



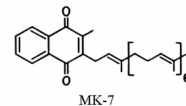
NATTO Essence

Science Behind

LEE Chee Cheow
Chief Scientific Officer



Vitamin K functions:



- Primary function is to regulate normal blood clotting
- Vitamin K₂ promote mineralization of bone, while inhibiting mineralization (calcification) of vessels.

• **Osteoporosis and Coronary Heart Disease are strongly associated with lower levels of K₂ (menaquinone).**

Causes of Vitamin K deficiency:

- Liver damage or disease (e.g. alcoholics), fibrosis, cirrhosis
- Gastrointestinal problems (decrease the absorption): Inflammatory bowel diseases, abdominal surgeries, obstructions in the bile duct, cystic fibrosis, sprue, Crohn's disease, colitis
- Medications (reduce the absorption): antibiotics.
- Stringent diets, taking anticoagulants.

Vitamin K

Phylloquinone (K₁)
 Natural K1
 Synthetic K1



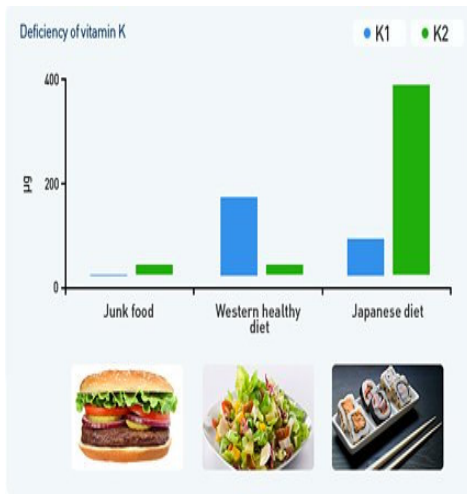
- Vitamin K₁ :**
- Leafy green vegetables such as spinach , cabbage, cauliflower, broccoli & brussels sprouts
 - Some fruits such as avocado, kiwifruit and grapes

Menaquinone (K₂)
 Menaquinone-4 MK4
 Menaquinone-7 MK7



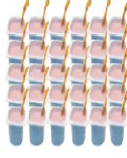





- MK-4 :**
 synthesized by animal tissues
 Found in meat, eggs, dairy
- MK-7 :**
 synthesized by bacteria during fermentation. Found in Natto

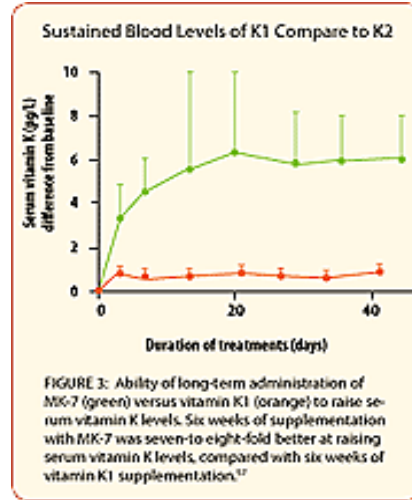
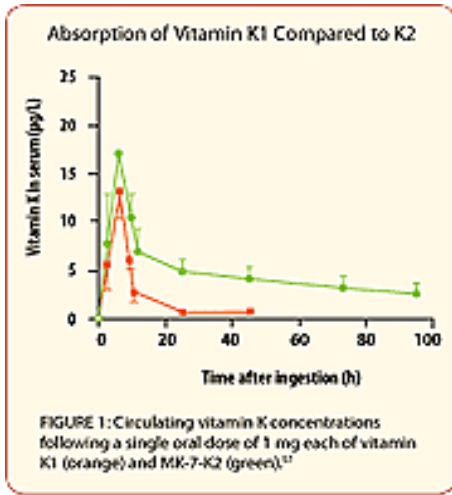
Vitamin K intake



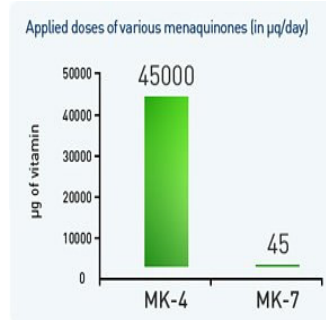
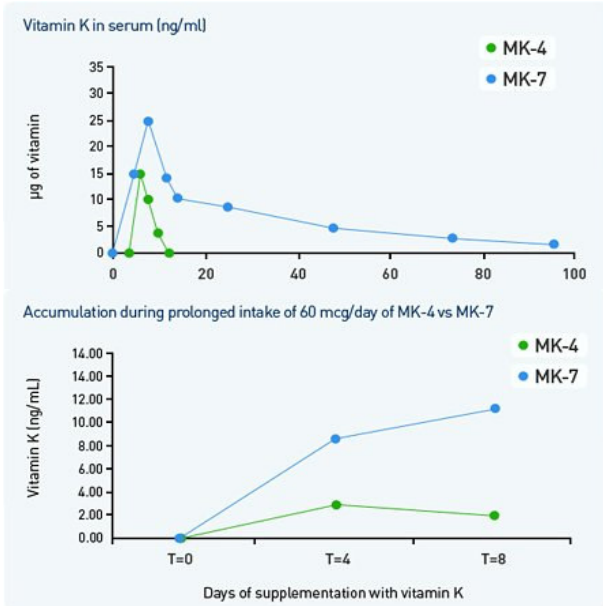
**To obtain 45 mcg of Vitamin K2
 one would have to eat:**

 beef 4090 g = 8.8 lbs	 milk 5 liters = 1.32 gallons	 whole yoghurt 5 liters = 1.32 gallons
 soft cheese 80 g = 0.175 lbs	 hard cheese 59 g = 0.129 lbs	 egg yolk 140 g = 8 yolks

Bioavailability K2 is superior to K1



Natural vitamin K₂ as menaquinone-7 (MK-7) is the most bioavailable, longest lasting and most bioactive form of Vitamin K2

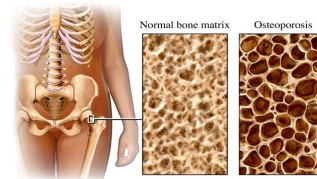


MK-4 has to be applied in very high pharmacological doses (milligrams) to demonstrate benefits for bone and heart health.

In case of MK-7, doses in micrograms – 1000x less - are sufficient for significant bioactive effect

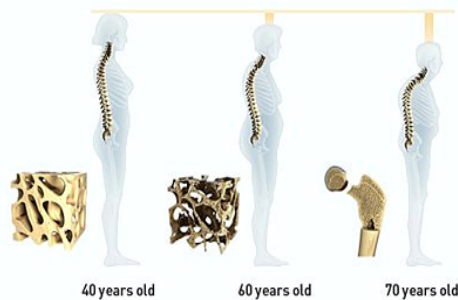
Osteoporosis

- A disease of bones that leads to reduced bone mineral density (BMD) and increased risk of fracture.



- **Primary type 1 : postmenopausal osteoporosis.** The form of osteoporosis most common in women after menopause
- **Primary type 2 : senile osteoporosis** occurs after age 75 and is seen in both females and males at a ratio of 2:1.

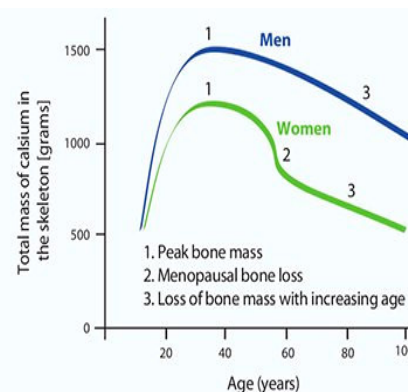
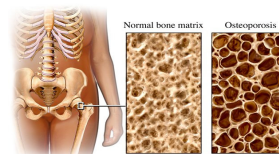
Osteoporosis



- **Secondary osteoporosis** may arise at any age and affects men and women equally:
 - chronic predisposing medical problems or disease
 - prolonged use of medications such as glucocorticoid (anti inflammation steroids hormone)

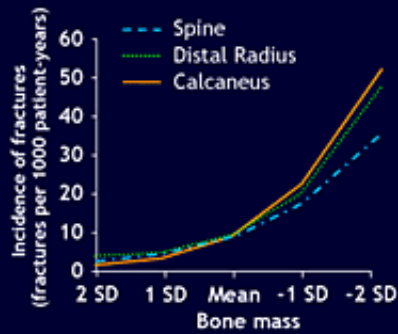
Osteoporosis Risk Factors

1. Women: estrogens deficiency following menopause
2. Men: decrease in testosterone levels
3. Excess alcohol
4. Vitamin D deficiency
5. Tobacco smoking
6. Malnutrition— low dietary calcium and/or phosphorus, magnesium, zinc, boron, iron, fluoride, copper, vitamins A, K, E and C
7. Diets high in animal protein (increased urinary calcium loss from the bones)
8. High Ratio of n6 to n3 fatty acids



Fracture Risk vs Bone Density

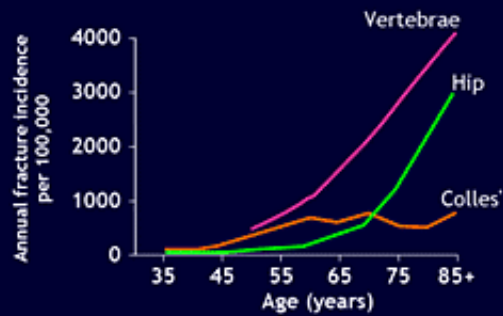
Exponential relationship between decreasing bone mass and increasing incidence of fractures



Wasnich RD et al. *J Nucl Med.* 1989;30:1166-1171.

Fracture Risk With Aging

Incidence rates for 3 common osteoporotic fractures*



*white women.

Riggs BL et al. *N Engl J Med.* 1986;314:1676-1686.

Universal Treatment Strategies

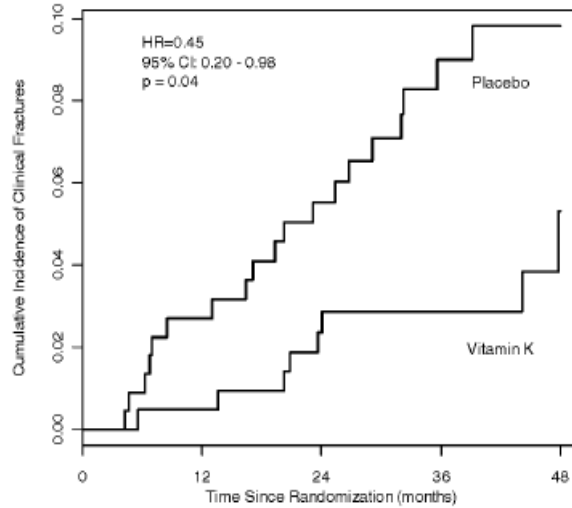
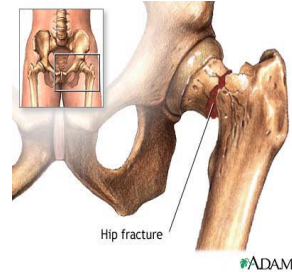
- Fall prevention
- Smoking cessation
- Hip protectors
- Weight-bearing exercise

- Diet
 - Calcium
 - Vitamin D

Does Not Improve BMD
Does Not Prevent Arterial Calcification

Yates AA et al. *J Am Diet Assoc.* 1998;98:699-706.
NIH Consensus Conference. *JAMA.* 1994;272:1942-1948.

Anti Osteoporosis: Vitamin K Reduce Fracture



No. at Risk	0	12	24	36	48
Placebo	223	213	195	127	42
Vitamin K	217	212	198	145	61

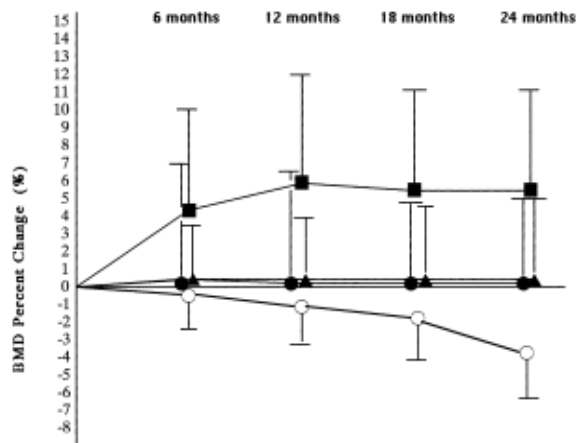
Vitamin K Supplementation in Postmenopausal Women with Osteopenia (ECKO Trial): A Randomized Controlled Trial; PLoS Med. 2008 October; 5(10): 1-12.

Vitamin K₂ + D₃

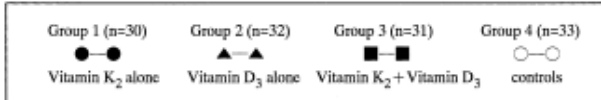
Can
Improve
BMD



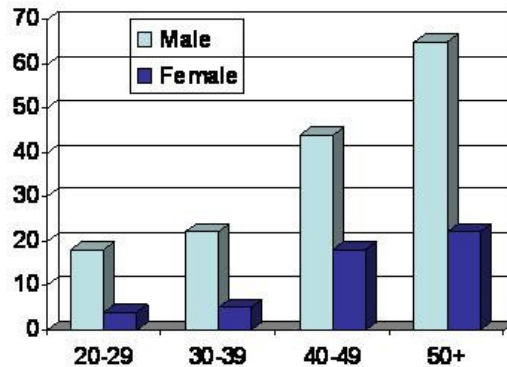
Effect of continuous combined therapy with vitamin K2 and vitamin D3 on bone mineral density and coagulofibrinolysis function in postmenopausal women; Maturitas 41 (2002) 211-221



Group 1—Group 2 ;	n.s.	n.s.	n.s.	n.s.
Group 1—Group 3 ;	P<0.01	P<0.01	P<0.01	P<0.01
Group 1—Group 4 ;	n.s.	n.s.	P<0.05	P<0.05
Group 2—Group 3 ;	P<0.001	P<0.001	P<0.001	P<0.001
Group 2—Group 4 ;	n.s.	n.s.	P<0.01	P<0.001
Group 3—Group 4 ;	P<0.001	P<0.001	P<0.001	P<0.001



Coronary Heart Disease



Prevalence of Coronary Artery Calcification

Coronary Artery Calcification Begins Earlier in Males

With Onset of Menopause, Women Lose Calcium From Bones and Increase Their Risk For Cardiovascular Disease by 360%

- Atherosclerosis is a process in which the inner lining of the arteries get fat deposition, on which calcium is also deposited and gradually the lumen gets narrowed.
- **Calcification of coronary arteries markedly increases heart attack risk**

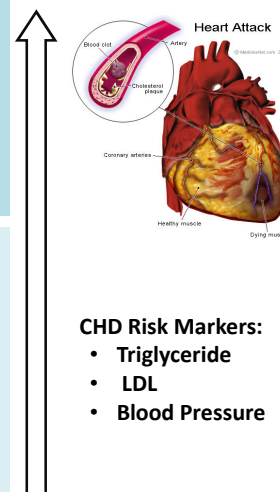
Current Prevention & Treatment of CHD

Medications Intervention

- Cholesterol lowering medications, such as statins.
- Nitroglycerin (vasodilator)
- ACE inhibitors (hypertension)
- Calcium channel blockers /beta-blockers (hypertension)
- Aspirin

Lifestyle changes

- Weight control
- Smoking cessation
- Exercise
- Healthy diet: reduction of animal based foods and an increase in plant based foods.
- **Increase omega-3 fatty acid intake**

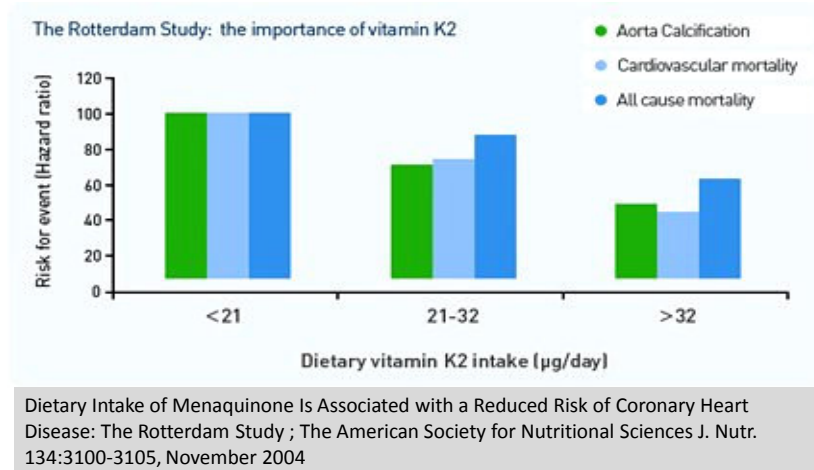


CHD Risk Markers:

- Triglyceride
- LDL
- Blood Pressure

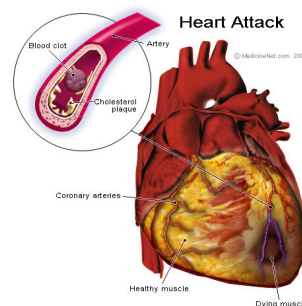
Vitamin K2 reverses arterial calcification

- Only natural vitamin K₂ consumption has been linked to the inhibition of arterial calcification



Prevention of coronary heart disease

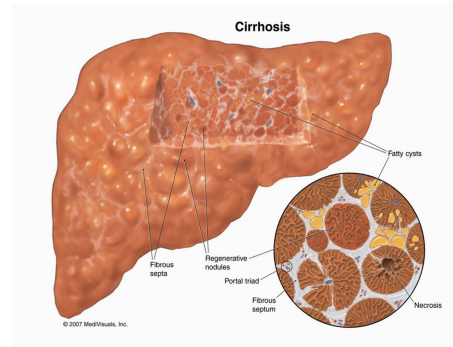
- For every 10mcg vitamin K₂ consumed, the risk of coronary heart disease was reduced by 9%



A high menaquinone reduces the incidence of coronary heart disease in women; Nutrition, Metabolism and Cardiovascular Diseases; J.numecd.2008.10.004

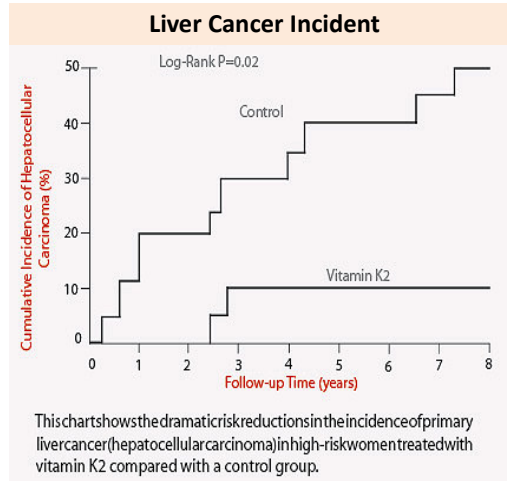
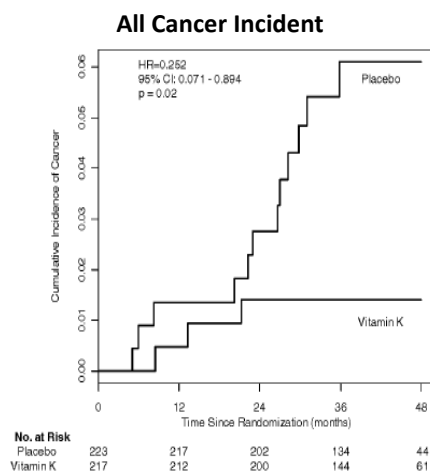
Alcoholic & Liver Diseases

- Vitamin K-dependent coagulation factors are synthesized in the liver.
- Consequently, severe liver disease results in lower blood levels of vitamin K-dependent clotting factors and an increased risk of uncontrolled bleeding



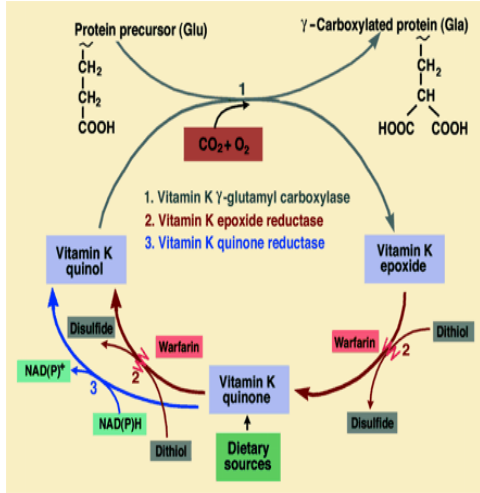
Vitamin K is used to reduce risk of bleeding in liver disease

Cancer Prevention



Role of Vitamin K2 in the Development of Hepatocellular Carcinoma in Women with Viral Cirrhosis of the Liver.
JAMA, July 21, 2004—Vol 292, No. 3

Person taking Anticoagulant



• A constant dietary intake of vitamin K is recommended (90-120 mcg/day) for patients on vitamin K antagonists like warfarin



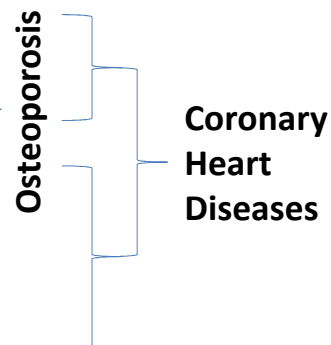
• Menaquinone K_2 is not inhibited by salicylates as happens with K_1 , so menaquinone supplementation can alleviate the chronic vitamin K deficiency caused by long term aspirin use

Vitamin K cycle

New Generation High Safety OTC Anti Osteoporosis & CHD prevention FORMULATION

Synergetic Formulation

Active Ingredients	Amount / 300mg softgel
Natto Extract natural Vitamin K2 as MK7	30 mg 60 μg
Vitamin D3	400 IU
Vitamin E	10 mg
Lecithin	20 mg
Omega-3 DHA	30 mg
Omega-3 EPA	45 mg



CLINICAL APPLICATION

INDICATIONS	Rx
Improve Bone Mineral Density Anti Osteoporosis	300mg b.i.d
Coronary Heart Diseases Cardiovascular Disease	300mg b.i.d
Cancer prevention Leukaemia, Lung, Prostate	300mg once
Liver Diseases: Alcoholic, Cirrhosis, Fibrosis Chronic Viral Hepatitis B & C	300mg b.i.d
Vitamin K deficiency: Inflammatory bowel diseases Long term Aspirin consumption	300mg b.i.d

Contra Indication:

Patients on warfarin potassium therapy

Warfarin exhibits an anticoagulant action and prophylactic action against thrombosis by inhibiting the metabolic cycle of vitamin K in the liver cell and producing non-coagulant blood coagulation factors. vitamin K2 preparation diminishes the action of warfarin when co administered with it.

Special Precaution: Children below 3 years

Direction: Best take after meals.

Vitamin K Products - Competitive Analysis

	VRP Ultra K2	Glakay	Fitness+ NATTO Essence
RSP (\$/Pack)	\$65.00	\$130.00	\$48.00
Dosage	x90 capsule	x30 cap	300mg x30 softgel
Vit K2	MK4 15mg	MK4 15mg	MK7 60mcg (=MK4 60mg)
Vit D3	-	-	400 IU
Vit E	-	-	10 mg
Others			Omega 3 75 mg
Cost /45 mg MK4 serving	\$2.16	\$13.00	\$1.60

