > 400 added up to 30 years to younger subjects

Calcium score < 10: Reduction in observed age by 10 years in subjects older than 70 years

Ref: Shaw et al. *Atherosclerosis* vol 188, p. 112 ; 2006

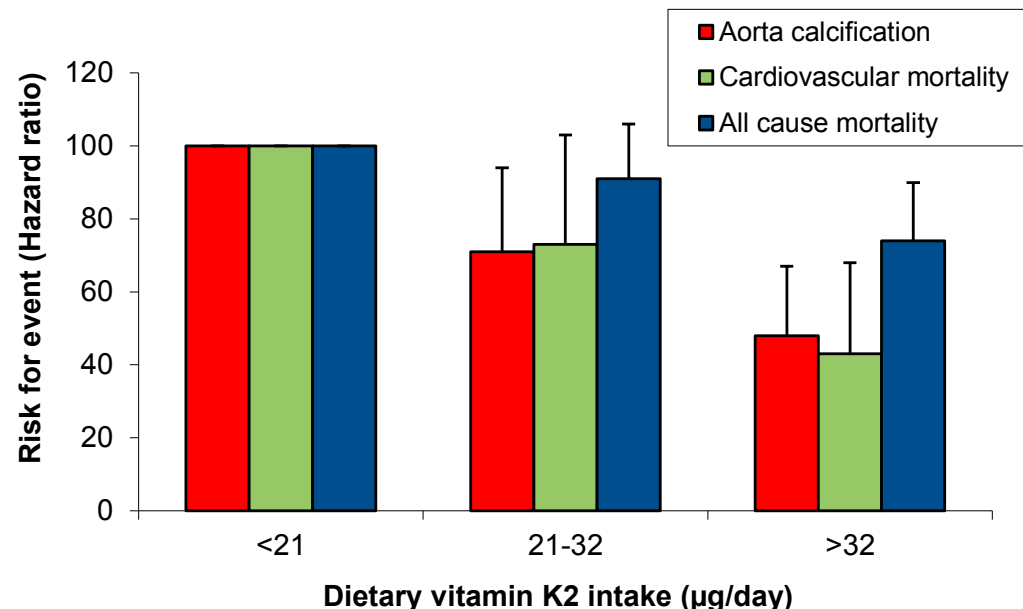
10377 asymptomatic individuals (♀ & ♂) referred by GP to coronary artery calcium screening in the US. 5 years follow-up for all-cause mortality

MenaQ7 helps decrease dp-ucMGP in HD patients



The Rotterdam Study: Importance of vitamin K2

- Over 4.800 people
- healthy elderly,
55 years and older
- 10 years follow-up
- Cross-sectional analysis
- **50% reduction of
arterial calcification**
- **50% reduction of
cardiovascular death**
- **25% reduction of
all cause mortality**

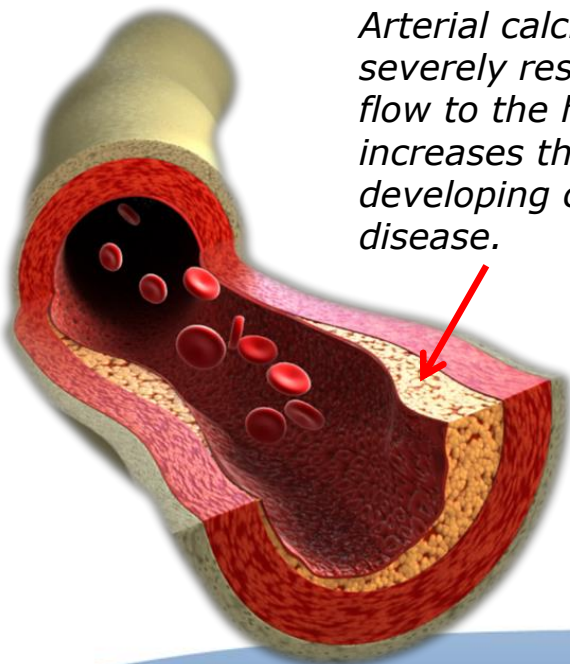


New study:

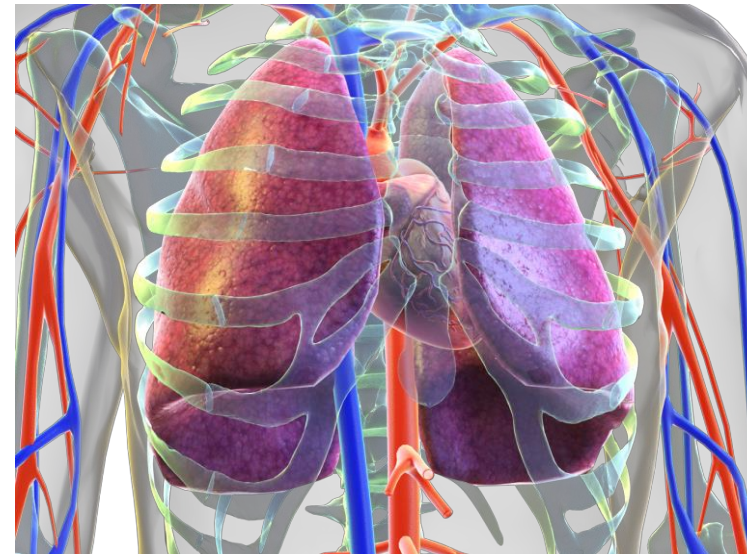
- 16,000 persons (aged 49-70)
- for every 10 µg increase in ingestion of vitamin K2 (higher menaquinones) the cardiovascular disease risk decreases by 9%. (Gast et.al, 2008)

MenaQ7[®] - Key to better heart health

- Healthy arterial tissues have been shown to contain 100 times more vitamin K2 than calcified tissues – and no K1!
- Increased consumption of natural vitamin K2 has been shown to significantly improve cardiovascular health and reduce the risk of a negative event.



Arterial calcification can severely restrict blood flow to the heart and increases the risk of developing cardiovascular disease.



General conclusions

- **New vital functions of vitamin K have been discovered not related to blood clotting**
- In all cases, vitamin K or K-related proteins play regulatory roles in important physiological processes
- **Vitamin K insufficiency of extra-hepatic tissues is widespread in healthy adults**
- No adverse effects of very high vitamin K intake have been observed
- **Increased vitamin K2 intake may improve public health and result in prolonged life expectation.**

MenaQ7[®]
Natural Vitamin K2

Exclusive MenaQ-7
Patent Protected

MenaQ7[®]
Natural Vitamin K2

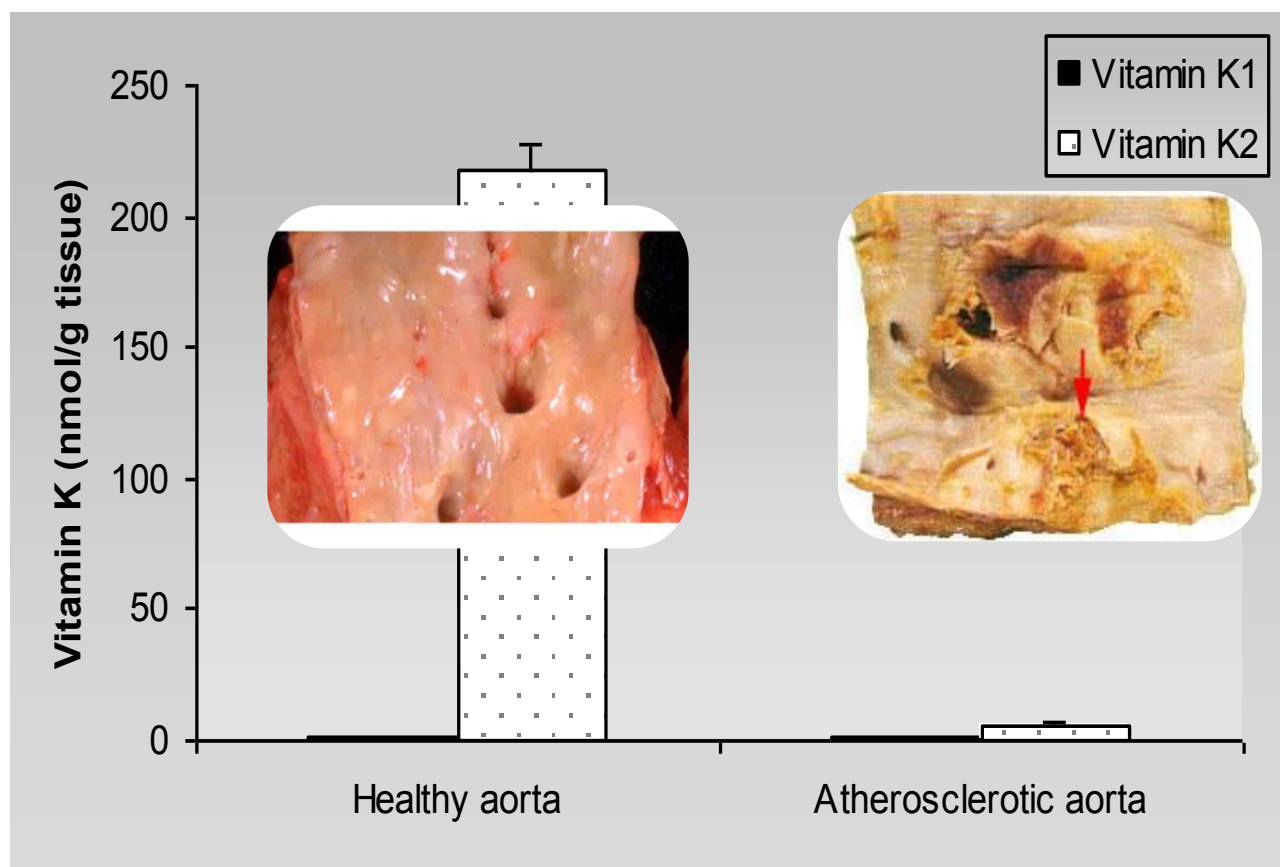
**The MenaQ7,
3-year clinical trial:**

Cardiovascular Health

NattoPharma[®]

Clinical results of vitamin K2 deficiency

K vitamins in healthy and atherosclerotic human aorta:
Biopsies from University Hospital Maastricht



Cardiovascular health: carotid artery ultrasound

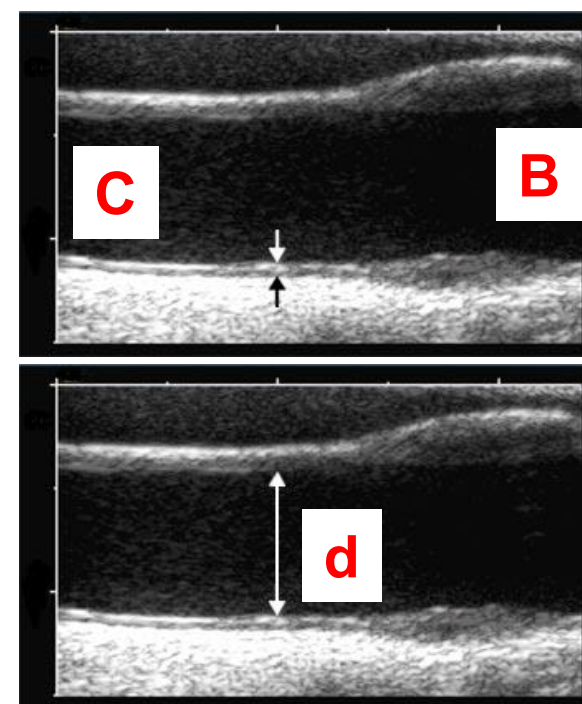
Ultrasound echography to determine vessel wall characteristics:

- Intima-media thickness (IMT)
- Diameter (**d**)
- Pulse pressure (PP)
- Distensibility coefficient (DC)
- Compliance coefficient (CC)
- Young's elasticity modulus (E)

$$DC = (2d\Delta d + \Delta d^2) / (d^2PP)$$

$$CC = \pi(2d\Delta d + \Delta d^2) / 4PP$$

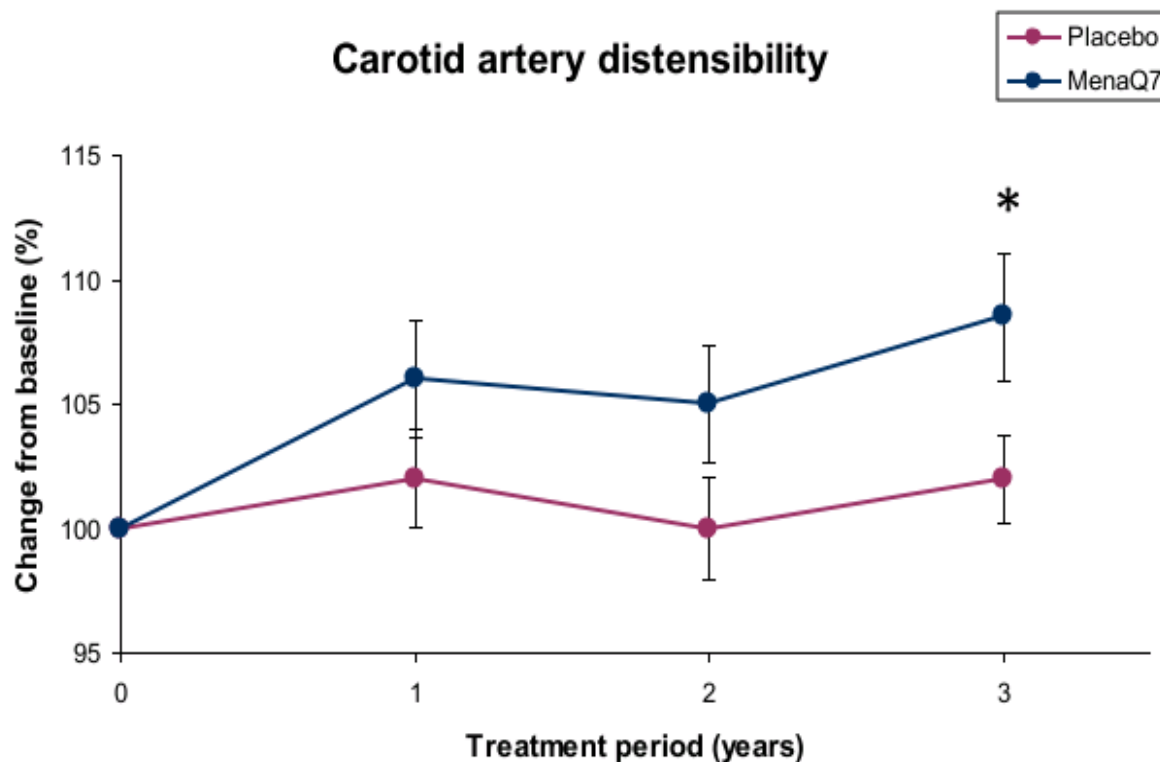
$$E = d / (IMT * DC)$$



Artery tested

- Common carotid artery **C** (before bifurcation **B**)

Cardiovascular health: carotid artery ultrasound

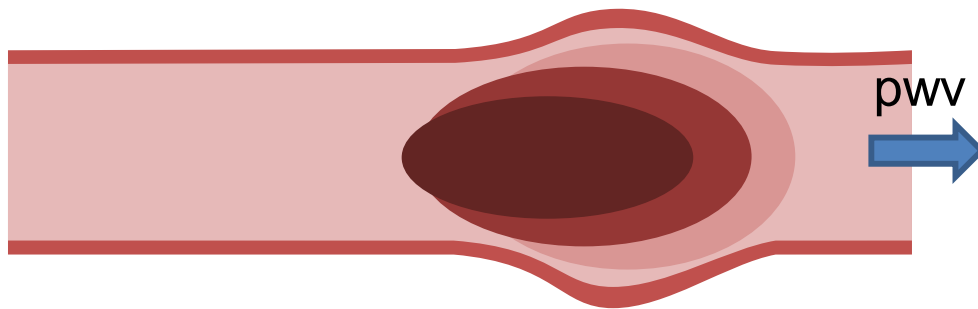


Distensibility (elasticity) is the ability for a blood vessel to stretch or dilate.

MenaQ7 gave a statistically significant increase in distensibility after **3 years** of treatment.

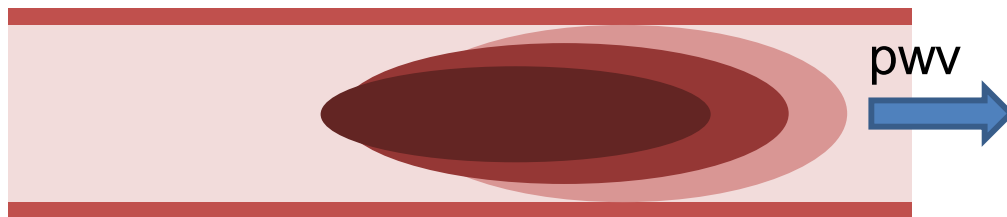
Distensibility and pulse wave velocity

Pulse wave velocity is a marker for arterial calcification



Larger effective cross section means lower pressure and slower flow = lower pulse wave velocity (pwv)

High distensibility
(elastic vessel wall)
More oxygen and nutrients delivered by the blood stream.



Smaller effective cross section means higher pressure and faster flow = higher pulse wave velocity (pwv)

Low distensibility
(stiff vessel wall)
Less oxygen and nutrients delivered by the blood stream.

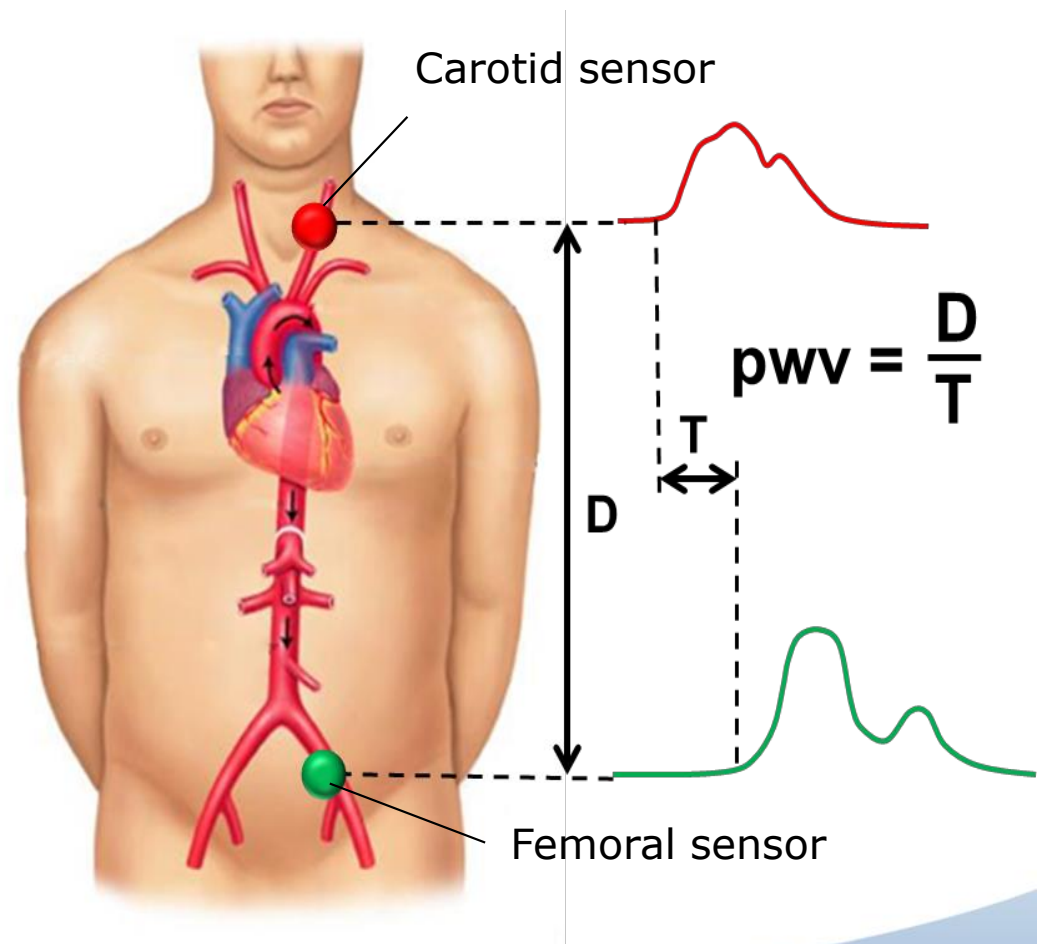
Cardiovascular health measurements

Pulse-wave velocity (PWV) to determine arterial stiffness

The passing of the systolic rise of the pulse wave is measured in two standardized places using ultra sound and the velocity of the wave (pulse wave velocity) is then calculated.

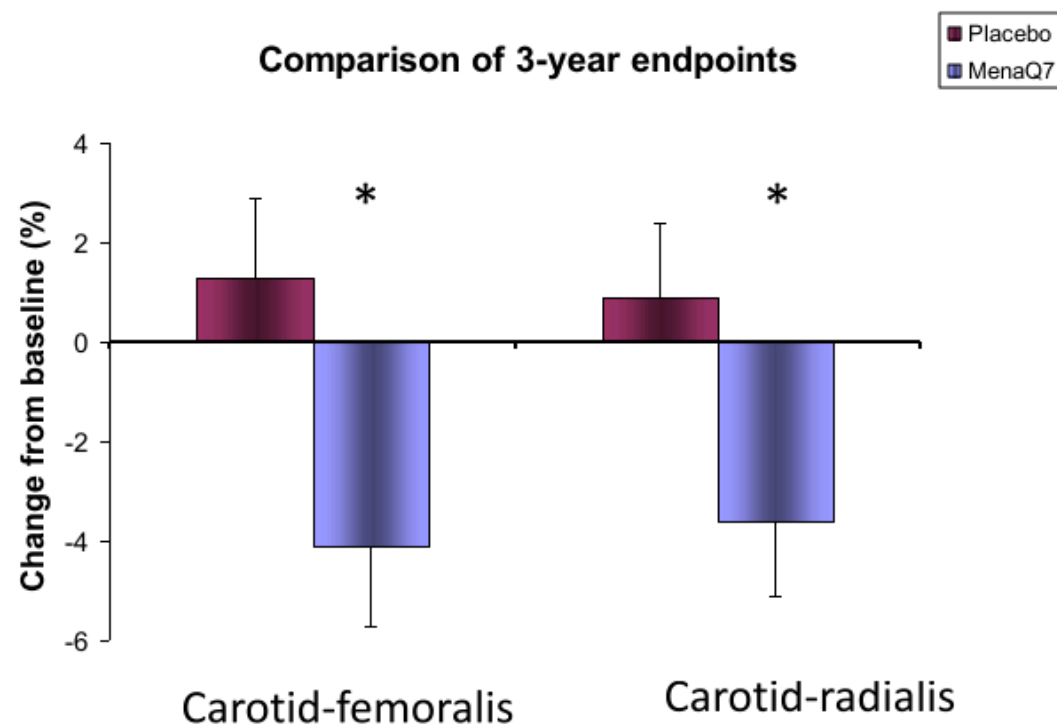


Complior SP



Pulse-wave velocity

- MenaQ7 **reduced** age-induced decrease in carotid-femoral PWV
- MenaQ7 significantly **improved** PWV

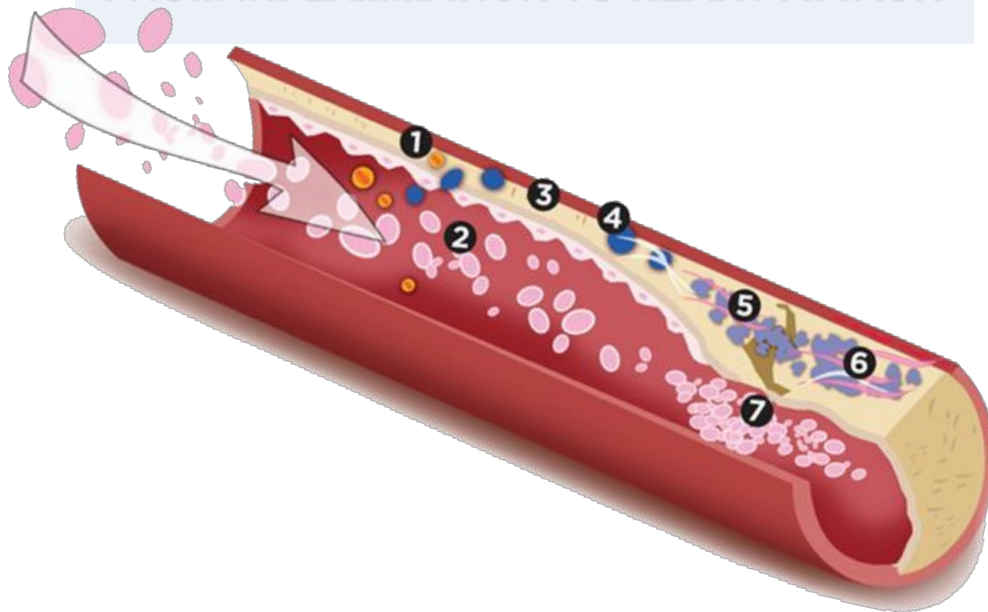


Three factors contributing to improved pulse wave velocity

- **Reduced** arterial calcification
- **More elastic** collagen in the vessel walls
- **Better physiological function** of the smooth muscle cells in the vessel walls

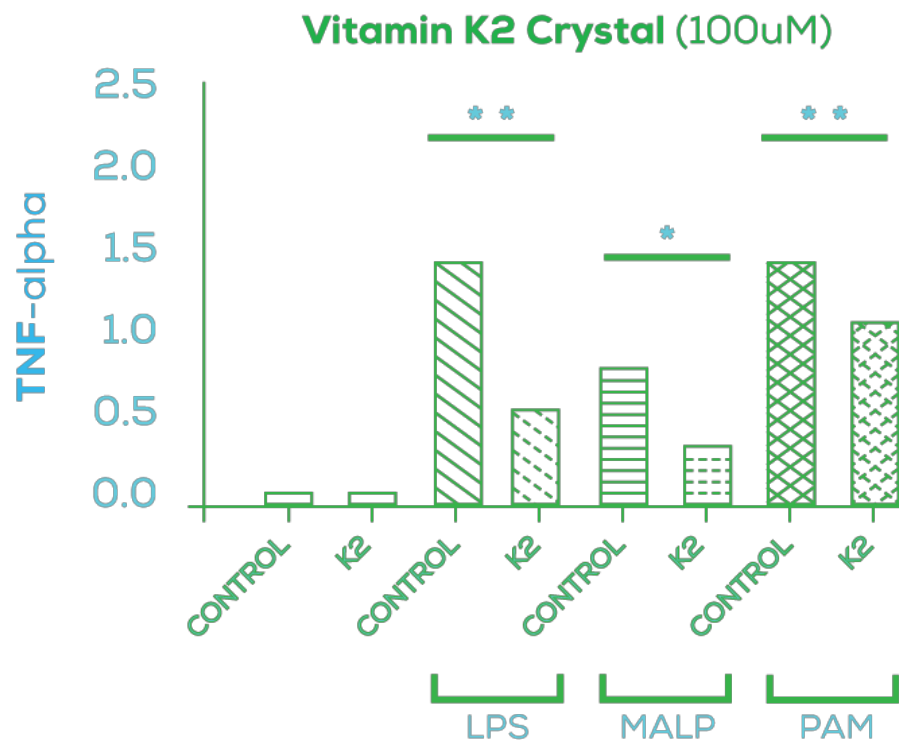
Inflammation as a Key Pathogenetic Mechanism in Atherosclerosis

FROM INFLAMMATION TO HEART ATTACK



- **Cardiovascular disease is a chronic disease** characterized by the presence of inflammation
- **Tumor necrosis factor- α (TNF- α)** is proinflammatory cytokine, which is implicated in the process of vascular calcification

MenaQ7[®]Crystals inhibits production of pro-inflammatory marker in human macrophages



- **High purity natural vitamin K2, 98% menaquinone-7 (MenaQ7[®]Crystals)** was evaluated for its potential to inhibit production of pro-inflammatory markers
- **Pretreatment of human monuclear cells with (MenaQ7[®]Crystals)** led to significant inhibition of TNF-alpha production after stimulation with TLR ligands (LPS, MALP, PAM)

Importance of MenaQ7 for vascular health

General:

- In the MenaQ7 group, pulse wave velocity was substantially and significantly lower than in the placebo group after 3 years of treatment
- Moreover, the pulse wave velocity also **significantly improved** relative to baseline in the MenaQ7 group
- **Thus: MenaQ7 not only prevents vascular damage, it also helps recover arteries from pre-existing stiffening**

This is the first time in history that vascular improvement by vitamin K (any form) was demonstrated in humans