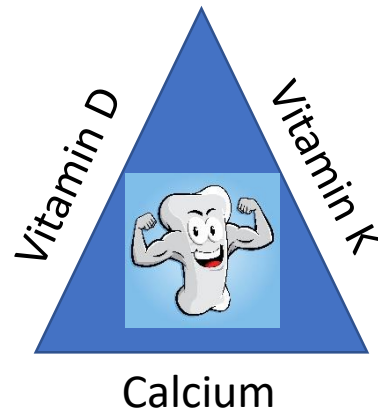


Hard arteries, soft bones – exploring the calcium, vitamin D and vitamin K triangle

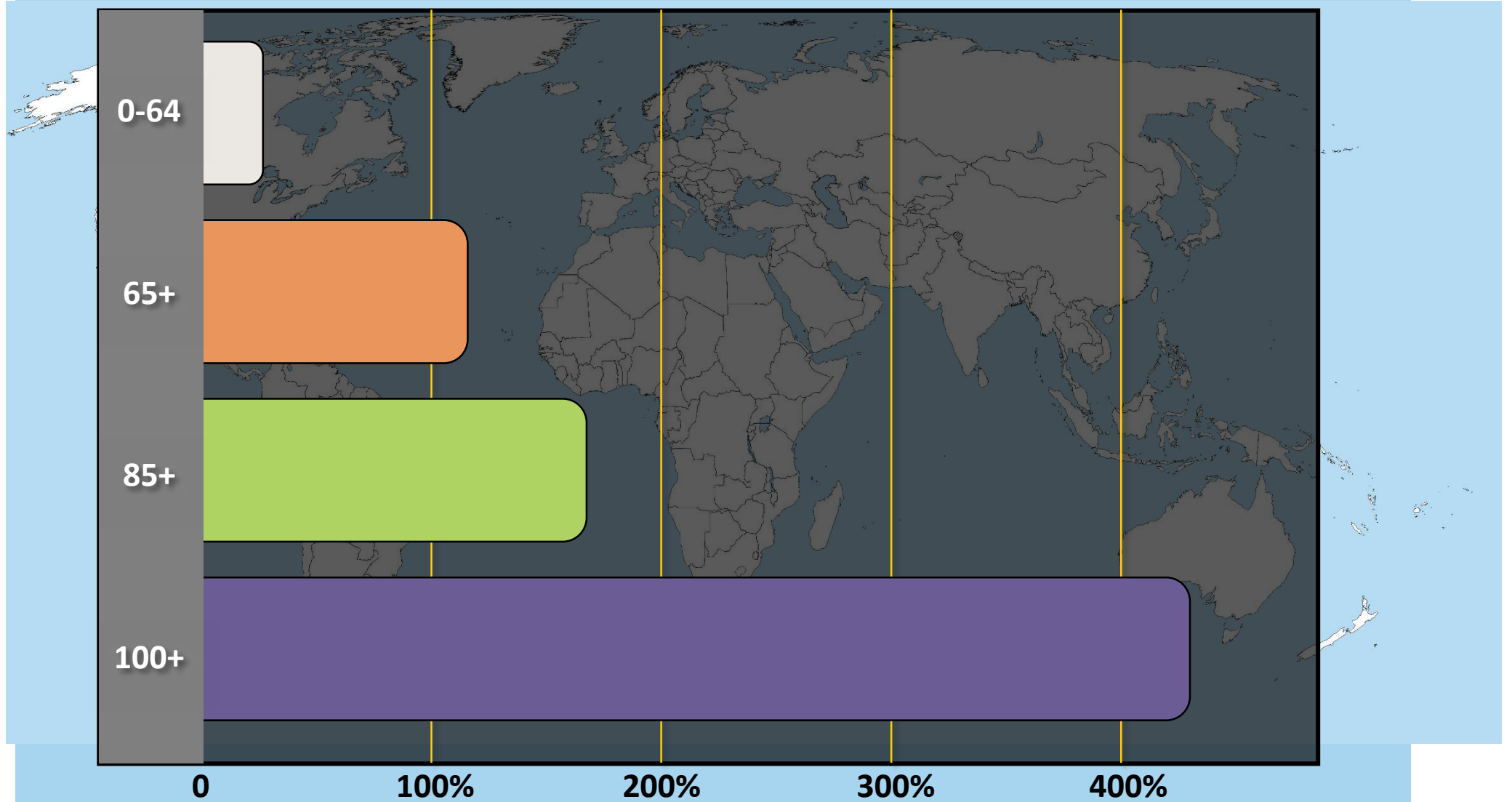


Dr Eamon Laird

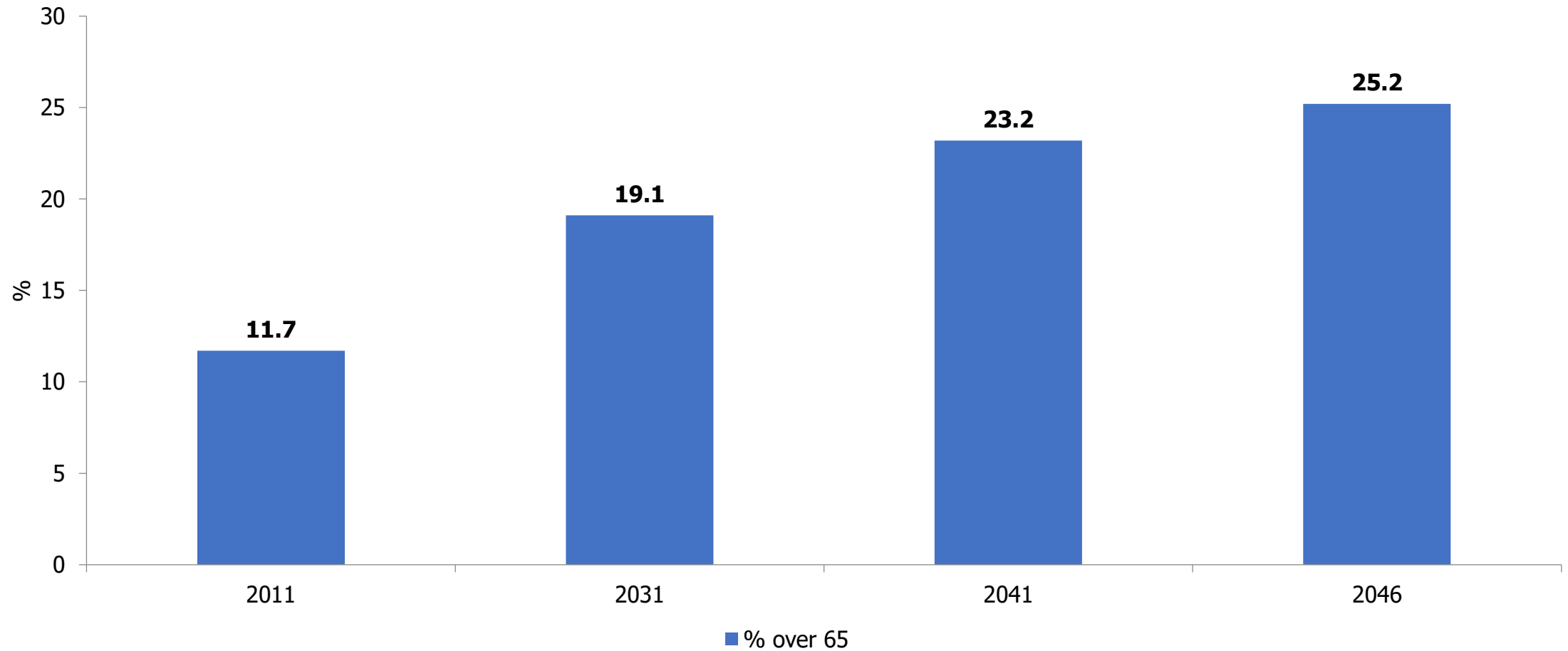
Plan

- Ageing & Chronic Disease
- Vitamin D & Calcium
- Vitamin K

Projected increase in Global Population between 2005 – 2030, by age



Population Aged >65 yrs Ireland, 2011-2046

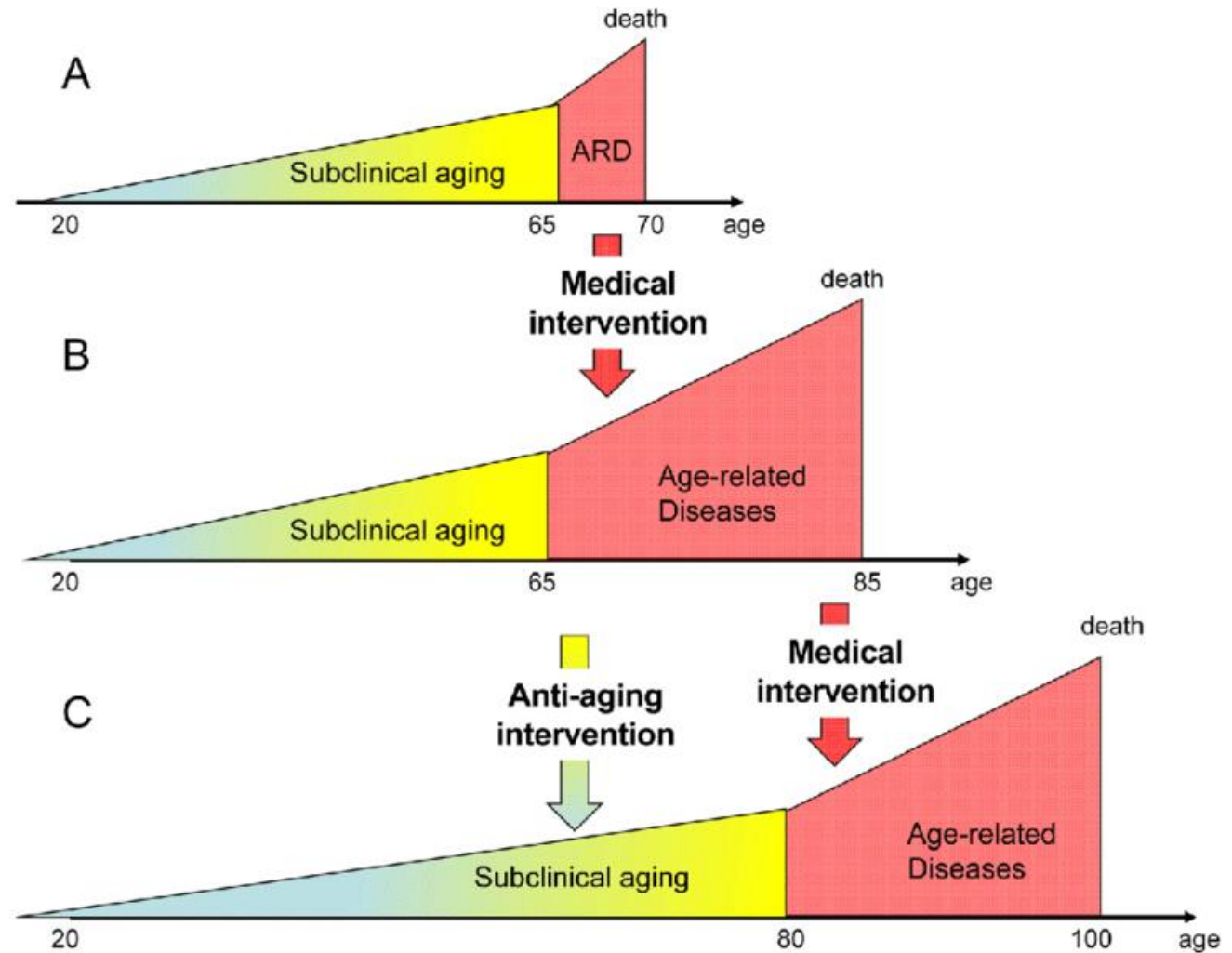
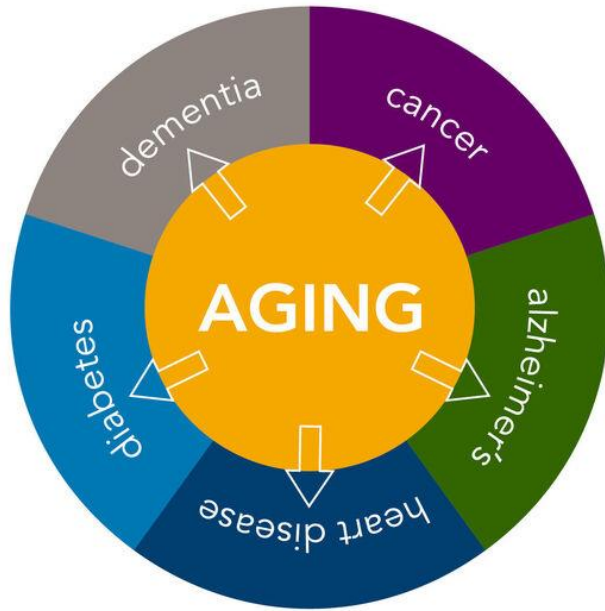


Sources:

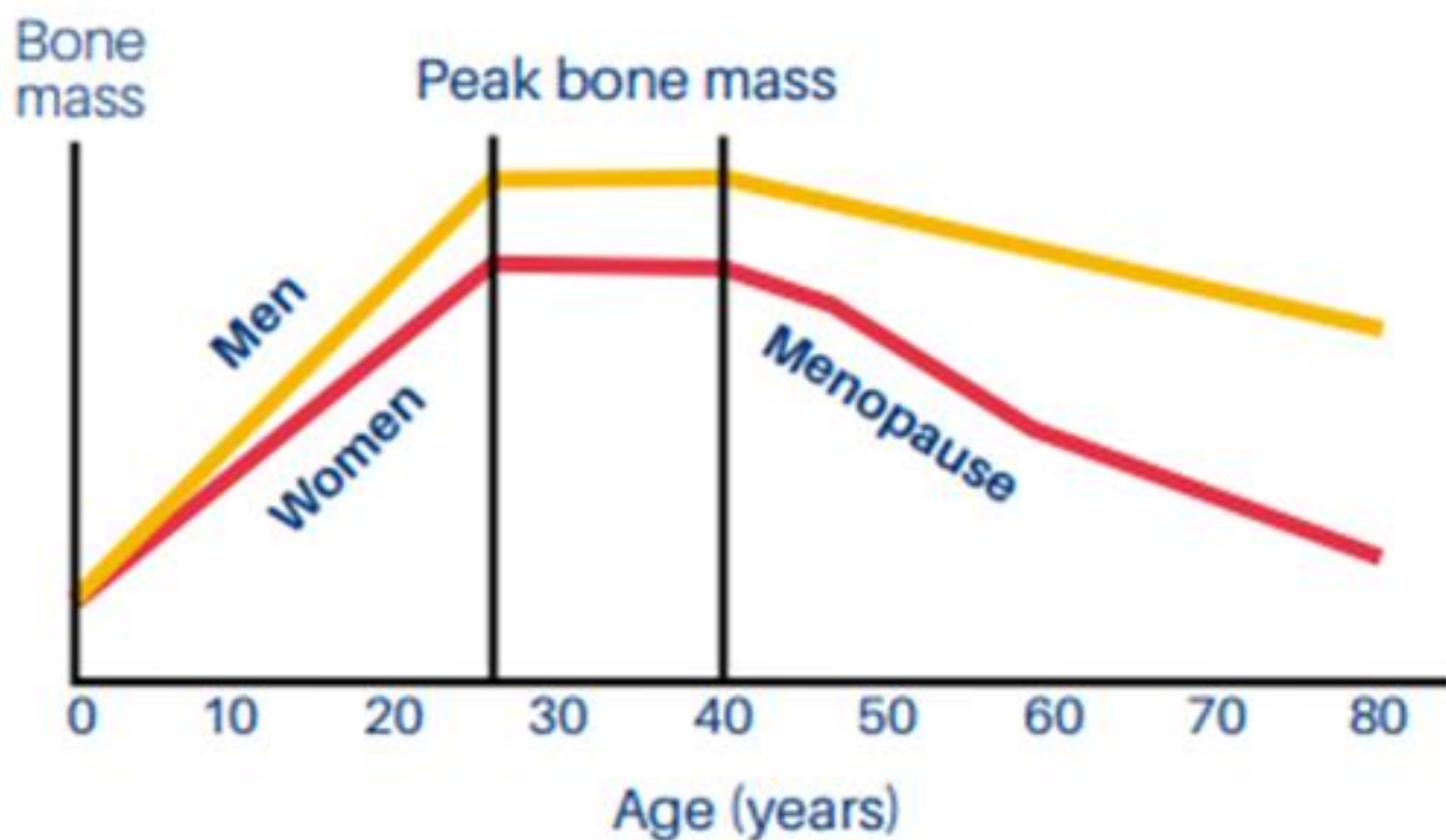
CSO Database Direct

CSO Population and Labour Force Projections 2016-2046 (M2F2 scenario)

Lifespan vs healthspan

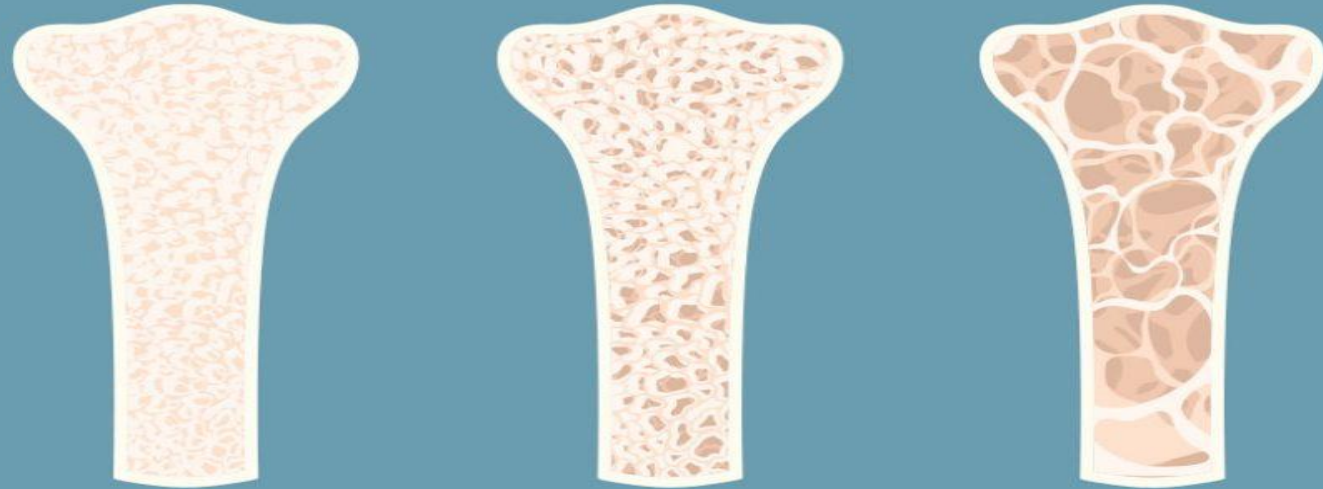


Changes in bone mass with age



Adapted from J Compston 1990

OSTEOPOROSIS STAGES



HEALTHY

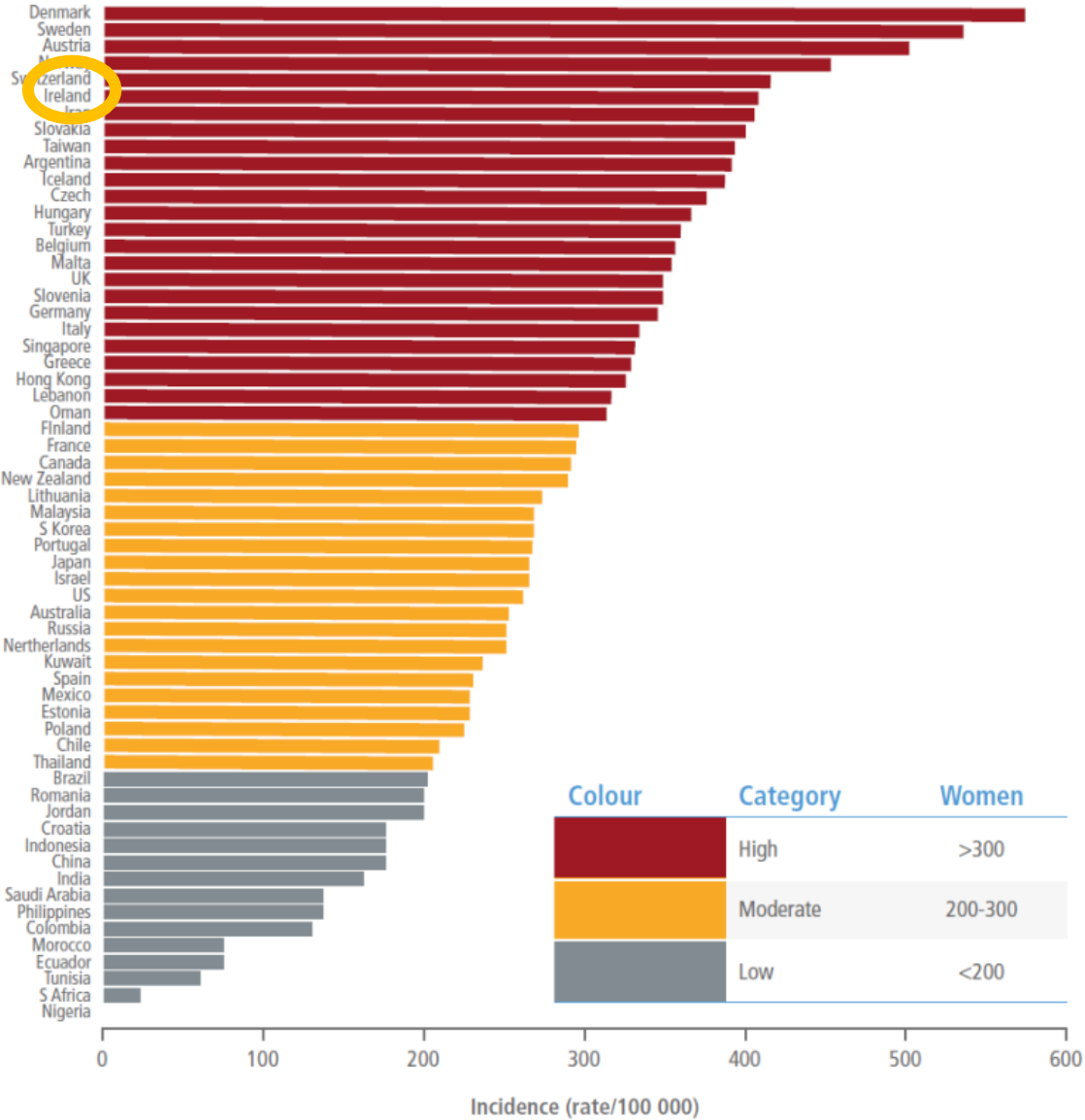


OSTEOPOROSIS



SEVERE
OSTEOPOROSIS

Osteoporosis Incidence global



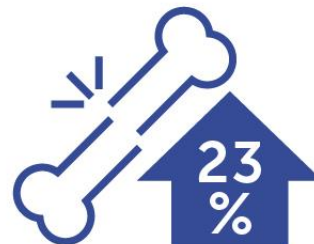
The estimated growing cost of osteoporosis and fragility fractures to healthcare systems in top 5 European countries*



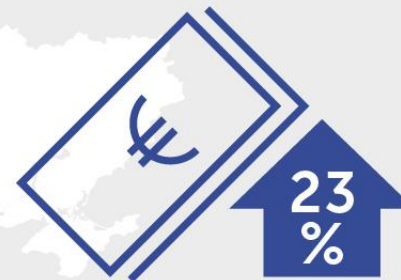
Every year, **2.5 million fractures** occur across the top 5 European countriesⁱ



with an associated healthcare cost of **€35 billion**ⁱ



This incidence rate is expected to rise by **23%** in 2030ⁱ



The annual expenditure is predicted to increase by **23%** to **€45 billion** by 2030ⁱ

*Based on GDP of Europe's five biggest countries (UK, Germany, France, Spain, Italy) in 2019^a

References

- i. IOF. BROKEN BONES, BROKEN LIVES: A roadmap to solve the fragility fracture crisis in Europe, 2018. Available at: http://share.iofbonehealth.org/EU-6-Material/Reports/IOF%20Report_EU.pdf. Last accessed: April 2021.
 - ii. Worldmeter. European Countries by population (2021). Available at: <https://www.worldometers.info/population/countries-in-europe-by-population/>. Last accessed: April 2021.
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Nutrition solutions

Evidence suggests that adequate nutritional status is one of the factors that can delay the onset of chronic disease

Thus the improvement of diet quality in older adults could be a cost effective health strategy

Vitamin D



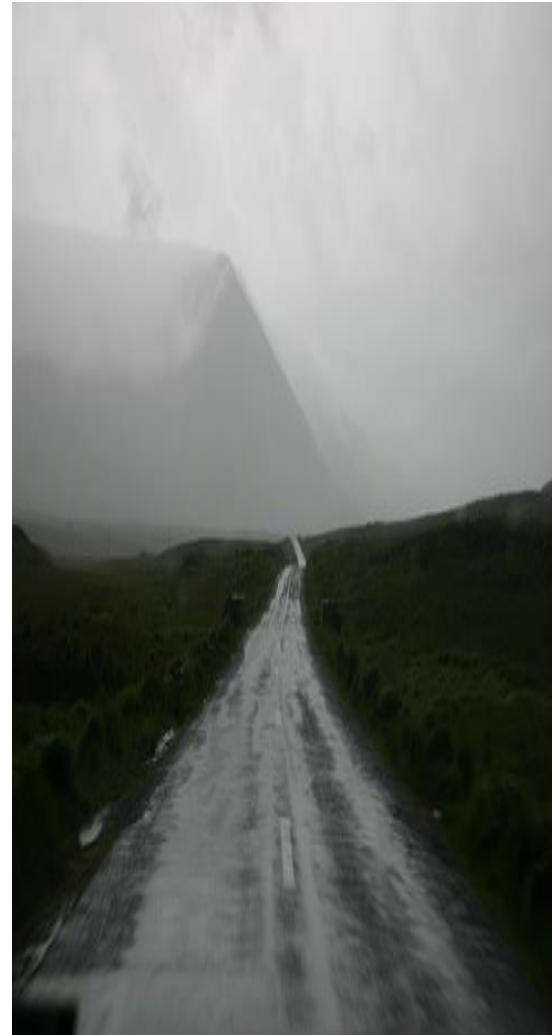
- Fat soluble vitamin found in two forms
 - Vitamin D₂ / ergocalciferol – synthesised in plants
 - Vitamin D₃ / cholecalciferol – synthesised in animals
- Two main forms in humans
 - 25(OH)D₃ (status measure – inactive form)
 - 1,25(OH)₂D₃ / calcitriol (active form)
- Primary source is dermal bio-synthesis following UVB exposure
- Geographical location is a major determinant of the rate of synthesis

Vitamin D synthesis Ireland


What we want & need!



Reality!!

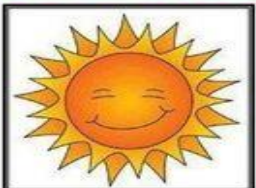


THE IRISH SUMMER...



MY FAVOURITE 2 DAYS OF THE YEAR...

MISSING



The Sun

HAVE YOU SEEN THIS?

Last seen in Ireland in early May.
If you have any information, or have seen the Sun, contact your local Gardai, or TD immediately

PLEASE - INFORMATION NEEDED



Wild Salmon =
700 Units Vit D /100g

Farmed Salmon =
200 Units Vit D /100g



1 Egg = 60 Units Vit D

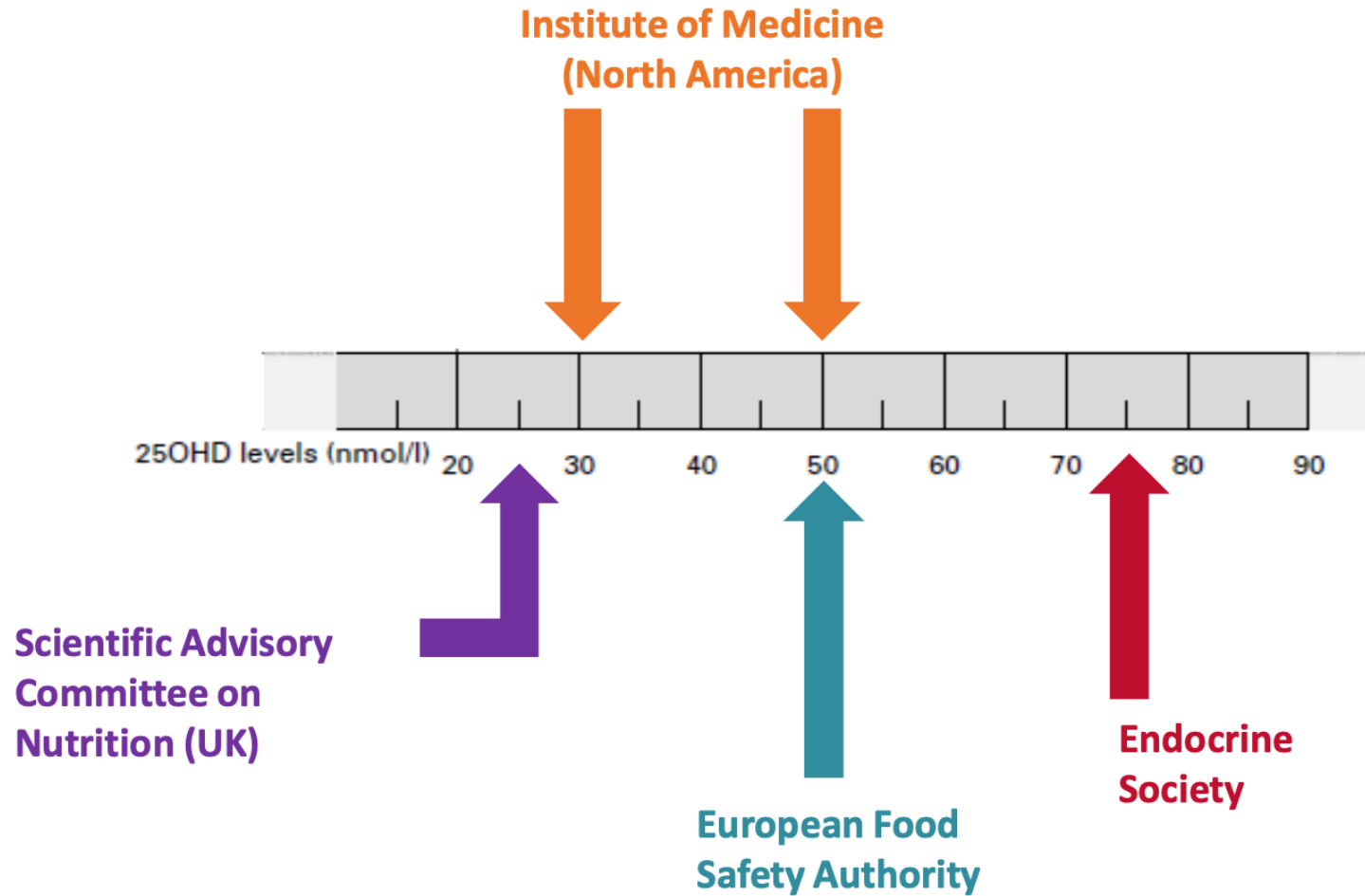


Fortified Cereals
One 35g Serving =
120 Units Vitamin D



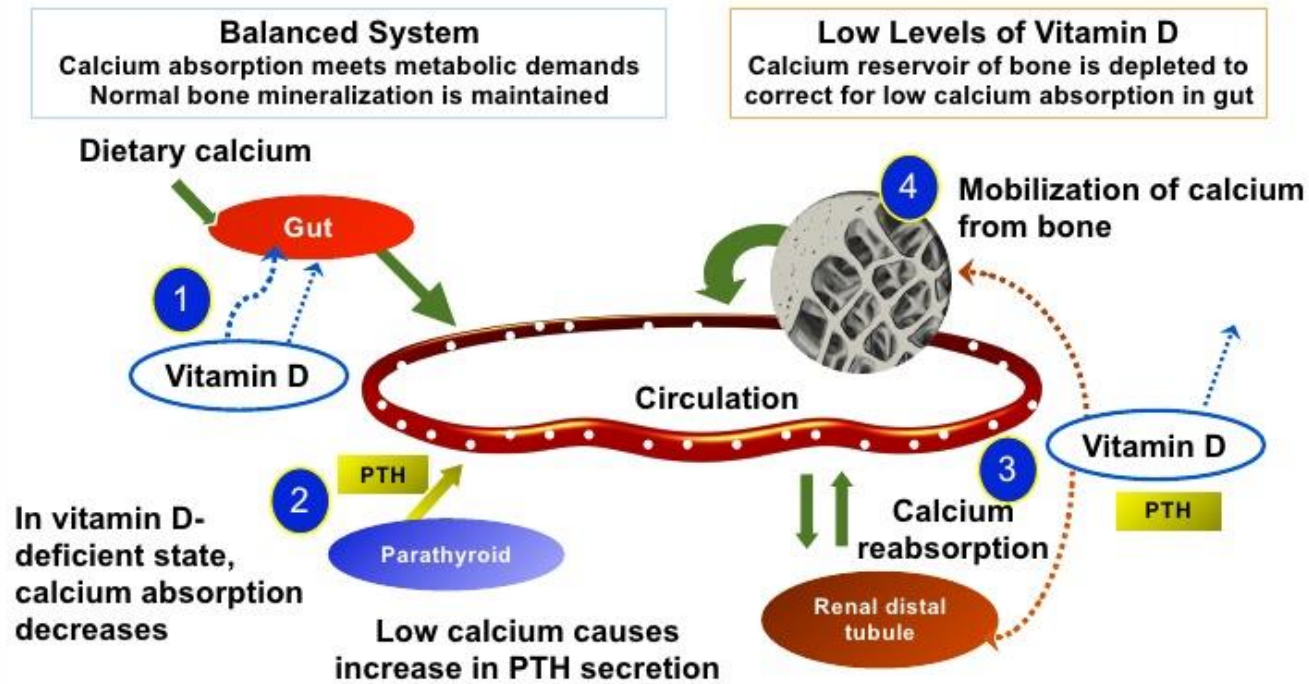
Ordinary Milk =
20 Units / Litre
**Super Milk =
800 Units / Litre**
**Other Fortified Milks
400 Units / L**

Cut-points 25(OH)D



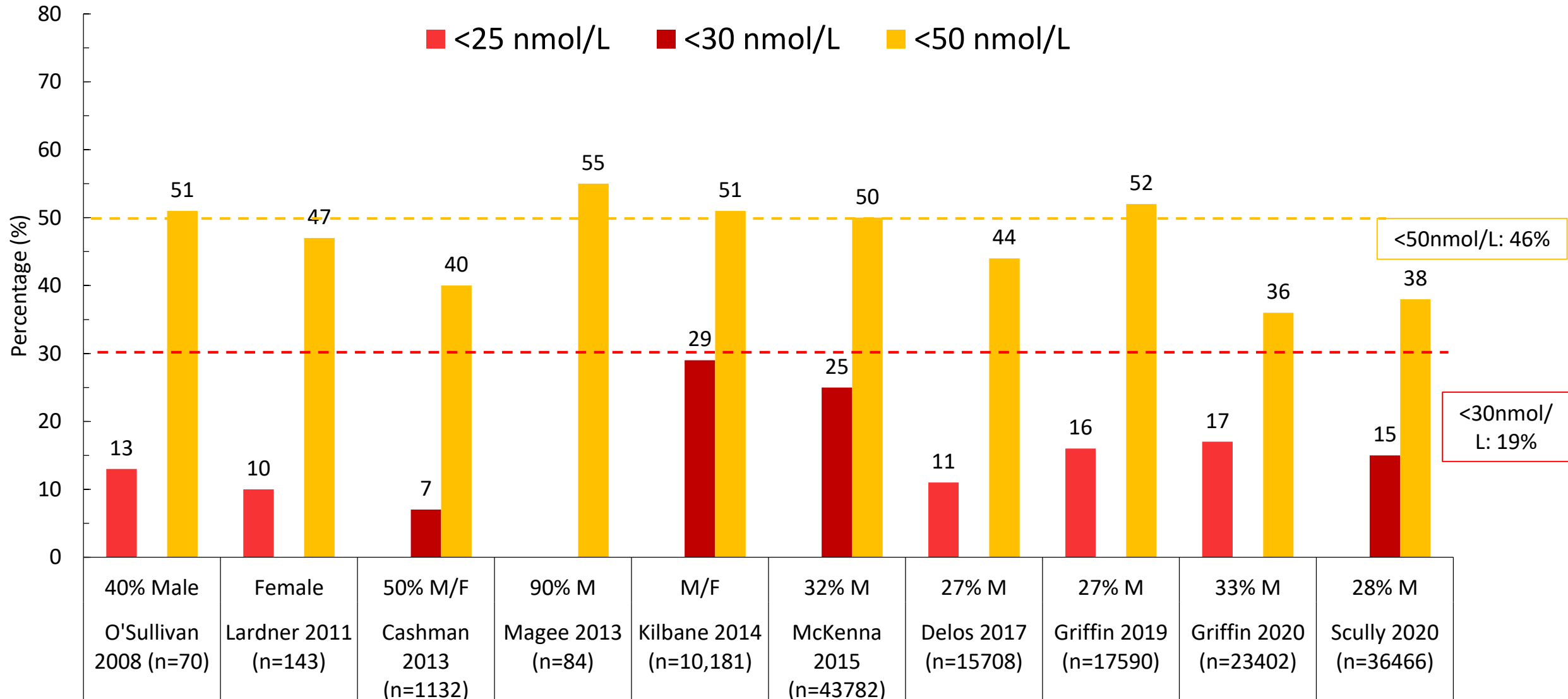
Bone health

Vitamin D and Bone Metabolism

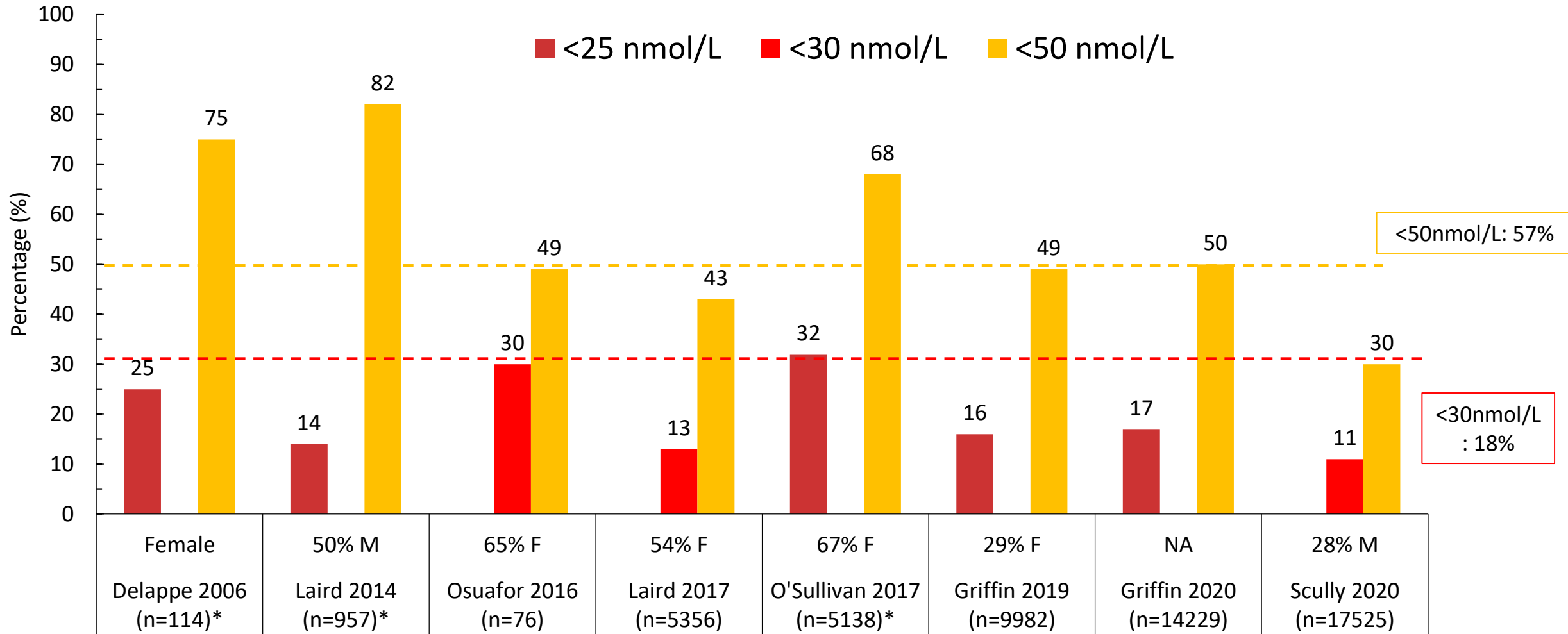


Adapted from Holick M. *Curr Opin Endocrinol Diabetes*. 2002;9:87-98; DeLuca HF. *Am J Clin Nutr*. 2004;80(suppl 1):1689S-1696S; Lips P. *Endocr Rev*. 2001;22:477-501; Holick MF. *J Nutr*. 2005;135:2739S-2748S.

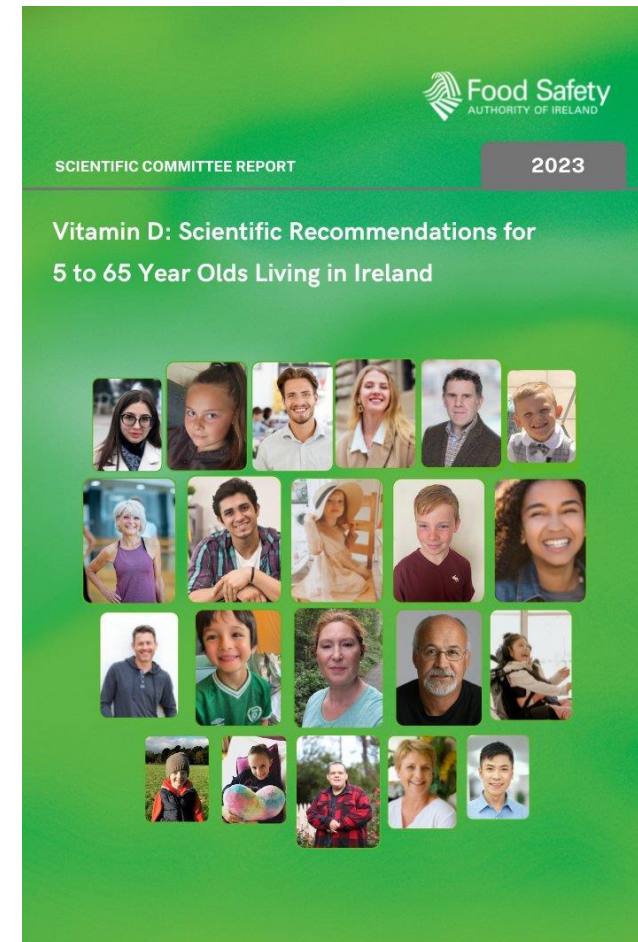
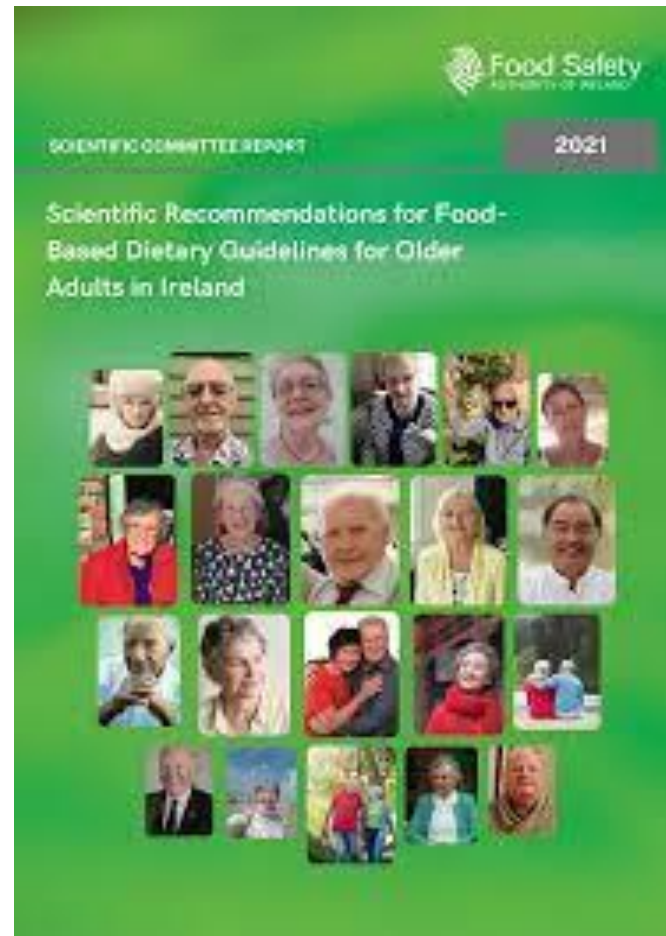
Vitamin D status adults



Vitamin D status older Adults



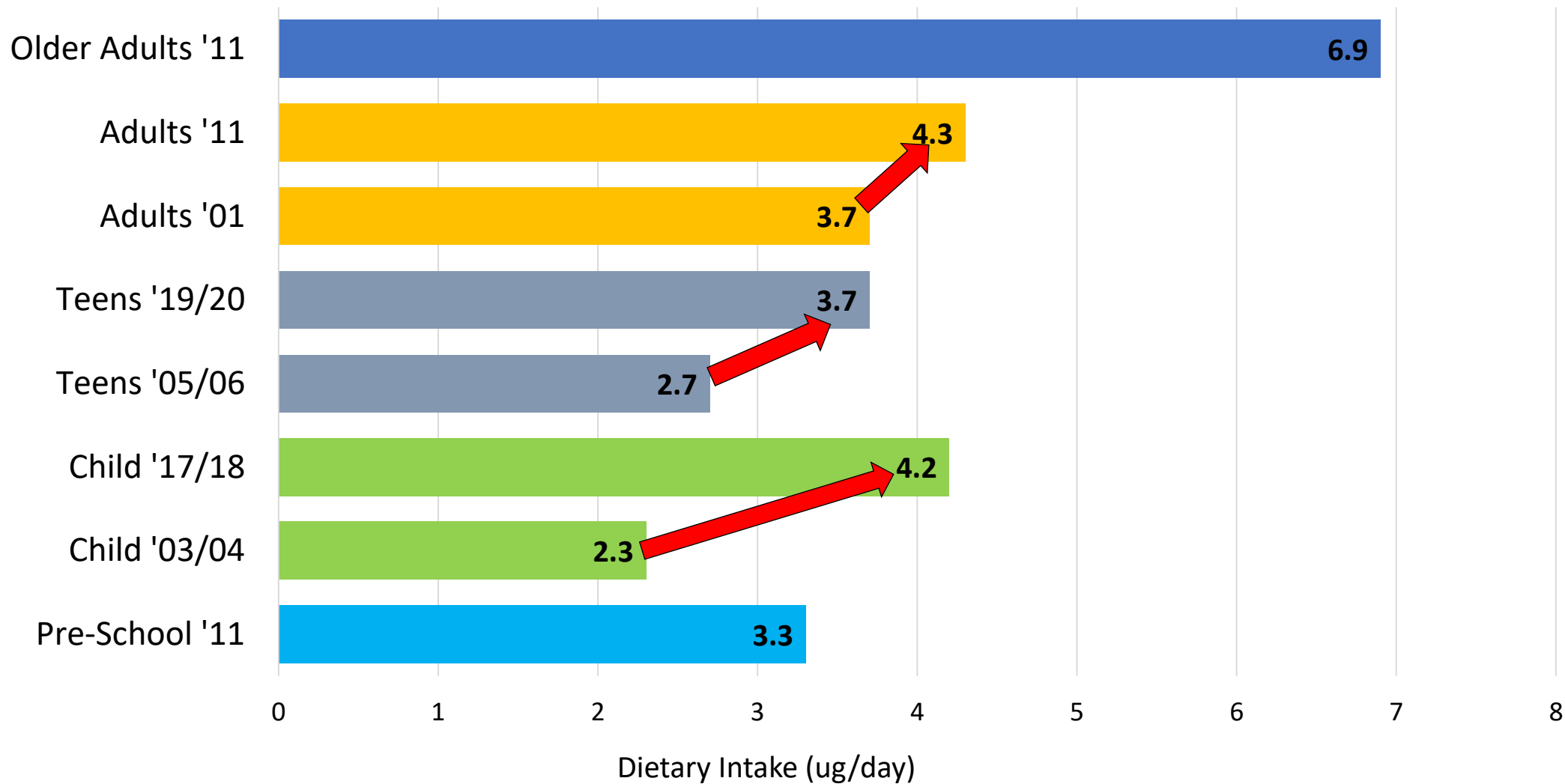
Vitamin D guidelines update Ireland



Vitamin D guidelines update Ireland

- For babies 0-12 months: 5ug/day (200IU) if breastfed or taking less than 300ml of infant formula a day
- For children aged 1-4 years: 5ug/day (200 IU) from Halloween (October 31st) to St Patrick's Day (March 17th)
- For healthy children (5-11 years) 10ug/day (400 IU) should be taken during extended winter (end of October to March) for those of fair-skin & throughout the full year for those of darker-skinned ethnicity
- For healthy teenagers and adults (12-65 years) 15µg/day (600 IU) should be taken during extended winter and all year round for pregnancy and those of darker-skinned ethnicity
- For older adults (>65 years) 15µg/day (600 IU) daily

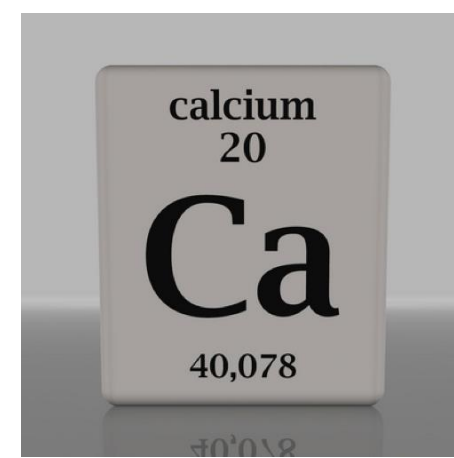
Vitamin D dietary intakes



Calcium

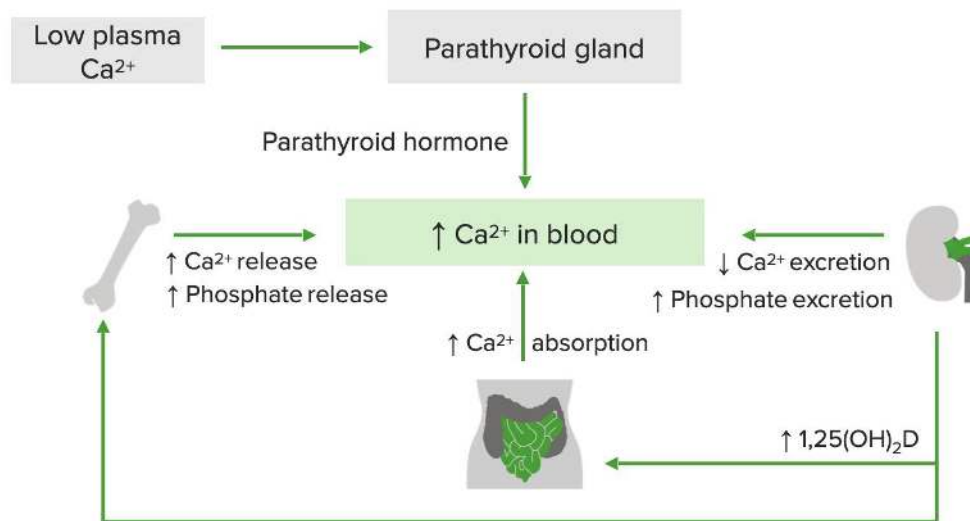
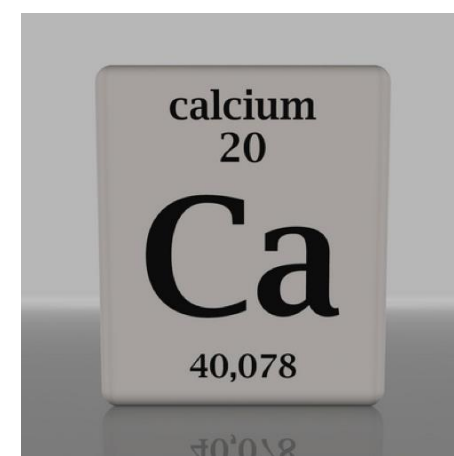
- Most abundant mineral in the body -99% found in bone
- Forms and maintains bone & teeth
- Acid-base balance
- Nerve impulse transmission
- Muscle contraction

Very tightly controlled in blood Range is 2.1 – 2.6 mmol/L



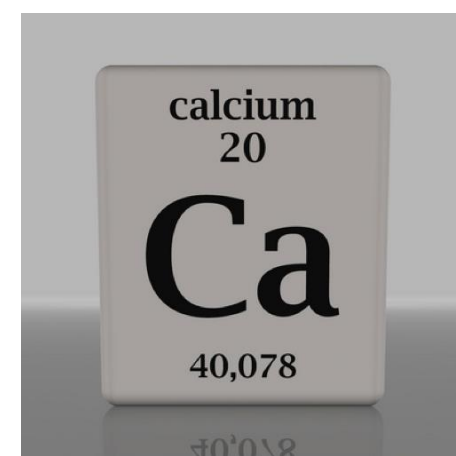
Low blood calcium

- Parathyroid (PTH) secretion is increased which can:
 - promote bone resorption to increase blood calcium concentrations to normal levels
 - stimulate calcium reabsorption in the small intestine



How much calcium is needed?

- Age 1-3 yrs: 450 mg (FAI)
- Age 4-6 yrs: 800 mg (FAI)
- Aged 4-10 yrs: 800mg (EFSA)
- Age 11-17 ys: 1150 mg (EFSA)
- Age 18 -24 yrs: 1000 mg (EFSA)
- Age 24-65 yrs: 950 mg (EFSA)
- Age >65 yrs: 1200 mg (NIH)



Dietary sources calcium

Food	Amount of calcium (mg per 100 g)	Adult portion size (household measurement)	Amount of calcium (mg per portion size)
Natural foods			
Low-fat milk	120	200 mL (1 cup)	240
Full-fat milk	130	200 mL (1 cup)	260
Skimmed milk	120	200 mL (1 cup)	240
Flavoured milk	120	200 mL (1 cup)	240
Natural or fruit yogurt	160	150 g (¾ cup)	240
Natural yogurt drink	120	200 mL (1 cup)	240
Fruit yogurt drink	120	200 mL (1 cup)	240
Flavoured yogurt drink	120	200 mL (1 cup)	240
Natural pouring yogurt	133	150 g (¾ cup)	200
Flavoured pouring yogurt	133	150 g (¾ cup)	200
Diet yogurt	140	150 g (¾ cup)	210
Cottage cheese	120	200 mL (1 cup)	240
Hard cheese	334–800	30 g (width and depth of 2 thumbs)	100–240 (depending on thumb size)
Soft cheese	267–734	30 g (width and depth of 2 thumbs)	80–220 (depending on thumb size)
Fortified foods*			
Low-fat fortified milk	160	200 mL (1 cup)	320
Fortified soya drink**	120	200 mL (1 cup)	240
Fortified almond drink**	120	200 mL (1 cup)	240
Fortified oat drink**	120	200 mL (1 cup)	240



Older adult calcium issues



- Principal source of calcium in older adults is dairy products
- Intake of dairy products in older adults is lower than in younger adults; most older adults do not achieve the recommended intake of three portions daily
- There is no biomarker available to assess calcium status

Intakes in older adults



- National Adult Nutrition Survey (NANs) reported mean daily calcium intake 908 mg for men & 985 mg for women
- However few consume dairy – NANs: 1.98 portions day; TUDA Study 1.16 portions daily; TILDA Study: 70% did not consume 3 portions of dairy per day (Note new 2023 guidelines state 3-4 portions dairy per day!)

FSAI New guidelines older adults

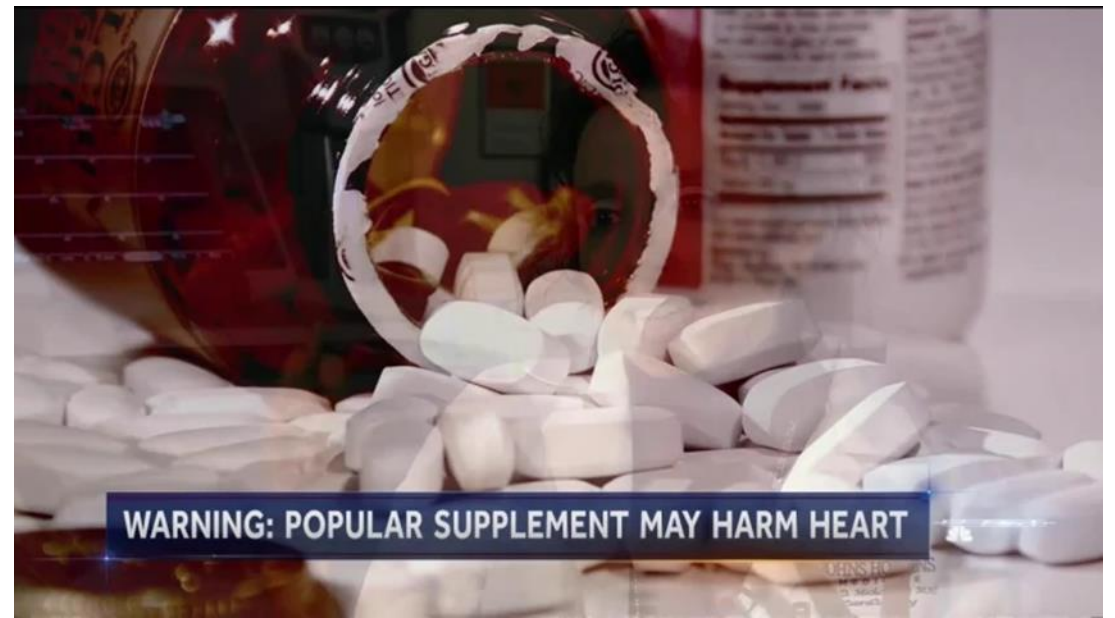
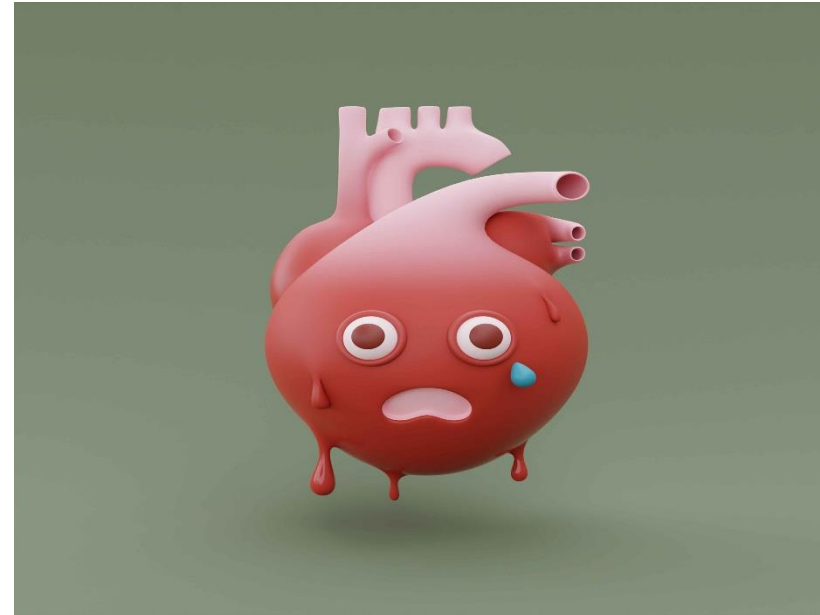
- Daily consumption of three portions of calcium-rich foods (such as milk, yogurt and cheese) is recommended in order to meet the requirement for older adults
- In those older adults who consume less than one portion of dairy products daily, a daily 500 mg calcium supplement is recommended

Benefits for bone health



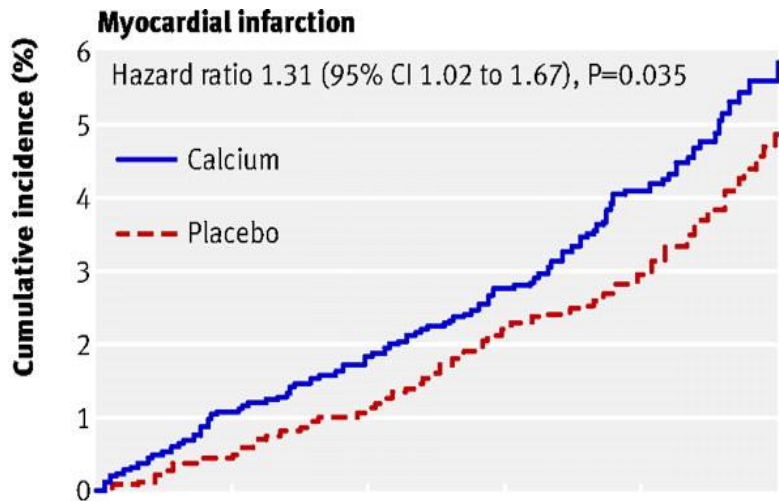
- Well established benefits for bone health
- 2021 study of 60 accredited residential aged care facilities: dietary calcium 600mg/day plus protein at 1g/kg bodyweight 2 years
- 7,000 residents 33% reduced risk all fractures, 46% hip fractures, 11% falls –no adverse effects reported
- Cost effective analysis: increasing dairy portions to 3.5 per day (resulting in 1,142 mg of calcium and 69 g of protein) reduced fractures at a daily cost of AU\$0.66 per resident. Equates to a saving of AU\$66,780,000 annually in Australia in fracture costs

But good for bones bad for heart??



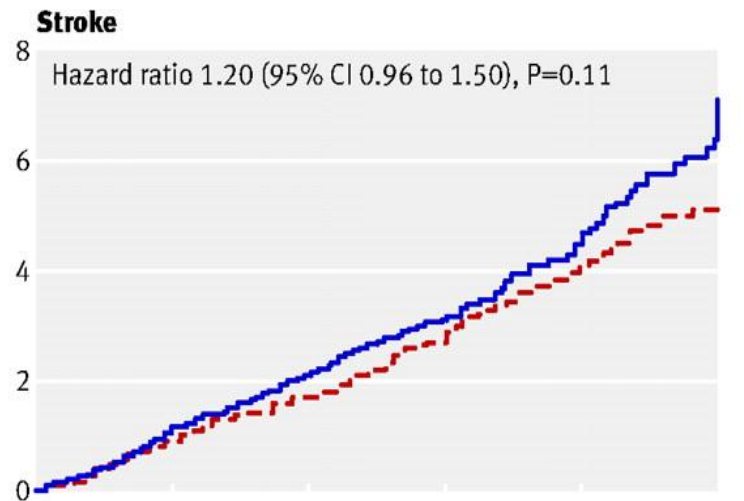
Previous work

- Bolland et al 2010: Systematic review & meta analysis of 15 RCTS; calcium supplements were associated with an increased risk of myocardial infarction by about 30%
- Myung et al 2021: Meta analysis of 13 RCTS; 15% increased risk of CVD in post menopausal women
- Levels >1000mg per day

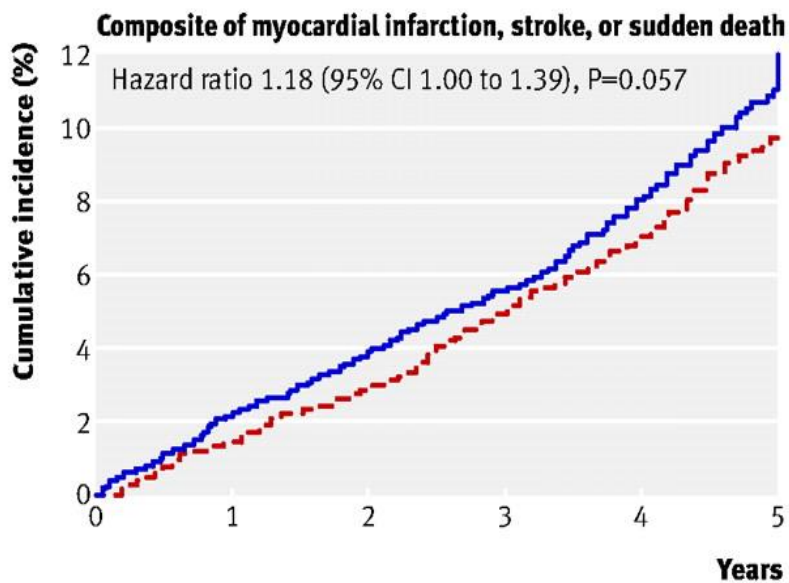


No at risk

Calcium	4097	3870	3539	2670	1294	373
Placebo	4054	3865	3588	2728	1320	388

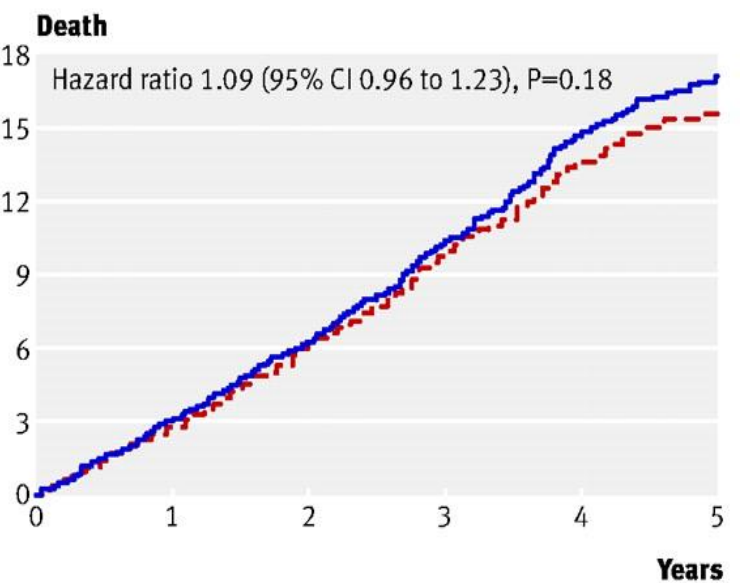


Calcium	4097	3865	3541	2659	1294	373
Placebo	4054	3859	3589	2730	1312	386



No at risk

Calcium	4097	3848	3517	2635	1271	360
Placebo	4054	3848	3566	2692	1292	376



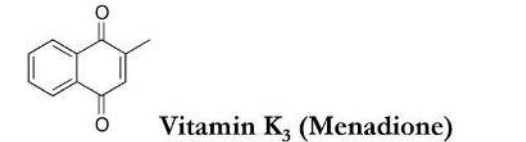
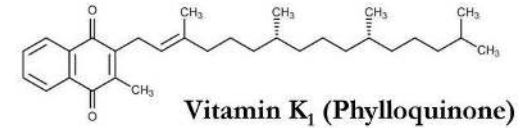
Calcium	4097	3889	3580	2699	1322	389
Placebo	4054	3875	3618	2767	1340	399

Mechanisms

- Vascular calcification primary mechanism
- Coagulability or altered vascular flow
- Most of evidence show restricted to calcium supplements and not dietary calcium
- Some evidence show higher dietary calcium levels associated with reduced risk of CVD- less immediate rise in levels? Other mechanisms?

Vitamin K

- Fat soluble vitamin exists in two forms in nature:
- Vitamin K1 (Phylloquinone)
- Vitamin K2 (Menaquinone)
- Synthetic water soluble version – vitamin K3 (Menadione)



Food	Vitamin K1 μg/100 g	Vitamin K2 μg/100 g
Kale ⁽¹⁰⁾	73.3	No data
Spinach ⁽¹⁰⁾	96.7	No data
Broccoli ⁽¹⁰⁾	146.7	No data
Sauerkraut ⁽¹⁰⁾	22.4	5.5
Beef ⁽¹⁰⁾	0.02	1.9
Liver (beef) ⁽¹⁰⁾	2.3	11.2
Chicken ⁽¹⁰⁾	Not detected	10.1
Cheddar (UK) ⁽¹²⁾	2.2	23.5
Cheddar (US) ⁽¹¹⁾	2.4	279
Brie ^(10,12)	4.9	12.5
Feta ⁽¹²⁾	1.4	11.7
Stilton ^(10,12)	3.6	49.4
Blue cheese (US) ⁽¹¹⁾	3.2	437
Mozzarella ⁽¹²⁾	1.5	6.2
Münster ^(10,12)	2.1	80.1

Dietary
sources

Key facts



- Vitamin K1 is more plentiful in the diet but vitamin K2 has higher efficacy and functional capacity
- Vitamin K1 forms 90% of the total vitamin K intake but only 10-15% of this is absorbed in the digestive tract
- Vitamin K2 intake is lower, difficult to quantify but its absorption is almost 100%
- Recommended dietary intake not established: BUT an adequate intake of $1 \mu\text{g}/\text{kg}$ body weight per day or $70 \mu\text{g}/\text{day}$ is suggested for all European adults

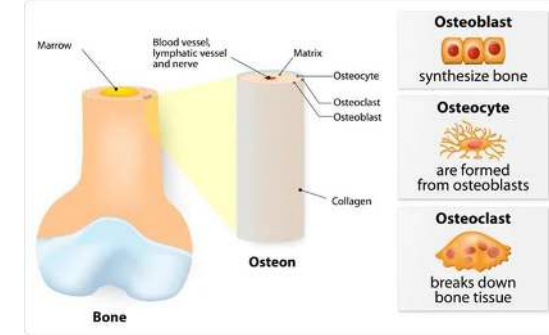
Vitamin K status

- Lack of population studies
- NANS study indicated that 55% of adults aged >18 yrs had vitamin K1 intakes below recommended levels
- Risk factors for low levels include:
 - Celiac disease
 - Cystic fibrosis
 - Intestinal or biliary tract (liver, gallbladder, and bile ducts) disorder
 - Antibiotics that interfere with vitamin K production and absorption

Vitamin K functions

- Vitamin K serves as an essential cofactor key vitamin K-dependent proteins include:
 - Coagulation proteins: factors II (prothrombin), VII, IX and X
 - Anticoagulation proteins: proteins C, S and Z
 - Bone proteins osteocalcin and matrix-Gla protein, and certain ribosomal proteins

Bone health



- Vitamin K facilitates mineralisation into bone tissue, through activation of osteocalcin. Osteocalcin is secreted by bone-building osteoblasts during synthesis of bone and dentine.
- Vitamin K2 in particular is associated with increases in both bone quality and strength
- Meta-analysis of vitamin K supplementation in adults showed that menaquinone was associated with 60% reduction in vertebral fractures, 77% reduction in hip fractures and 81% reduction in all non- vertebral fractures

Vitamin K - Calcium

- When the vitamin K dependant matrix-gla protein (MGP) is activated, it has a high affinity for calcium and can inhibit vascular calcification and associated with improved vascular elasticity
- May also alter the gene expression involved in calcification process
- Combined supplementation with vitamin D has been shown to increase BMD though increased phosphorylated carboxylated osteocalcin
- In the absence of vitamin K, calcium supplementation (non dietary) may not be ideal for those with low vitamin K status

Vitamin K CVD

- Rotterdam study – 4,800 participants 57% lower mortality from heart disease in those with highest menaquinone intakes
- Recent Norwegian study that higher intakes of vitamin K2, but not K1, were associated with lower CVD risk
- Vascular calcification is highly prevalent in CKD patients and is a strong predictor of cardiovascular mortality – these patients also high levels of vitamin K deficiency
- Similar in T2DM patient groups

Summary

- Population is ageing and increased risk of osteoporosis and fractures
- Also rise in other chronic conditions which may impact treatment
- Dairy foods are essential for older adults however intakes are poor
- Dairy can help provide triangle of calcium, vitamin D and vitamin K along with protein for optimal bone health
- Risks with supplemental calcium for CVD
- Dairy food excellent source of dietary calcium along with protective vitamin K