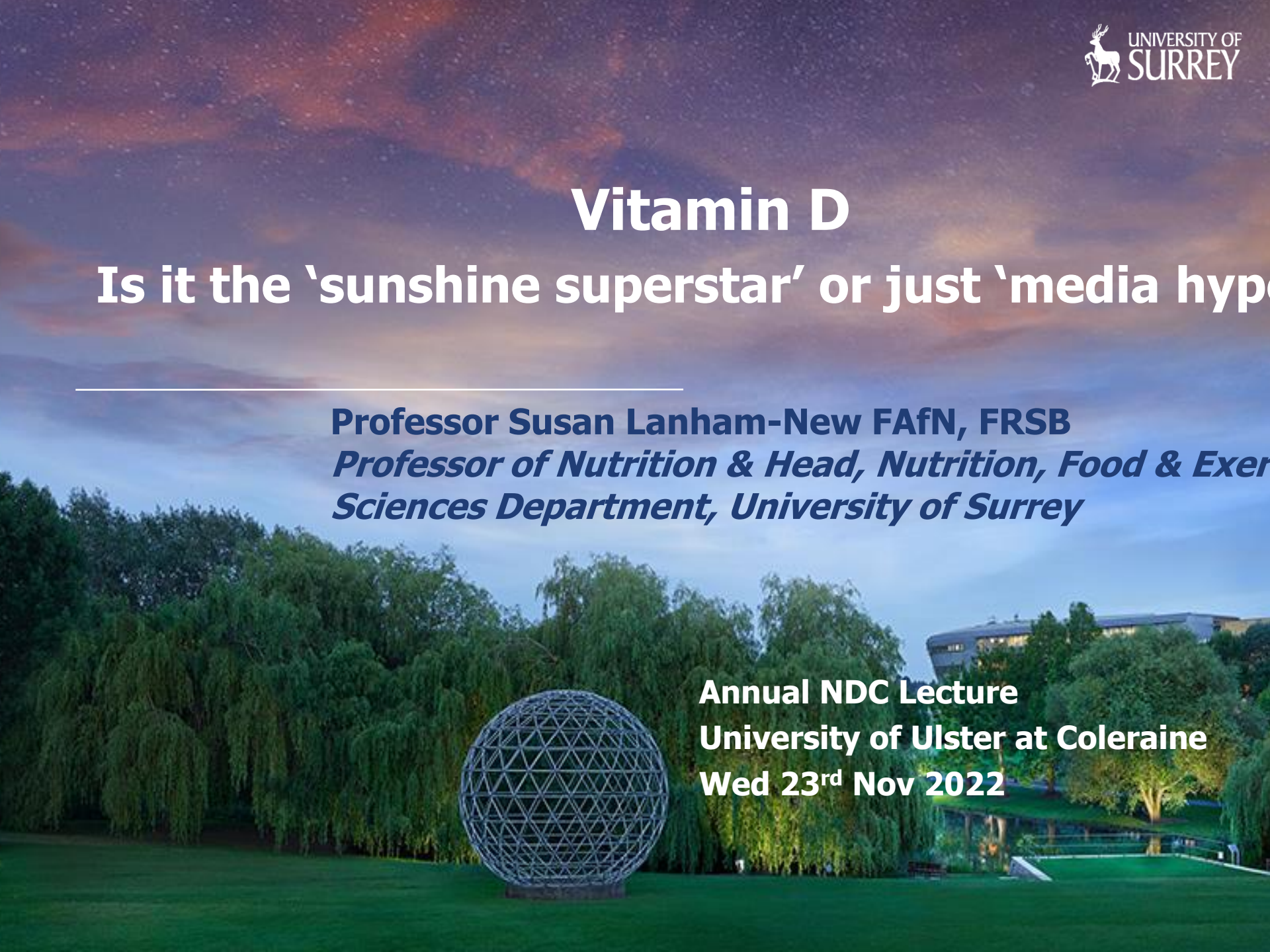
Vitamin D

Is it the 'sunshine superstar' or just 'media hyp

Professor Susan Lanham-New FAfN, FRSB
Professor of Nutrition & Head, Nutrition, Food & Exer
Sciences Department, University of Surrey



Annual NDC Lecture
University of Ulster at Coleraine
Wed 23rd Nov 2022

Presentation plan

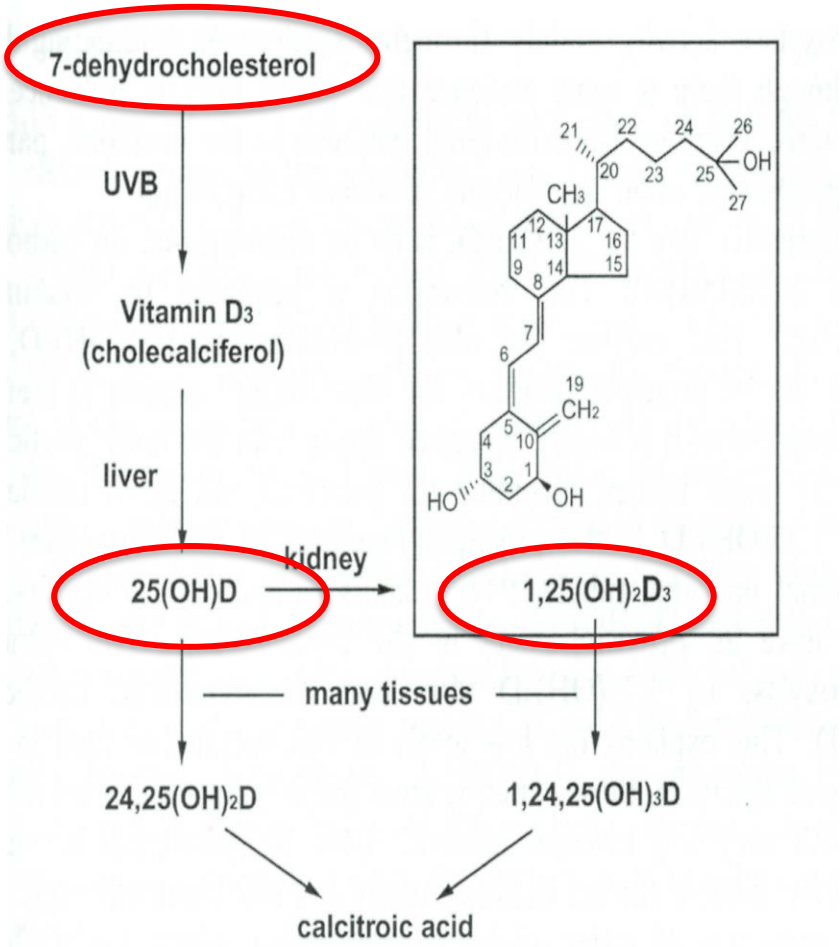
NDC Annual Lecture, University of Ulster at Coleraine. Wed 23rd Nov 2022

UNIVERSITY OF SURREY

- Overview of key vitamin D concepts
  Definition; metabolism, UVB exposure, dietary sources requirements;
- Importance of vitamin D (and calcium) to health – current controversies
  MSK, immune function, upper/acute respiratory tract infections, influenza
- The vitamin D2 vs. vitamin D3 debate
  Current Controversies
- Current scientific evidence for COVID-19 and vitamin D
  Review of international scientific studies; UK Biobank; media reports
- Practical ways for ensuring vitamin D adequacy
- Concluding remarks

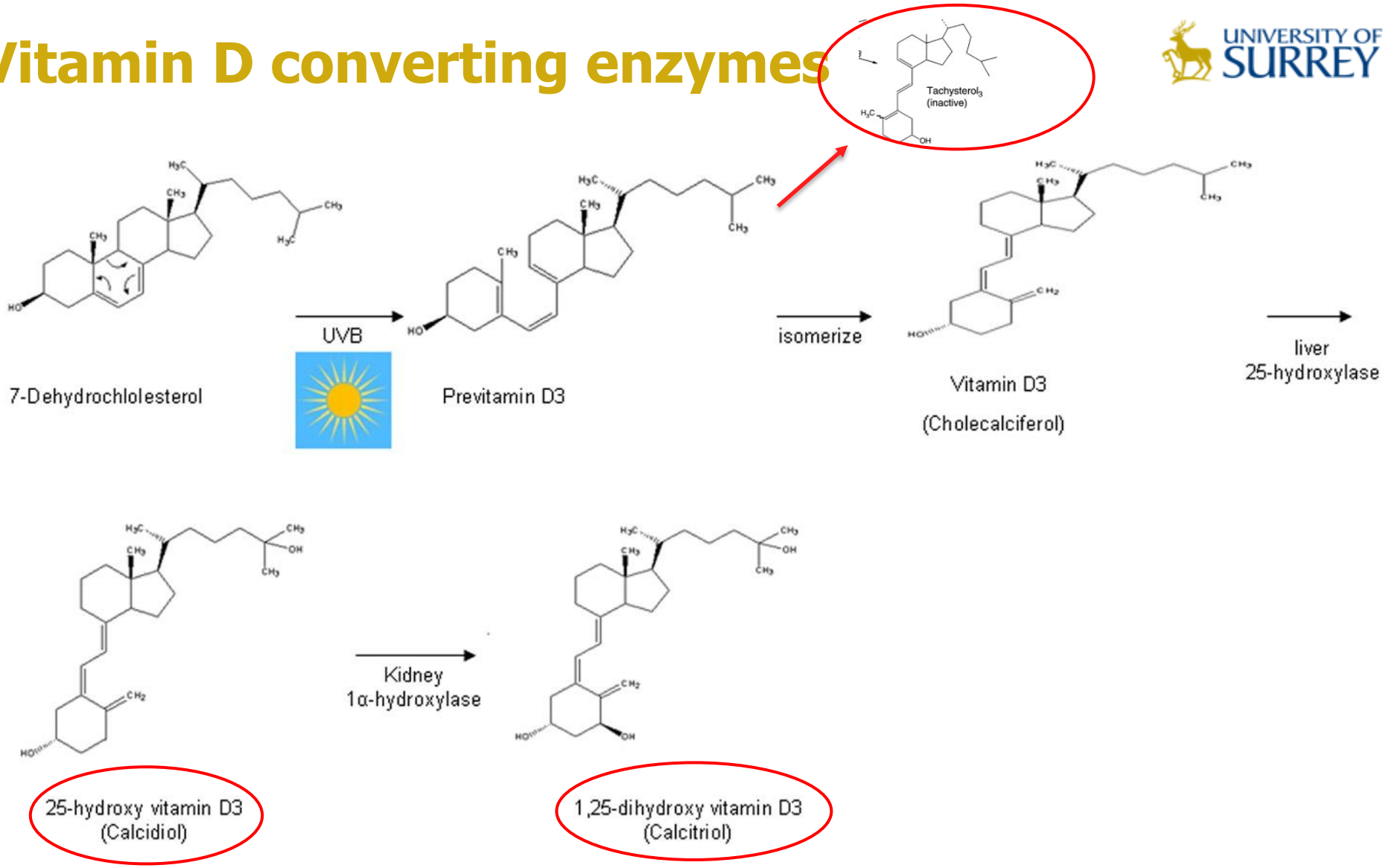

Vitamin D is NOT a Vital Amine!

Vitamin D – Introductory Comments



- The term 'Vitamin D' is a mis-nomer: is not a '***vital amine***' in the true sense of the word. It is a pro-hormone.
- Only nutrient where main source is not one of diet but UVB exposure
- UVB exposure must be at 290-315nm
- In the UK, we **only** make vitamin D from sunlight between April to September

Vitamin D converting enzymes

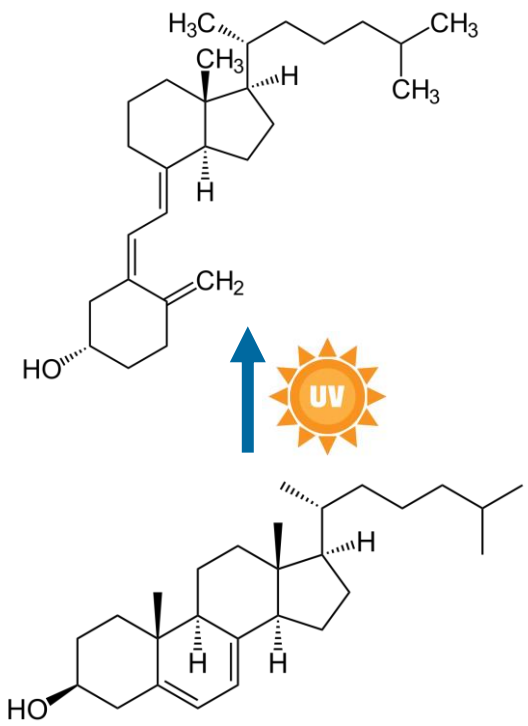


Active Hormone

Manbir S. Sandhu, MD,* and Thomas B. Casale, MD**__The role of vitamin D in asthma__ *Ann Allergy Asthma Immunol. 2010;105:191–199*

Problem of Vitamin D Deficiency - Worldwide

Vitamin D_3



Provitamin D_3

Geographical Area	Prevalence (%) <25nmol/l or <30nmol/l	Prevalence (%) <50nmol/l
Global	6.7%	37.3%
USA	5.9%	24.0%
Europe	13.0%	40.4%
UK*	13.0-19.0%	40.2%
China	20.7%	63.2%
Middle East	50.0%	90.0%

WHO estimates that 2 billion people in Low to Middle Income Countries (LMIC) are vitamin D deficient.

*NDNS Years 9-11; 2016-2017 & 2018-2019

Food Standards Agency
Public Health England

UNIVERSITY OF SURREY

2 BILLION

WHO estimation of the number of people in LMIC

£ 100 MILLION

NICE – Primary Care costs for treating vitamin D deficiency in the UK alone - per year

Dr Dame Harriette Chick DBE, PhD, FRSM

6 January 1875 – 9 July 1977

THE LANCET
Volume 200, Issue 5157, 1 July 1922, Pages 7-11

THE ÆTIOLOGY OF RICKETS IN INFANTS : PROPHYLACTIC AND CURATIVE OBSERVATIONS AT THE VIENNA UNIVERSITY KINDERKLINIK. ☆

Harriette Chick D.SC., ElsieJ. Dalyell M.B., Margaret Hume M.R.C.P., H.Henderson Smith R.R.C., HelenM.M. Mackay M.D., HAMS WIMBERGER, M.D., RADIOLOGIST TO THE UNIVERSITY KINDERKLINIK, VIENNA.

- British microbiologist, protein scientist and nutritionist.
- She is best remembered for demonstrating the roles of sunlight and cod liver oil in preventing rickets.

TABLE 1 The incidence of rickets in infants on different diets and in different seasons in the main study in Vienna with diagnosis based on radiographs[1]

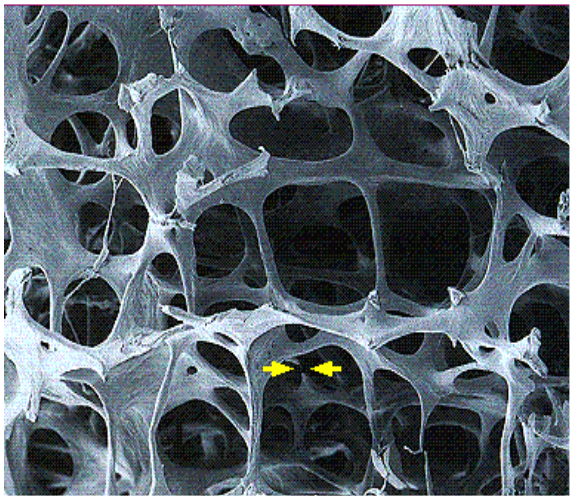
Season	Diet	With rickets/total
		n
Summer (May–Oct.)	I (milk + sucrose)	0/15
	II (milk + CLO)	0/23
Winter (Nov.–Apr.)	I (milk + sucrose)	13/25
	II (milk + CLO)	0/21

Why is vitamin D so important?

Vitamin D is absolutely critical to health

Children Rickets
Adults Osteomalacia; osteoporosis

Heart Disease
Diabetes
Cancer
TB
The Common Cold!

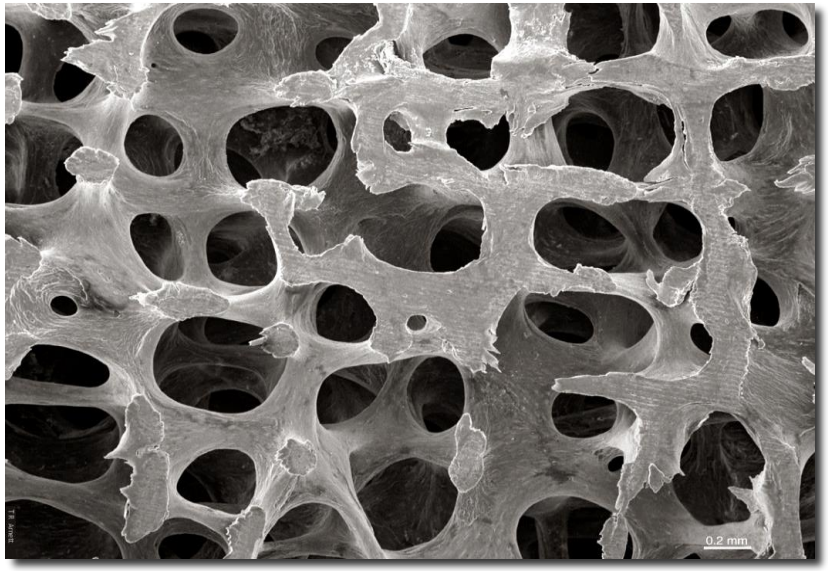


In the UK, we can only make vitamin D between April to September

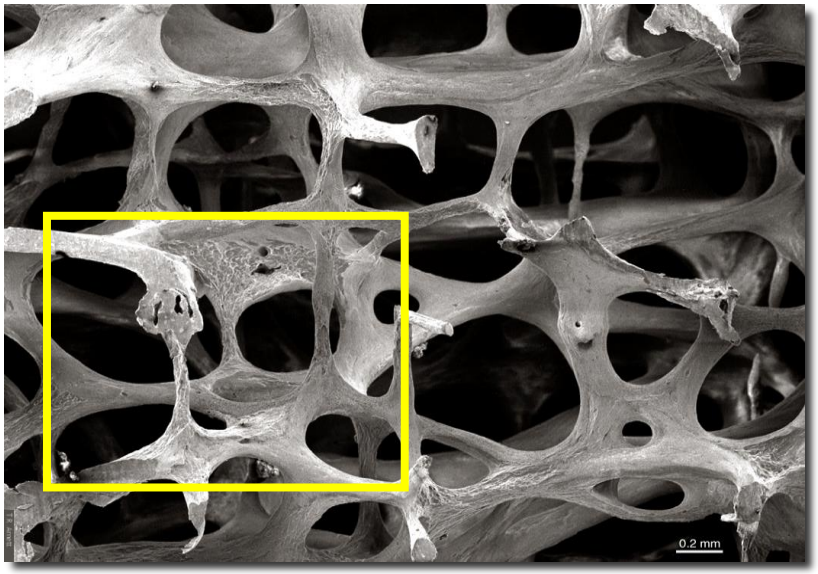
British Winter is a huge challenge for vitamin D health!

Definition of osteoporosis (*osteo* - bone; *porosis* - porous)

Normal bone architecture in the 3rd lumbar vertebra: 30 year old woman

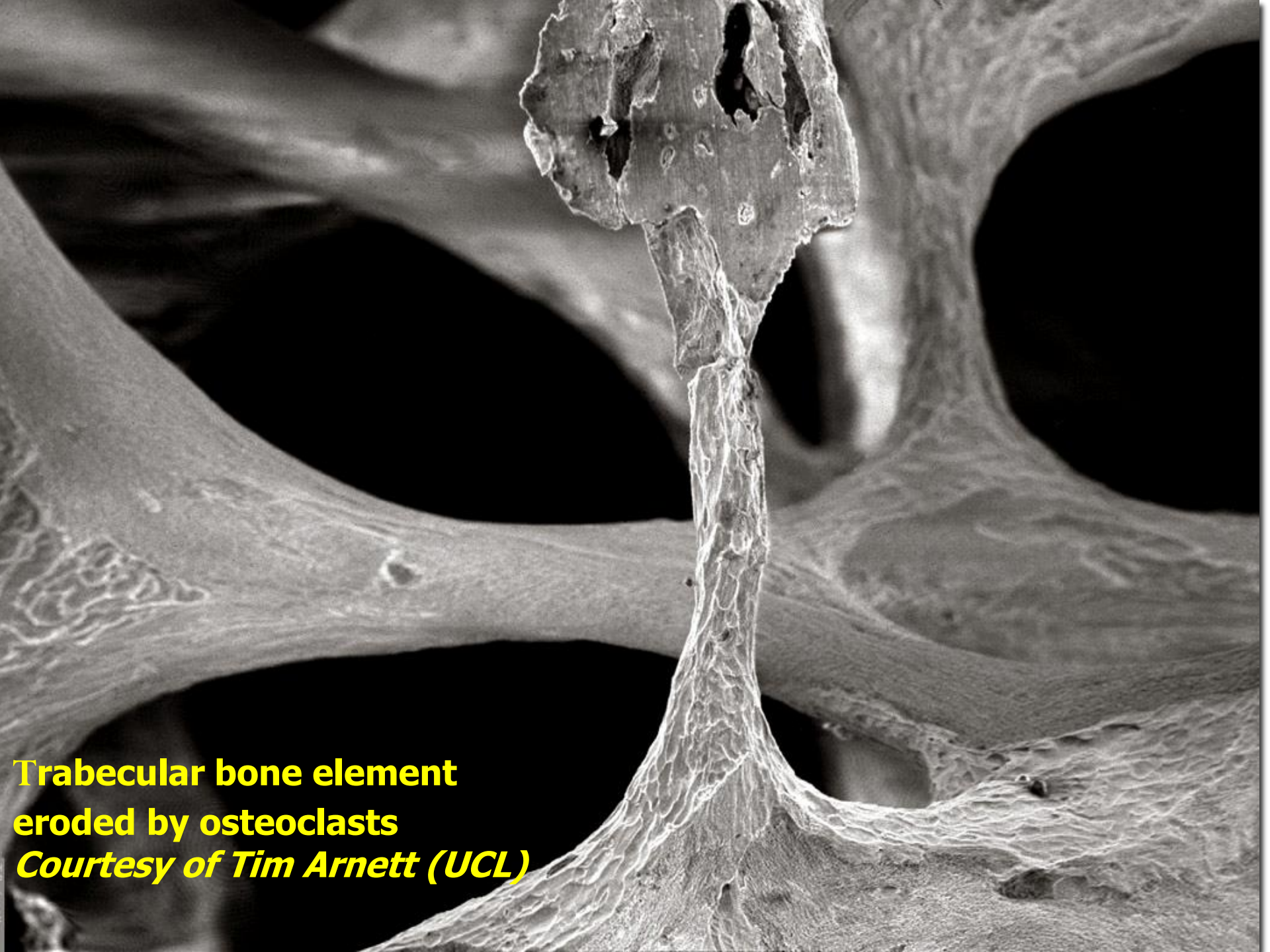


Osteoporotic bone architecture in the 3rd lumbar vertebra: 71 year old woman



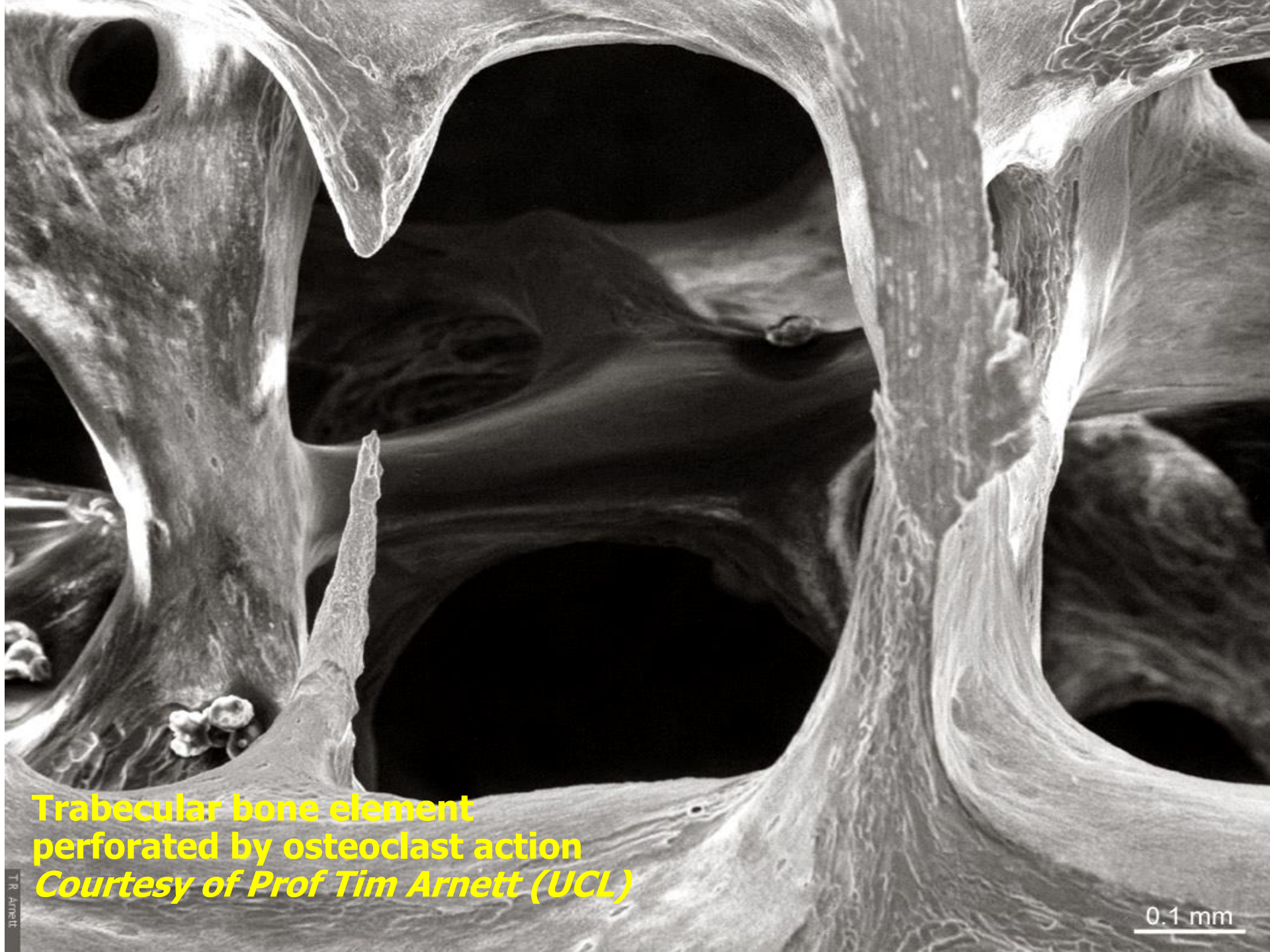
"A progressive *systemic* skeletal disease characterized by *low bone mass* and micro architectural deterioration of bone tissue, with consequent increase in *bone fragility* and susceptibility of *fracture*."[1]

1. World Health Organisation 1991



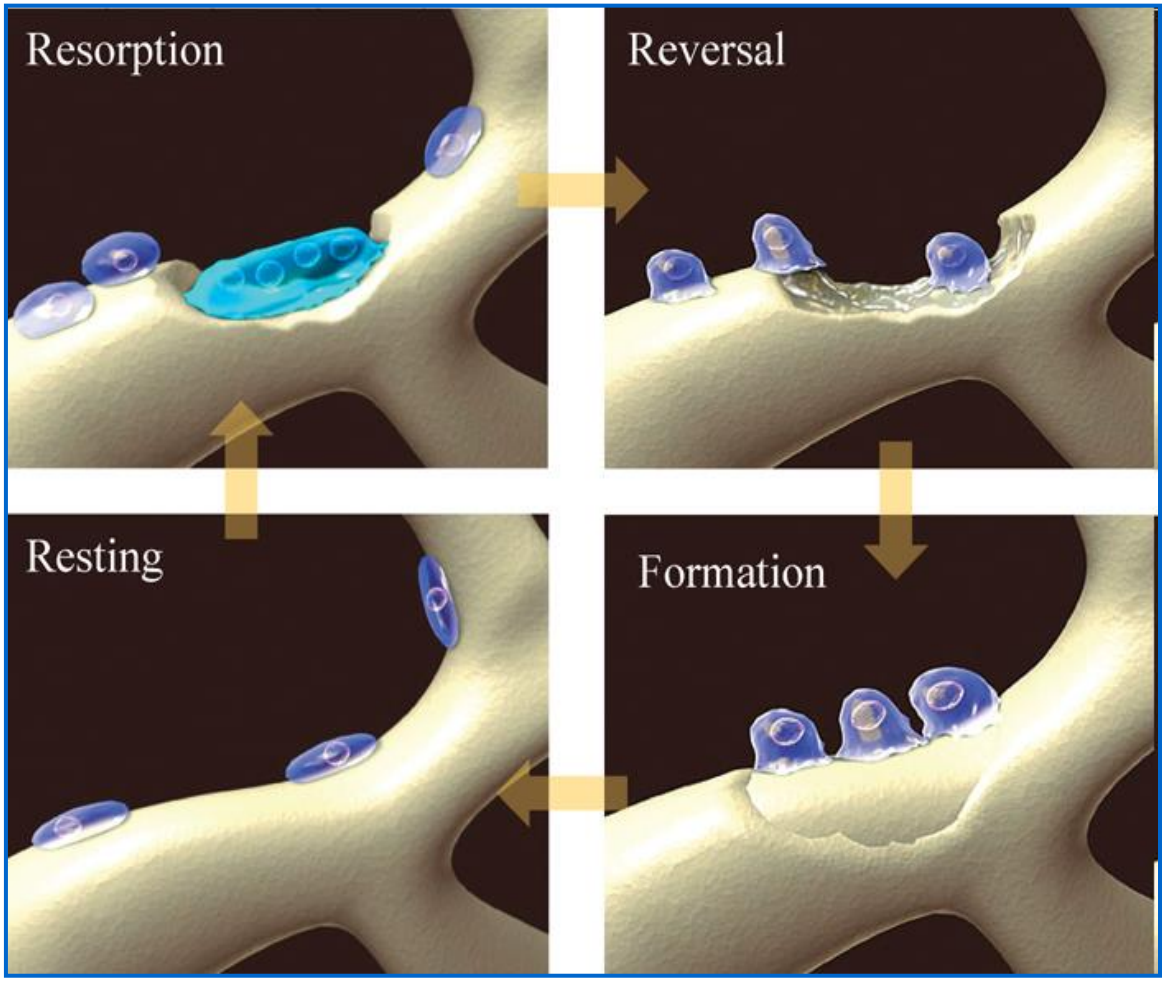
Trabecular bone element eroded by osteoclasts

Courtesy of Tim Arnett (UCL)


Trabecular bone element
perforated by osteoclast action
Courtesy of Prof Tim Arnett (UCL)
0.1 mm
T.R. Arnett

The osteoclast
Courtesy of Prof Tim Arnett (UCL)

Process of bone turnover



Ref: Bone Research Society

Resorption

Osteoclasts break down bone creating a resorption cavity

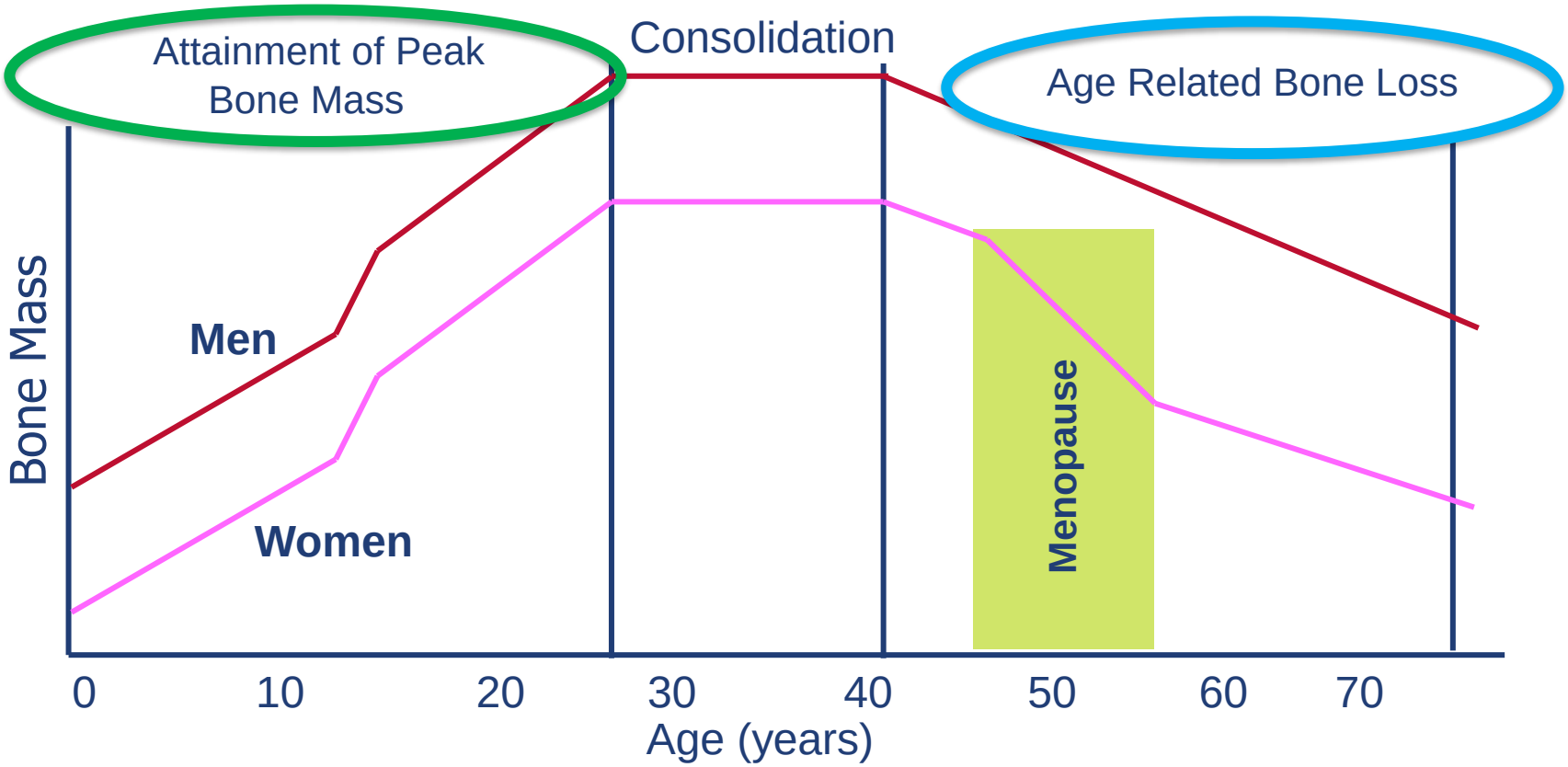
Formation

Osteoblasts make new bone matrix which is then mineralised, filling the remodelling space

Enables bone to

- adapt to mechanical loading
- repair damage
- regulate circulating Ca levels
- contribute to acid/base balance

Change in bone mass with ageing



Ref: Royal Osteoporosis Society 2019

Public health impact of osteoporosis

More than

3 million people in the UK

are estimated to *have osteoporosis* and there are estimated t

be over **500,000** *fragility fractures* that occur in the UK each yea

Many of those fractures could be prevented with earlier identification and intervention

Fragility fractures are estimated to cost the UK around ***£4.4 billion each year.***

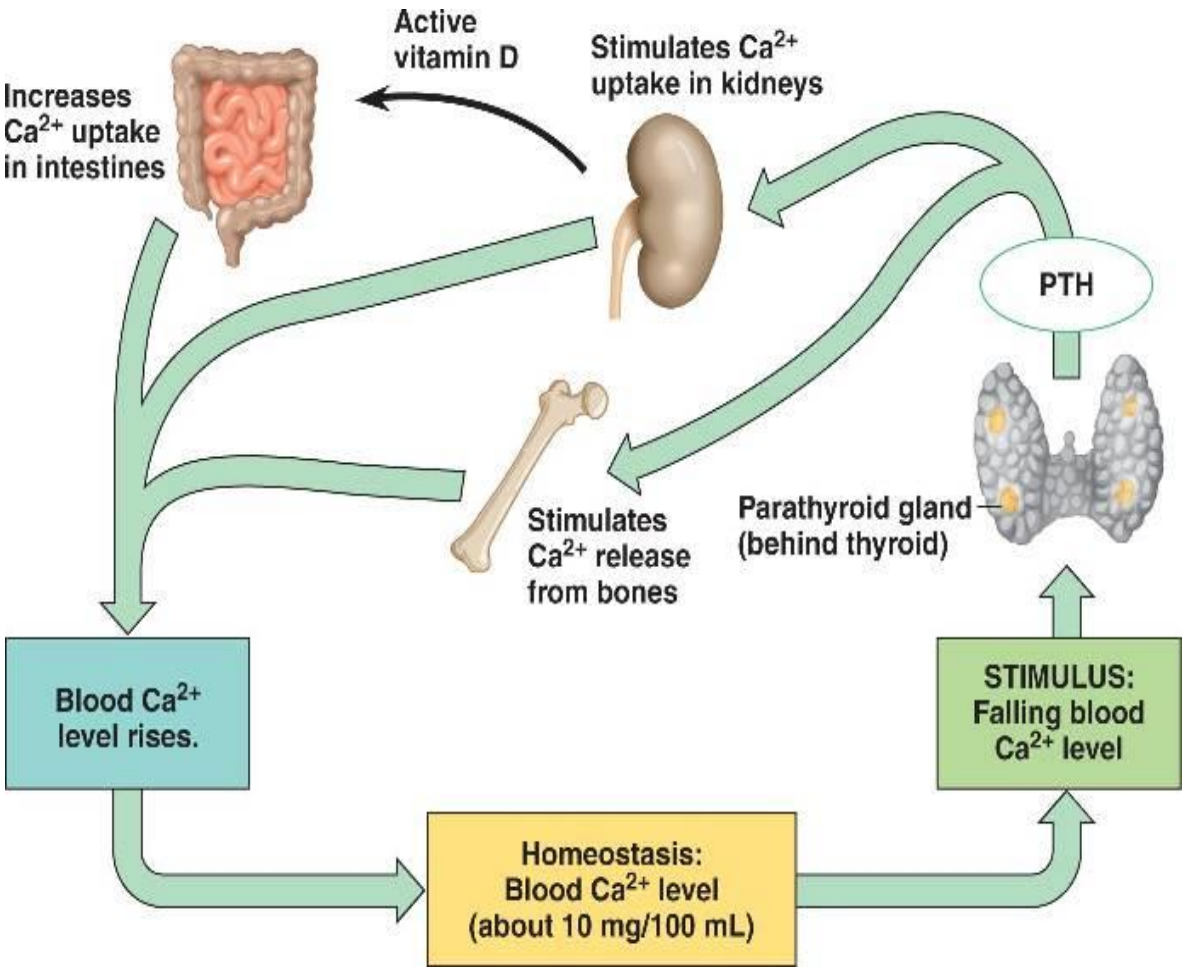
£

Hip fractures alone account for ***69,000 emergency admissions*** into English hospitals, adding up to ***1.3 million bed days*** and a cost of ***£1.5 billion each year.***

Ref: NOS Research Strategy, October 2017; NHS RightCare scenario: The variation between sub-optimal and optimal pathways, February 2017

Calcium influences on bone health

Calcium homeostasis



Calcium Requirements I

Institute of Medicine (USA) RDA

Age	0-6 m	6-12 m	1-3 y	4-8 y	9-18 y	19-50 y	51-70 y	>70 y
All	1000mg[U]	1500mg[U]	700mg	1000mg	1300mg	1000mg	1000mg	1200mg
Female*							1200mg	1200mg

Department of Health (UK) RNI

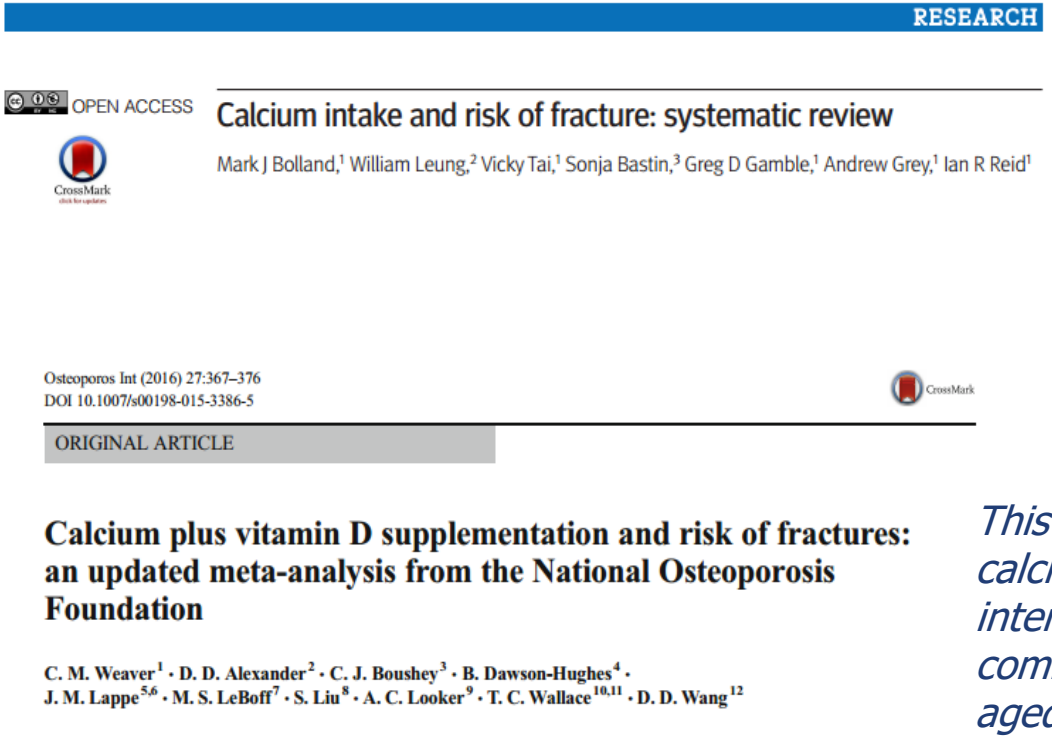
Age	0-12 m	1-3 y	4-6 y	7-10y	11-18 y	19-50 y	>50 y
All	525mg	350mg	450mg	550mg	1000mg	700mg	700mg
Female*					800mg		

RDA Recommended Dietary Allowance; RNI Reference Nutrient Intake; m months; y years; [U] Upper Level Intake; *where different from recommendation for males.

Lower Reference Nutrient Intake (LRNI) is 400mg/d

Slide courtesy of Dr Louise Durrant (nee Wilson)

Conflicting Data



RESEARCH

OPEN ACCESS

Calcium intake and risk of fracture: systematic review

Mark J Bolland,[1] William Leung,[2] Vicky Tai,[1] Sonja Bastin,[3] Greg D Gamble,[1] Andrew Grey,[1] Ian R Reid[1]

Osteoporos Int (2016) 27:367–376
DOI 10.1007/s00198-015-3386-5

ORIGINAL ARTICLE

Calcium plus vitamin D supplementation and risk of fractures: an updated meta-analysis from the National Osteoporosis Foundation

C. M. Weaver[1] · D. D. Alexander[2] · C. J. Boushey[3] · B. Dawson-Hughes[4] · J. M. Lappe[5,6] · M. S. LeBoff[7] · S. Liu[8] · A. C. Looker[9] · T. C. Wallace[10,11] · D. D. Wang[12]

Dietary calcium intake is not associated with risk of fracture, and there is no clinical trial evidence that increasing calcium intake from dietary sources prevents fractures. Evidence that calcium supplements prevent fractures is weak and inconsistent.

This meta-analysis of RCTs supports the use of calcium plus vitamin D supplements as an intervention for fracture risk reduction in both community-dwelling and institutionalized middle-aged to older adults.

Conflicting Data

RESEARCH

OPEN ACCESS

Calcium intake and risk of fracture: systematic review

PROSPECTS

Journal of Cellular Biochemistry 116:494–501 (2015)

Dietary calcium intake is not associated with risk of fracture, and there is no clinical trial evidence that increasing

Journal of Cellular Biochemistry

es calcium veak

Osteoporos Int (2016) 27:367–376
DOI 10.1007/s00198-015-3386-5

ORIGINAL ARTICLE

Calcium plus vit
an updated meta
Foundation

C. M. Weaver[1] · D. D. Alexander[2] · C. J. Boushey[3] · B. Dawson-Hughes[4] · J. M. Lappe[5,6] · M. S. LeBoff[7] · S. Liu[8] · A. C. Looker[9] · T. C. Wallace[10,11] · D. D. Wang[12]

Cardiovascular Complications of Calcium Supplements

Ian R. Reid,[1,2*] Sarah M. Bristow,[1] and Mark J. Bolland[1]

[1]*University of Auckland, Auckland, New Zealand*

[2]*Department of Endocrinology, Auckland District Health Board, New Zealand*

se of

intervention for fracture risk reduction in both community-dwelling and institutionalized middle-aged to older adults.

Calcium supplements in the media

The Telegraph

Calcium pills 'double heart attack risk'

Calcium supplements taken by millions of people every day can double the risk of heart attacks, according to a study, while researchers say they do little to protect bones against fractures.

Mail Online

Calcium pills taken by hundreds of thousands of women 'double risk of heart attack and could do more harm than good'

NHS

Calcium supplements and heart attacks 'linked'

Calcium pills "do more harm than good' the Daily Mail has reported. By contrast, the Telegraph tells us there is "no need to panic over new calcium heart attack research". So, which to believe?

Are Calcium Supplements Safe?

Kidney stones are a known risk, but studies have investigated other potential safety concerns, including an increased risk of death, cancer and heart disease.

The Telegraph

No need to panic over new calcium heart attack research, say British Heart Foundation

There is no need for alarm over new research that says calcium supplements may be linked to heart attacks, says senior cardiac nurse Natasha Stewart.

Slide courtesy of Dr Marcela Moraes-Mendes

ORIGINAL ARTICLE

JBMR®

biobank uk
Improving the health of future generations

Calcium and Vitamin D Supplementation Are Not Associated With Risk of Incident Ischemic Cardiac Events or Death: Findings From the UK Biobank Cohort

Harvey *et al* 2018

Nicholas C Harvey,[1,2] Stefania D'Angelo,[1] Julien Paccou,[1,3] Elizabeth M Curtis,[1] Mark Edwards,[1,4] Zahra Raisi-Estabragh,[5] Karen Walker-Bone,[1] Steffen E Petersen,[5*] and Cyrus Cooper[1,2,6*]

ABSTRACT

We investigated associations between calcium/vitamin D supplementation and incident cardiovascular events/deaths in a UK population-based cohort. UK Biobank is a large prospective cohort comprising 502,637 men and women aged 40 to 69 years at recruitment. Supplementation with calcium/vitamin D was self-reported, and information on incident hospital admission (ICD-10) for ischemic heart disease (IHD), myocardial infarction (MI), and subsequent death was obtained from linkage to national registers. Cox proportional hazards models were used to investigate longitudinal relationships between calcium/vitamin D supplementation and hospital admission for men/women, controlling for covariates. A total of 475,255 participants (median age 58 years, 55.8% women) had complete data on calcium/vitamin D supplementation. Of that number, 33,437 participants reported taking calcium supplements; 19,089 vitamin D; and 10,007 both. In crude and adjusted analyses, there were no associations between use of calcium supplements and risk of incident hospital admission with either IHD, MI, or subsequent death. Thus, for example, in unadjusted models, the hazard ratio (HR) for admission with myocardial infarction was 0.97 (95% confidence interval [CI] 0.79–1.20, $p = 0.79$) among women taking calcium supplementation. Corresponding HR for men is 1.16 (95% CI 0.92–1.46, $p = 0.22$). After full adjustment, HR (95% CI) were 0.82 (0.62–1.07), $p = 0.14$ among women and 1.12 (0.85–1.48), $p = 0.41$ among men. Adjusted HR (95% CI) for admission with IHD were 1.05 (0.92–1.19), $p = 0.50$ among women and 0.97 (0.82–1.15), $p = 0.77$ among men. Results were similar for vitamin D and combination supplementation. There were no associations with death, and in women, further adjustment for hormone-replacement therapy use did not alter the associations. In this very large prospective cohort, there was no evidence that use of calcium/vitamin D supplementation was associated with increased risk of hospital admission or death after ischemic cardiovascular events.

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Eatwell Guide

Use the Eatwell Guide to help you get a balance of healthier and more sustainable food. It shows how much of what you eat overall should come from each food group.

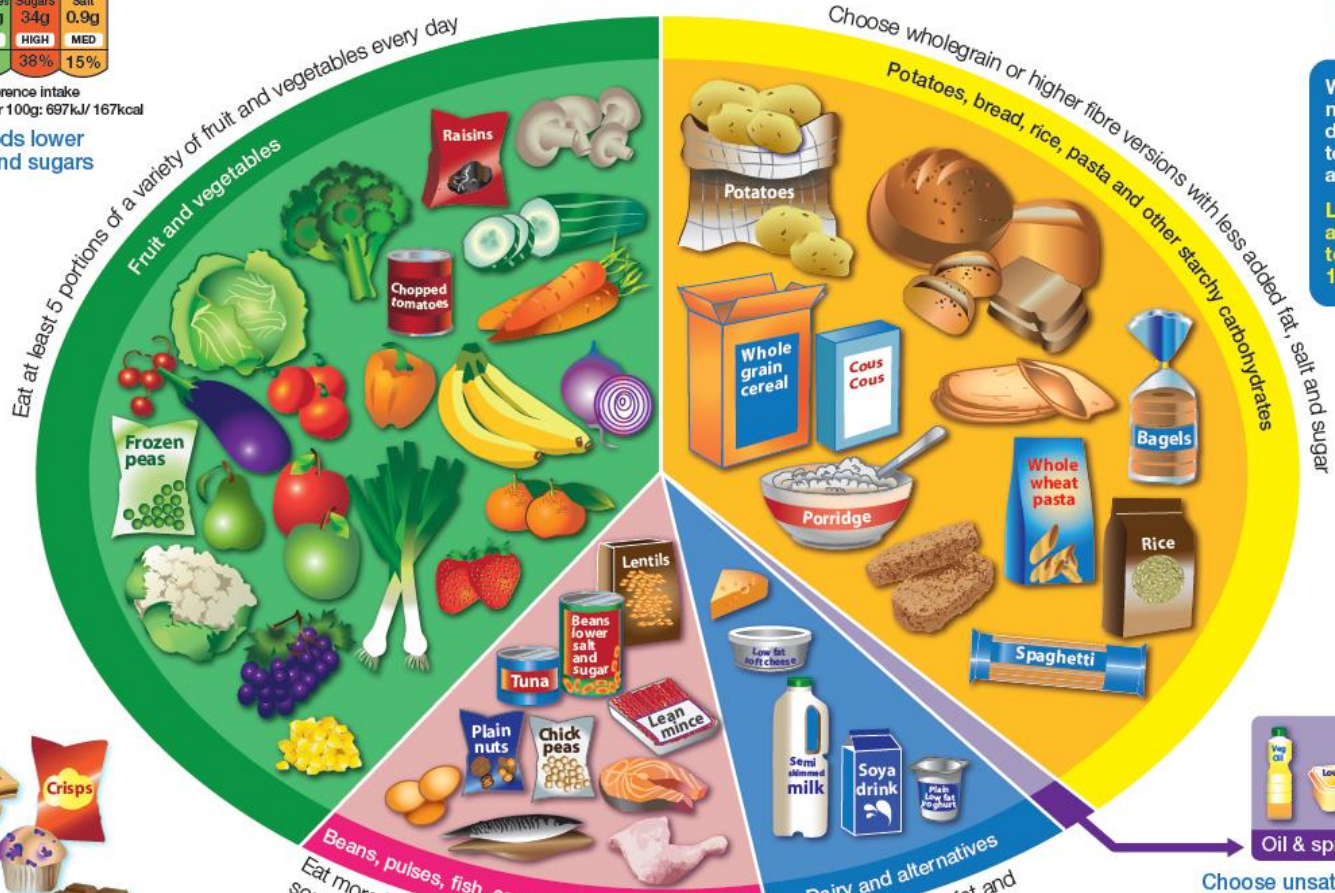
Check the label on packaged foods

Each serving (150g) contains

Energy	Fat	Saturates	Sugars	Salt
1046kJ 250kcal	3.0g	1.3g	34g	0.9g
	LOW	LOW	HIGH	MED
13%	4%	7%	38%	15%

of an adult's reference intake
Typical values (as sold) per 100g: 697kJ/ 167kcal

Choose foods lower in fat, salt and sugars



6-8 a day

Water, lower fat milk, sugar-free drinks including tea and coffee all count.

Limit fruit juice and/or smoothies to a total of 150ml a day.

Eat less often and in small amounts

Eat more beans and pulses, 2 portions of sustainably sourced fish per week, one of which is oily. Eat less red and processed meat

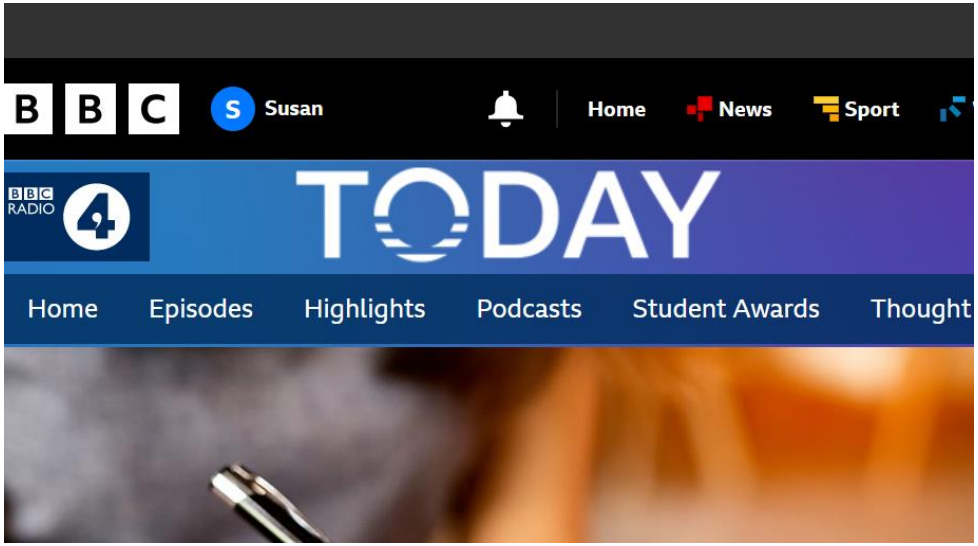
Choose lower fat and lower sugar options

Choose unsaturated oils and use in small amounts

Per day 2000kcal 2500kcal = ALL FOOD + ALL DRINKS

Source: Public Health England in association with the Welsh Government, Food Standards Scotland and the Food Standards Agency in Northern Ireland

Controversies in Nutritional Sciences!



Royal Osteoporosis Society Media Launch

April 2018 to current

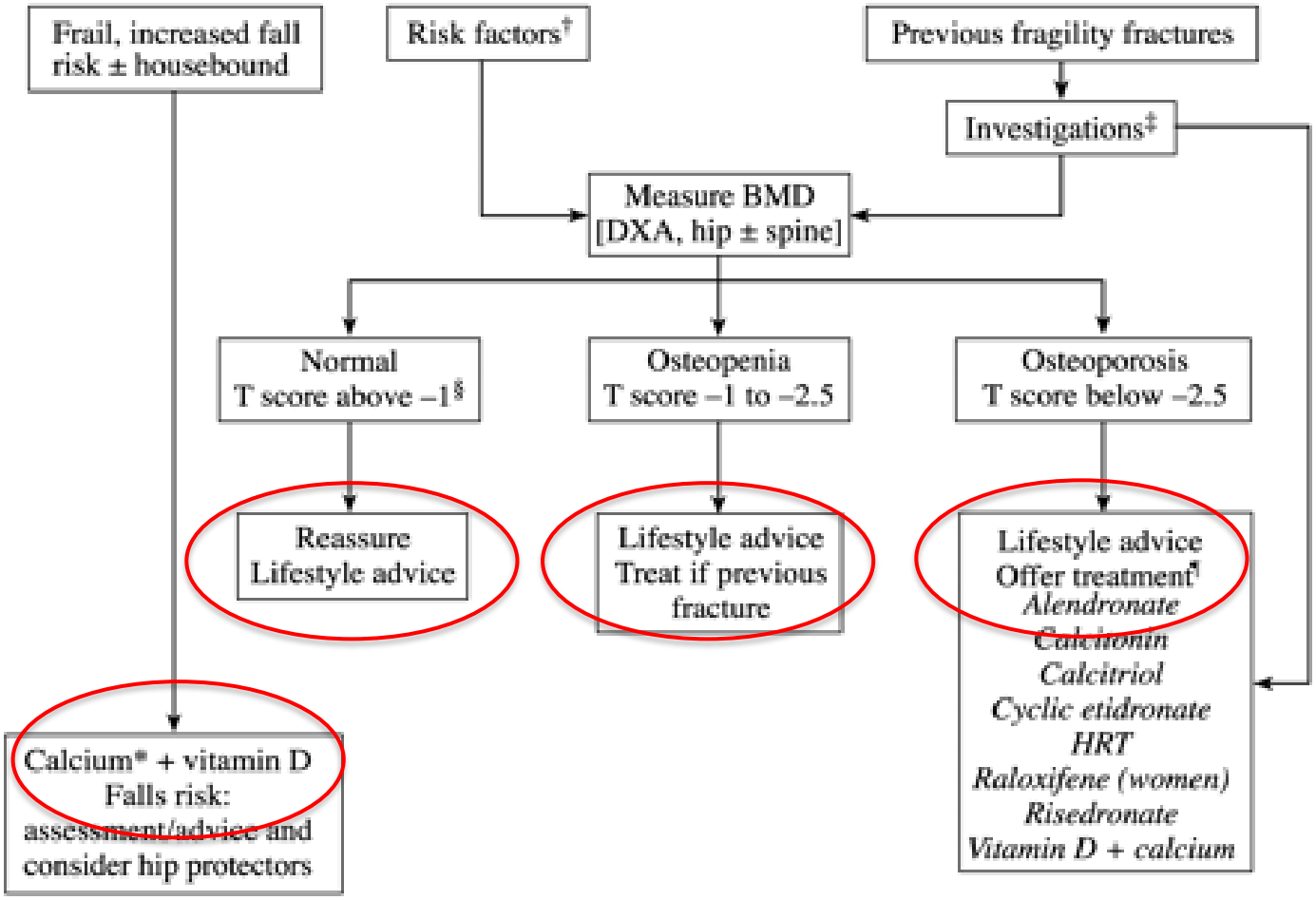
Problems with Social Media ‘Health’ Information

Dairy-free diets warning over risk to bone health

12 April 2017 | Health

Prof Susan Lanham-New, head of nutritional sciences at the University of Surrey and clinical advisor to the National Osteoporosis Society, said: "Diet in early adulthood is so important because by the time we get into our late 20s it is too late to reverse the damage caused by poor diet and nutrient deficiencies and the opportunity to build strong bones has passed."

Royal College of Physicians Guidelines



Royal College of Physician Guidelines (2000); Compston *et al* 2017;**12**:43

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 28, 2022 VOL. 387 NO. 4

Supplemental Vitamin D and Incident Fractures in Midlife and Older Adults

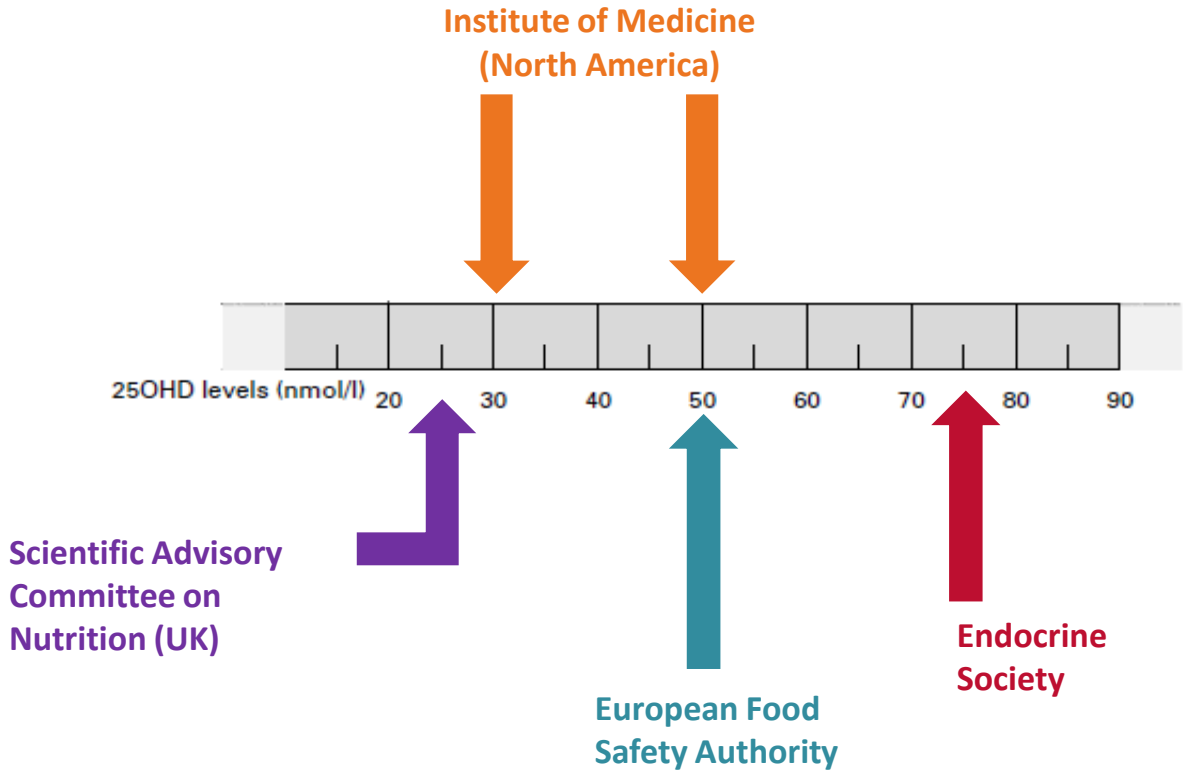
Meryl S. LeBoff, M.D., Sharon H. Chou, M.D., Kristin A. Ratliff, B.A., Nancy R. Cook, Sc.D., Bharti Khurana, M.D., Eunjung Kim, M.S., Peggy M. Cawthon, Ph.D., M.P.H., Douglas C. Bauer, M.D., Dennis Black, Ph.D., J. Chris Gallagher, M.D., I-Min Lee, M.B., B.S., Sc.D., Julie E. Buring, Sc.D., and JoAnn E. Manson, M.D., Dr.P.H.

VITAL Findings — A Decisive Verdict on Vitamin D Supplementation

Steven R. Cummings, M.D., and Clifford Rosen, M.D.

An estimated one third or more of U.S. adults 60 years of age or older take vitamin D supplements, not including those who take multivitamins or other compounds containing vitamin D.[1] Yet controversy continues about its overall benefits. In this issue of the *Journal*, LeBoff and

Defining Vitamin D Deficiency/Adequacy



Slide courtesy of Dr Taryn Smith

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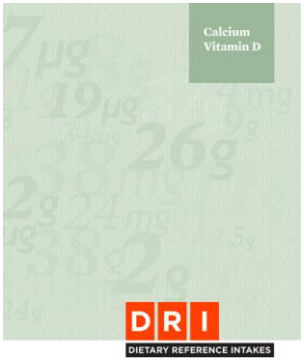
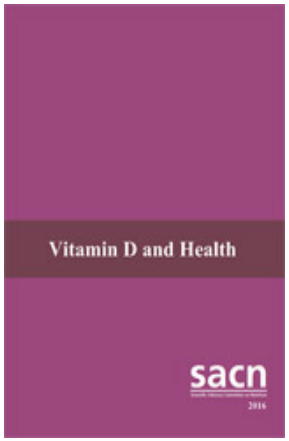
Worldwide Vitamin D Recommendations





SCIENTIFIC OPINION

efsa
European Food Safety Authority

ADOPTED: 29 June 2016

doi: 10.2903/j.efsa.2016.4547

Dietary reference values for vitamin D

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)

Health Council of the Netherlands

Evaluation of dietary reference values for vitamin D

norden

Nordic Nutrition Recommendations 2012

Integrating nutrition and physical activity

Annals of Nutrition & Metabolism

Original Paper

Ann Nutr Metab 2012;60:241–246
DOI: 10.1159/000337547

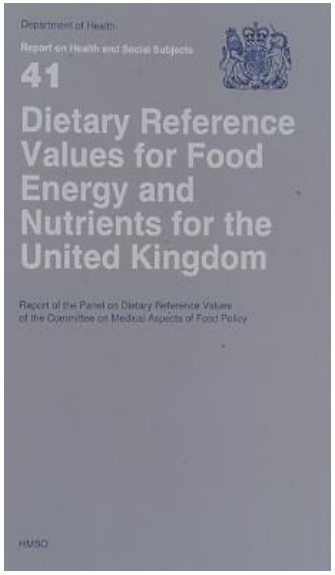
Received: February 23, 2012
Accepted: February 23, 2012
Published online: June 1, 2012

New Reference Values for Vitamin D

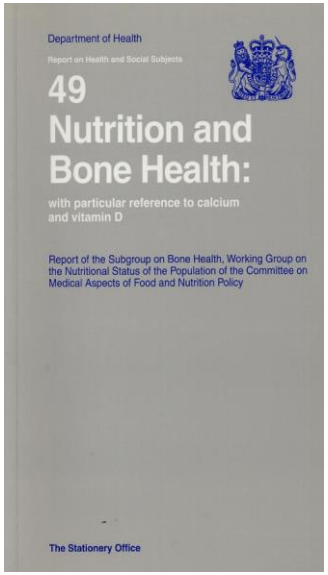
German Nutrition Society, Bonn, Germany

UK Recommendations

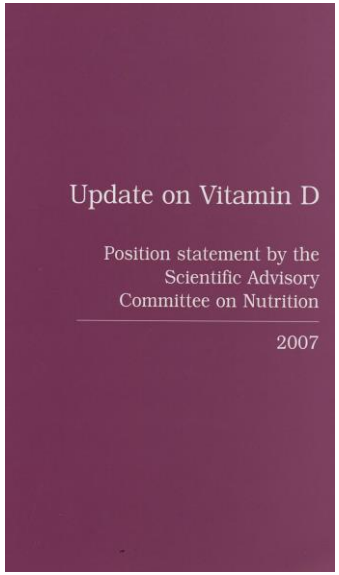
1991



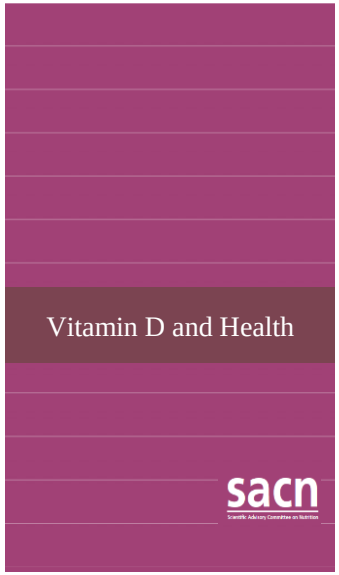
1998



2007



2016



0 µg/day recommendation

10 µg/day

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Vitamin D

Innovations – Public health policy

Age group	Old Recommendation (Department of Health, 1991)	New Recommendation (Public Health England, 2016)
0-6 months	0 µg	8.5 µg (340 IU)
7 mo - 3 y	0 µg	7 µg (280 IU)
4 - 50 years	0µg	10 µg (400 IU)
51 - 64 years	0 µg	10 µg (400 IU)
65 – 70 years	10 µg (400 IU)	10 µg (400 IU)
71 + years	10 µg (400 IU)	10 µg (400 IU)

The new recommendation represents a significant challenge to the UK population since we would achieve no more than 3.5 µg/ 140IU per day in our diet


When your shadow is *longer* than your height . . . . .
You make no vitamin D

Background

Shadow Method for Sun Protection

You can only make vitamin D in the sunshine once your shadow is shorter than your height.

SIR,—To protect the public from skin damage by the sun's ultraviolet (UV) rays, doctors warn their patients to avoid the midday sun between 1100 h and 1500 h or during similar periods when the radiation from the sun is assumed to be at maximum intensity. Unfortunately, these rules based on clock time are flawed and do not tell people when midday truly occurs or for how long it lasts. The strength of the sun's UV-B radiation depends mainly on the height of the sun in the sky, but clock time is often a poor indicator of solar height because of seasonal changes, wide time zones, daylight saving time, and the large differences in latitude and longtitude in various locations. When clock rules are working as intended, the limits of the unsafe period correspond roughly to times when the sun is halfway between the horizon and the overhead point (ie, at 45°).

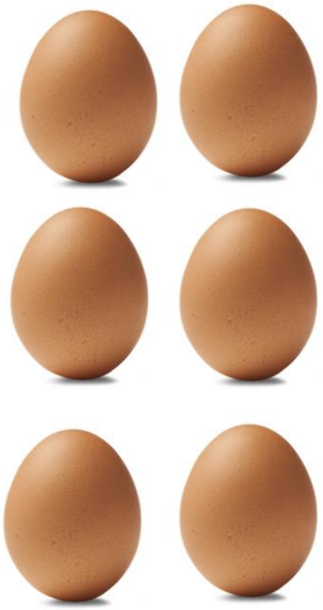
A simple, more accurate, and direct method for estimating the height of the sun and thereby the strength of its UV-B rays is to observe the lengths of shadows outdoors. When shadow lengths on level surfaces are equal to the height of objects casting them, the sun is at 45°. Shorter shadows imply stronger radiation. The shadow method is therefore a better approximation of the information that clock rules are trying to provide. Physical measurements of the

Holloway L, *Lancet* Feb 24, 1990, pg 484

Practical ways of increasing vitamin D intake

Table 2 Dietary sources of vitamin D (PHE 2019)

	Vitamin D content (µg per 100 g/100 ml)
Fish and shellfish	
Grilled herring	16.1
Canned pink salmon in brine	13.6
Grilled salmon	7.8
Grilled kipper fillet	9.0
Baked rainbow trout fillet	8.2
Smoked mackerel	8.2
Tinned sardines in tomato sauce	3.3
Milk and milk products	
Build-up powdered sachet (shake)	1.7
Fortified soya milk	0.8
Skimmed milk, dried	0.8
Custard, confectioners'	0.8
Horlicks, powder	18.5
Animal products	
Lamb leg, roast	0.7
Beef, roast	0.8
Corned beef, canned	1.3
Grilled bacon back rashers	0.8
Grilled pork sausages	1.1
Fried lamb's liver	0.9
Chicken's egg, raw	3.2
Non-animal based products	
Fortified, low-fat spread, polyunsaturated	8.4
Baking fat/margarine	8.8
Bran type cereal, fortified	3.9
Breakfast cereal, cornflakes, fortified	4.7



Mushrooms

x 4 tins of sardines in tomato sauce (71g/ tin)

x 4 Bowls of fortified cereal (cornflakes; 30g)

1.33 litres of fortified dairy-free alternative milk

Slide courtesy of Dr Saskia Wilson-Barnes

Key Work in Vitamin D from the University of Ulster NICHE Group

Proceedings of the Nutrition Society (2021), **80 (OCE3)**, E140 doi:10.1017/S0029665121002639

Irish Section Conference, 22–24 June 2021, Nutrition, health and ageing — translating science into practice – Part A

Improving vitamin D content in pork meat by UV bio-enrichment

H.R. Neill[1], C.I.R. Gill[1], E.J. McDonald[2], W.C. McRoberts[3], E.J. Rosbotham[1], R. Boland[1] and L.K. Pourshahidi[1]

[1]*Nutrition Innovation Centre for Food and Health (NICHE), School of Biomedical Sciences, Ulster University, Coleraine, UK,*
[2]*Devenish Nutrition Ltd., Belfast, UK and*
[3]*Agri-Food and Biosciences Institute, Belfast, UK*

Trained & Mentored by the late Professor Julie Wallace

Key Work in Vitamin D from the University of Ulster NICHE Group

Eur J Nutr (2017) 56:1577–1587
DOI 10.1007/s00394-016-1202-4

ORIGINAL CONTRIBUTION

Vitamin D_3 supplementation using an oral spray solution resolves deficiency but has no effect on VO_2 max in Gaelic footballers: results from a randomised, double-blind, placebo-controlled trial

Joshua J. Todd[1] · Emeir M. McSorley[1] · L. Kirsty Pourshahidi[1] · Sharon M. Madigan[2] · Eamon Laird[3] · Martin Healy[4] · Pamela J. Magee[1]

Trained & Mentored by the late Professor Julie Wallace

Key Work in Vitamin D from the University of Ulster NICHE Group

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Journals of Gerontology: Medical Sciences
cite as: *J Gerontol A Biol Sci Med Sci*, 2018, Vol. 73, No. 4, 519–525
doi:10.1093/gerona/glx168
Advance Access publication September 2, 2017

OXFORD

Research Article

The Prevalence of Vitamin D Deficiency and the Determinants of 25(OH)D Concentration in Older Irish Adults: Data From The Irish Longitudinal Study on Ageing (TILDA)

Eamon Laird, PhD,[1] Aisling M. O'Halloran, PhD,[1] Daniel Carey, PhD,[1] Martin Healy, PhD,[2] Deirdre O'Connor, MSc,[1] Patrick Moore, PhD,[1] Tom Shannon, Bsc,[2] Anne M. Molloy, PhD,[3] and Rose Anne Kenny, PhD[1,3,4]

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Sources of vitamin D

YES – but the content is not as high as in other foods.
TIP – put your mushrooms in the sun!

Vitamin D

Innovations – D-FINES Study (£0.7M, FSA funded)

Aim:

Effect of diet and sunlight on vitamin D status.

Outcome:

Extensive vitamin D issues in white Caucasian and South Asian populations.

Impact:

Informed DoH, PHE; Led to new significant funding from BBSRC.

FOOD STANDARDS AGENCY

D-FINES

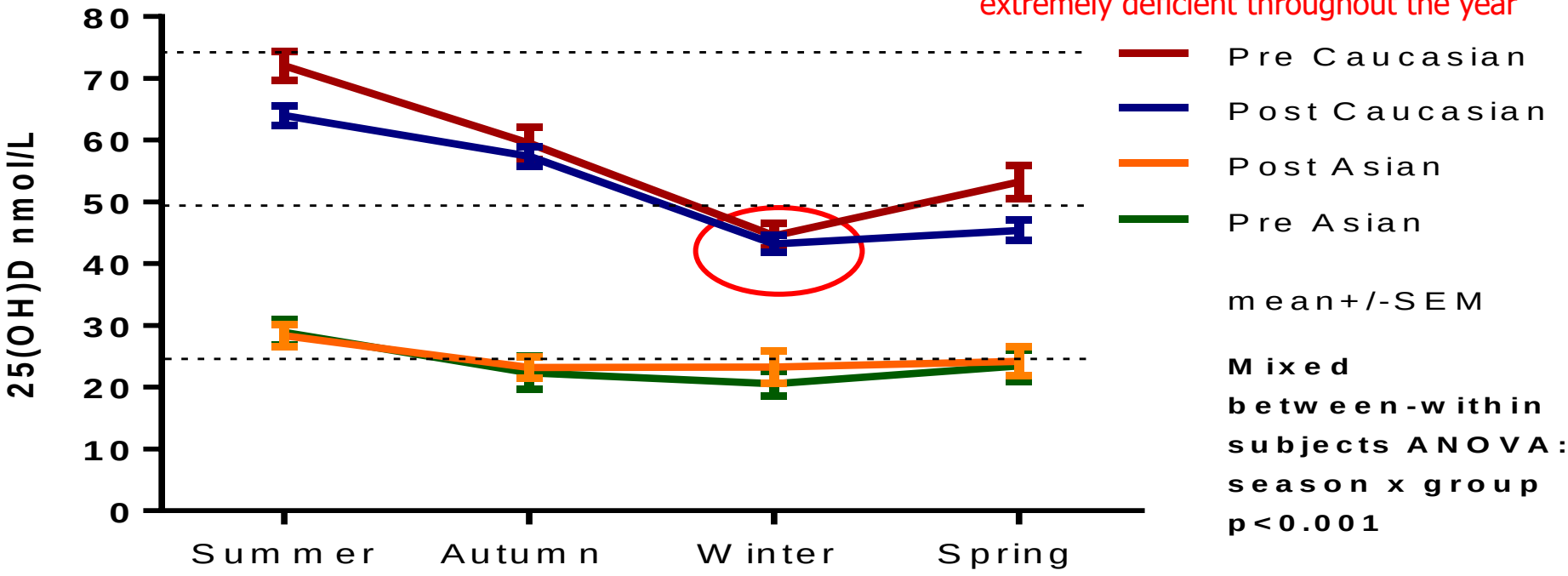
MANCHESTER 1824

UNIVERSITY OF SURREY

Key Findings from D-FINES Study

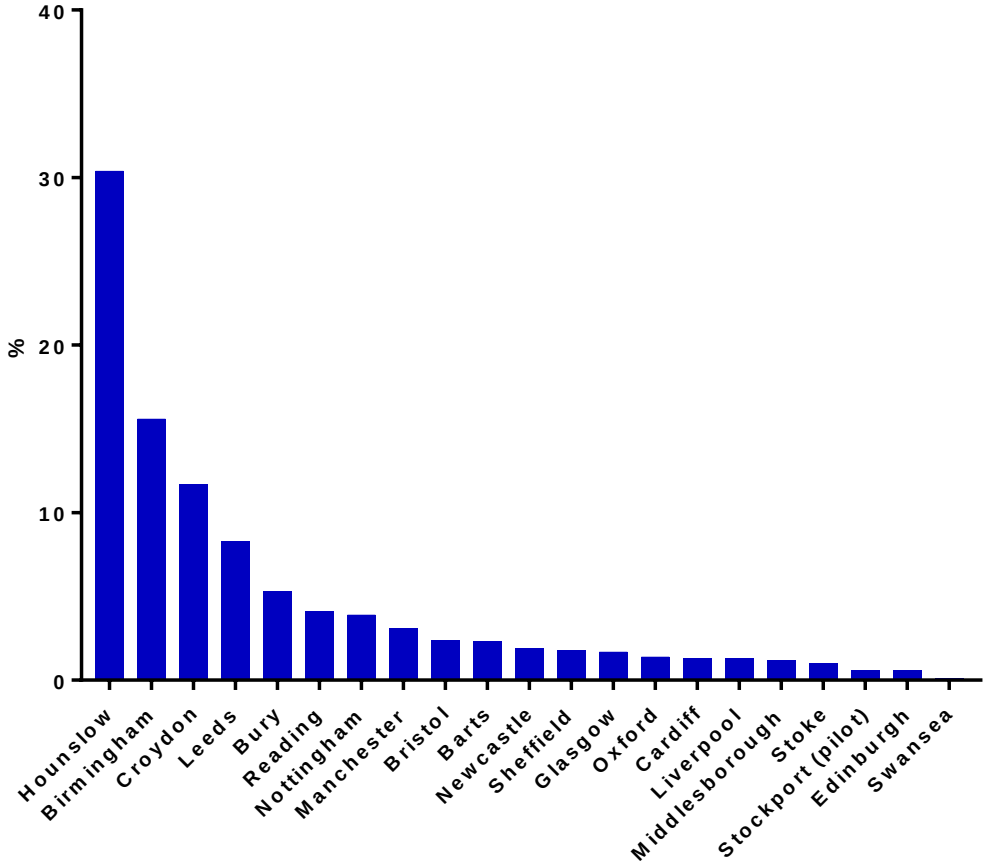
Darling et al. Osteoporosis International 2011, 2012)

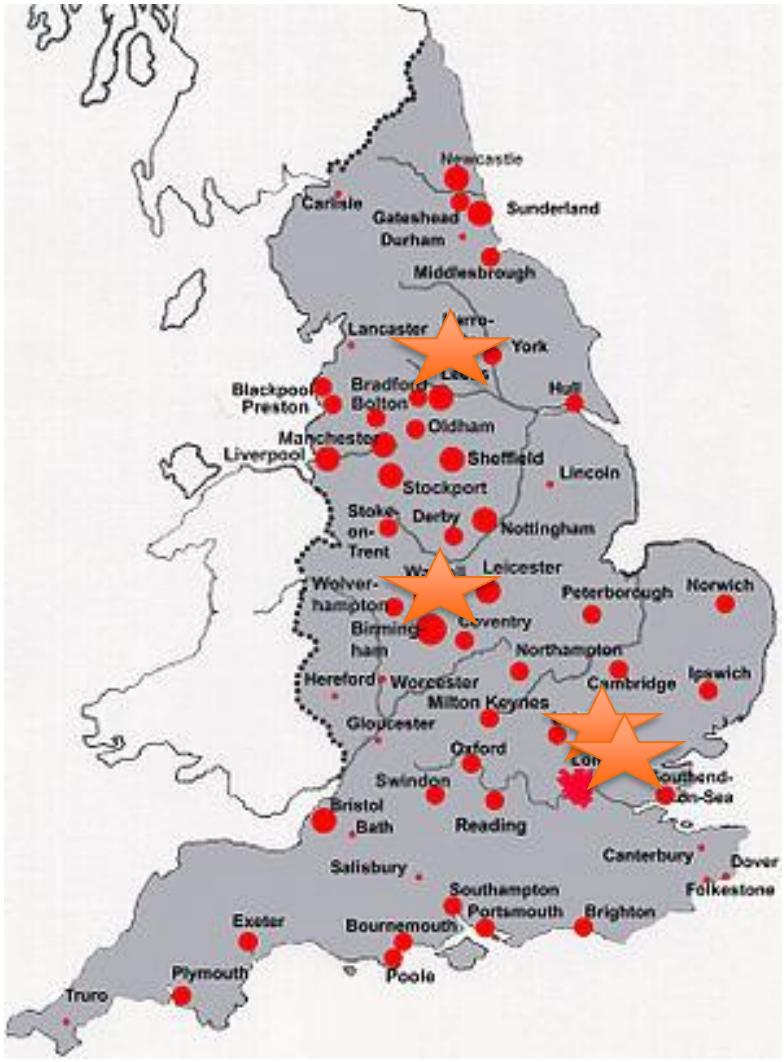
Caucasian women consistently higher 25OHD, with seasonal change
Considerable vitamin D 'insufficiency' in Caucasian women in late autumn and winter. Asian women extremely deficient throughout the year



UK Biobank study of serum 25(OH)D

Of the n 8024 UK Biobank South Asians, 2/3 from Hounslow, Birmingham, Croydon and Leeds



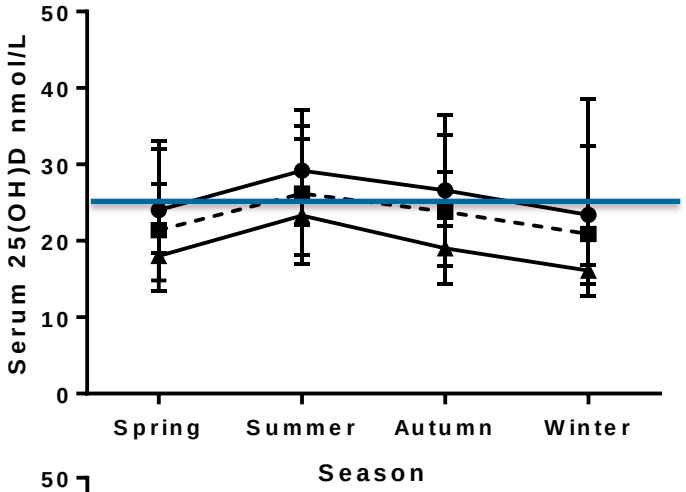


#uniofsurrey

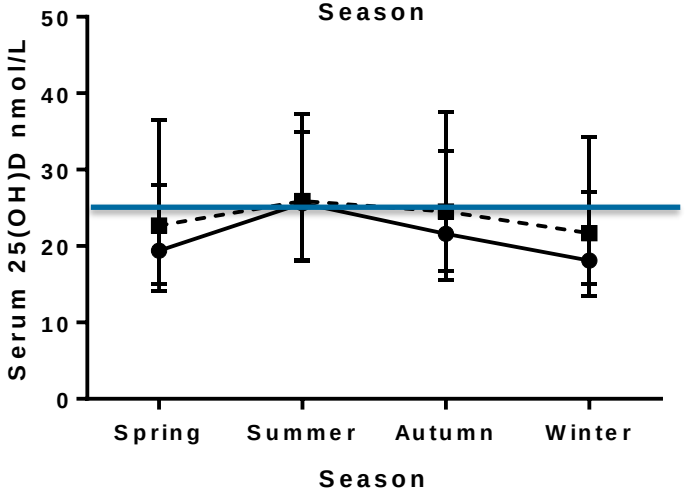
Serum 25(OH)D by ethnic group and gender

Vitamin D deficiency is *almost universal* in UK South Asians with *92% <50nmol/L, 55% <25nmol/L and 20% <15nmol/L*. 10% were below detection limit (10nmol/L). The general population are likely to be even lower.

Each person has one measurement in one season only (data are not repeated measures).



Median +/- IQR
Two way between subject ANOVA:
Ethnic x season P=0.13
Main effect ethnic P<0.0001
Main effect season P<0.0001



Median +/- IQR
Two way between subject ANOVA:
Gender x season P<0.0001

Note: these figures exclude n=824 participants who had values below (or above) the limit of detection

Public Health Nutrition Paper 2018

Public Health Nutrition: page 1 of 11 doi:10.1017/S1368980018001404

Vitamin D supplement use and associated demographic, dietary and lifestyle factors in 8024 South Asians aged 40–69 years: analysis of the UK Biobank cohort

Andrea L Darling*, David J Blackbourn, Kourosh R Ahmadi and Susan A Lanham-New
Department of Nutritional Sciences, School of Biosciences and Medicine, Faculty of Health and Medical Sciences, University of Surrey, Guildford, Surrey, GU2 7XH, UK

Public Health Nutrition

Table 1 Characteristics of 8024 South Asian UK Biobank participants by ethnic group: continuous data split by ethnic sub-group (Bangladeshi, Indian, Pakistani)

	Bangladeshi (*n* 236)					Indian (*n* 5951)					Pakistani (*n* 1837)					
	Mean	SD	*n*	Lower 95 % CI	Upper 95 % CI	Mean	SD	*n*	Lower 95 % CI	Upper 95 % CI	Mean	SD	*n*	Lower 95 % CI	Upper 95 % CI	*P**
Age (years)	50[a,b,c]	9	236	49	51	54[a,b,c]	8	5951	54	54	51[a,b,c]	8	1837	51	52	<0·001
BMI (kg/m^2)	26[b]	4	229	26	27	27[a]	4	5769	27	27	28[a,b]	5	1790	28	29	<0·001
Waist-to-hip ratio	0·9[a]	0·1	229	0·9	0·9	0·9[a,b]	0·1	5889	0·9	0·9	0·9[b]	0·1	1789	0·9	0·9	<0·001
	Median	IQR	*n*			Median	IQR	*n*			Median	IQR	*n*			
Vitamin D intake (µg/d)	3·0[a,c]	3·7	34			1·0[a,b]	1·6	1852			1·5[b,c]	1·9	320			<0·001

[a,b,c]Values within rows with like superscript letters were significantly different in *post hoc* tests ($P<0·05$).
*One-way ANOVA, except Kruskal–Wallis test (with Dunn's multiple-comparison *post hoc* tests) for vitamin D intake.

Equivalent NDNS data: 1.8-3.2 micrograms/day, suggest Indian and Pakistani intakes are lower than the National average

Vitamin D

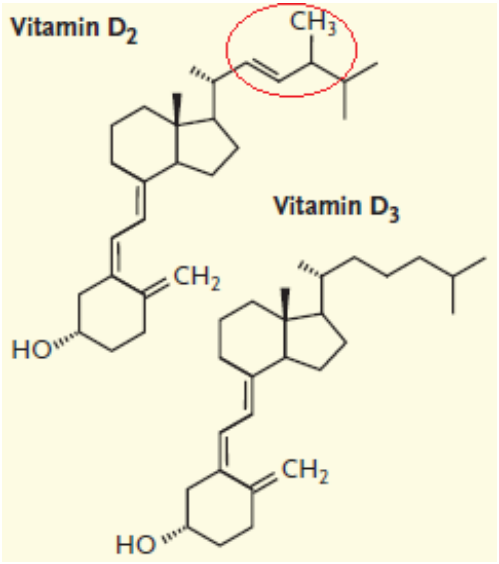
Innovations – D2 v D3 Study (£0.75M, BBSRC DRINC I)

Aim:
Does it matter if you give vitamin D2 (plant source) or vitamin D3 (animal sources)?

Impact:
Key information for DoH, PHE and the food industry…

Led to exciting bid for further significant funding from BBSRC DRINC II.

Outcome:
Vitamin D3 was 50% better at raising vitamin D levels in white Caucasian and South Asian populations.



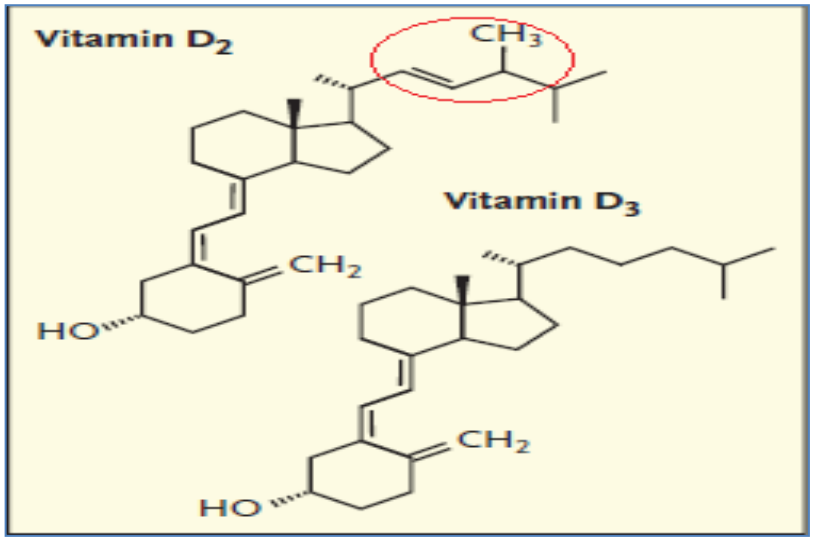
BACKGROUND: Vitamin D2 vs. Vitamin D3

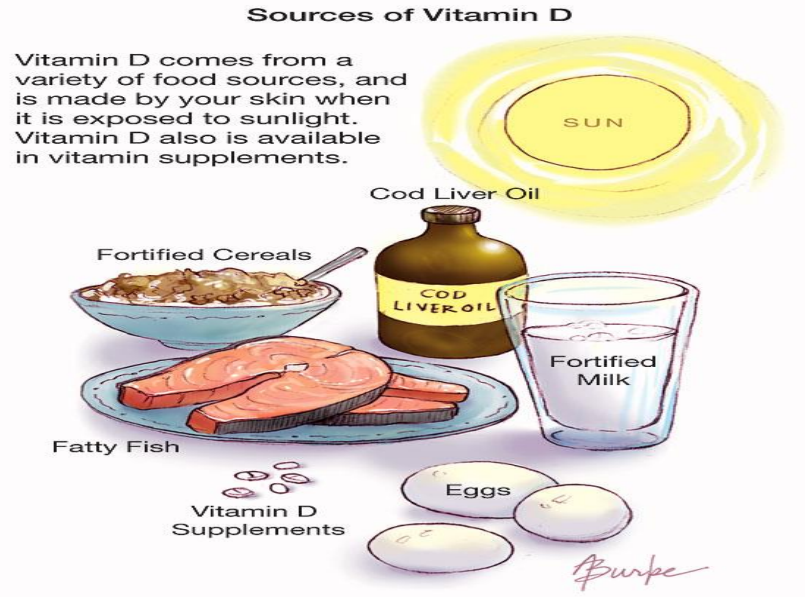
Vitamin D –

generic term for two molecules:

1) Ergocalciferol (Vitamin D2) – derived from UV irradiation of ergosterol that is widely distributed in plants and other fungi

2) Cholecalciferol (Vitamin D3) – formed from the action of UV irradiation on the skin: form that is found in fish, eggs etc.





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DRINC • DIET AND HEALTH RESEARCH INDUSTRY CLUB

Fortification of orange juice with vitamin D_2 or vitamin D_3 is as effective as an oral supplement in maintaining vitamin D status in adults[1–4]

Rachael M Biancuzzo, Azzie Young, Douglass Bibuld, Mona H Cai, Michael R Winter, Ellen K Klein, Allen Ameri, Richard Reitz, Wael Salameh, Tai C Chen, and Michael F Holick

ABSTRACT

Background: Vitamin D has been added to calcium-fortified orange juice. It is unknown whether vitamin D is as bioavailable from orange juice as it is from supplements.

Objective: The objective was to compare the bioavailability of vitamin D_2 and vitamin D_3 from orange juice with that from vitamin D_2 and vitamin D_3 supplements. A secondary aim was to determine which form of vitamin D is more bioavailable in orange juice.

Design: A randomized, placebo-controlled, double-blind study was conducted in healthy adults aged 18–84 y (15–20/group) who received 1000 IU vitamin D_3, 1000 IU vitamin D_2, or placebo in orange juice or capsule for 11 wk at the end of winter.

Results: A total of 64% of subjects began the study deficient in vitamin D (ie, 25-hydroxyvitamin D [25(OH)D]) concentrations <20 ng/mL). Analysis of the area under the curve showed no significant difference in serum 25(OH)D between subjects who consumed vitamin D–fortified orange juice and those who consumed vitamin D supplements ($P = 0.084$). No significant difference in serum 25(OH)D_3 was observed between subjects who consumed vitamin D_3–fortified orange juice and vitamin D_3 capsules ($P > 0.1$). Similarly, no significant difference in serum 25(OH)D_2 was observed between subjects who consumed vitamin D_2–fortified orange juice and vitamin D_2 capsules ($P > 0.1$). No significant overall difference in parathyroid hormone concentrations was observed between the groups ($P = 0.82$).

Conclusion: Vitamin D_2 and vitamin D_3 are equally bioavailable in orange juice and capsules. *Am J Clin Nutr* 2010;91:1621–6.

INTRODUCTION

malabsorption and avoid drinking milk (35–37). According to the US Department of Agriculture, 49% of Americans older than 2 y drink more than one glass (236.6 mL; 8 fluid oz) of juice every day. Tangpricha et al (38) reported that orange juice fortified with 1000 IU vitamin D_3/236.6 mL increased the serum 25-hydroxyvitamin D [25(OH)D] concentrations of adults by >150% over 12 wk, which indicated that the fortification of orange juice with vitamin D_3 is an effective way to increase vitamin D intake in adults.

Bread has been fortified with vitamin D since the 1930s (1). It was observed that fortifying wheat and rye bread with 400 IU vitamin D_3/100 g per serving resulted in a significant increase in serum 25(OH)D concentrations but no significant change in parathyroid hormone (PTH) concentrations after 3 wk compared with a control group (39). However fortification of bread with 5000 IU vitamin D_3/serving for 1 y not only increased serum 25(OH)D concentrations but also caused significant reductions in the PTH concentrations (40). A 3-wk bioavailability study showed comparable elevations in blood 25(OH)D concentrations between subjects who ingested wild mushrooms and those who ingested 400 IU vitamin D_2 (41).

Whether vitamin D_2 is equally as effective as vitamin D_3 at maintaining blood concentrations of 25(OH)D is still under discussion. A study of the bioavailability of 4000 IU vitamin D_2 and vitamin D_3 ingested in alcohol for 2 wk (42) or as a single 50,000-IU dose (43) suggested that vitamin D_2 was less effective than vitamin D_3 in raising and maintaining blood concentrations of 25(OH)D. However, elevations in blood 25(OH)D concen-

[1] From the Endocrine Section, Department of Medicine, Boston Univ

The American Journal of Clinical Nutrition

Study Limitation:

n 12-13 in each group but *n* 65 needed for appropriate study power

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DRINC • DIET AND HEALTH
RESEARCH INDUSTRY CLUB

Vitamin D_2 and vitamin D_3 comparisons: fundamentally flawed study methodology

Dear Sir:

The recent article by Biancuzzo et al (1) presents data showing that vitamin D is equally bioavailable from orange juice and gel caps. This equivalence of vehicle was shown for both vitamin D_2 and vitamin D_3. The article is important because it has implications for health policy.

However, health professionals, scientists, and the public alike are interpreting this article as evidence that vitamin D_2 is equivalent to vitamin D_3, which is an issue that was not addressed by Biancuzzo et al (1). The results present no direct comparison of the area under the curve (AUC) for serum 25-hydroxyvitamin D for vitamin D_2 compared with vitamin D_3.

We are writing to emphasize that the conclusion of the article by Biancuzzo et al (1) is unfortunately ambiguous and hence subject to misinterpretation; the authors failed to make it clear that their study was not designed to compare vitamin D_2 with vitamin D_3. Without such clarification, the true interpretation of the findings of Biancuzzi et al will be lost to most who read their article.

The authors had no conflicts of interest to declare.

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Reinhold Vieth

Department of Nutritional Sciences
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Toronto
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Robert Heaney

Reply to S Lanham-New et al

Dear Sir:

We were pleased that Lanham-New et al appreciated that this article has important implications for health policy. It is, however, surprising and disappointing that these 3 experts did not fully understand the design, outcomes, and conclusions of our study. This study was designed to compare not only the bioavailability of vitamin D_2 and vitamin D_3 in orange juice with that in capsules, but it also was designed to confirm the previous report (1) that vitamin D_2 is equally as effective as vitamin D_3 in raising and maintaining total serum 25-hydroxyvitamin D [25(OH)D] concentrations. In our article (2), we clearly showed that serum 25-hydroxyvitamin D_2 [25(OH)D_2] and 25-hydroxyvitamin D_3 [25(OH)D_3] increased in identical fashion, and thus the results were not ambiguous—ie, vitamin D_2 was equally as effective as vitamin D_3 in both orange juice and in capsular form in vitamin D_3 or vitamin D_2 (**Table 1**). Therefore, on the basis of all of these analyses, it can be concluded with a high degree of certainty that vitamin D_2 is equally as effective as vitamin D_3 in raising and maintaining serum total 25(OH)D concentrations and that vitamin D_2 is equally as bioavailable as vitamin D_3.

None of the authors declared a conflict of interest.

Rachael M Biancuzzo
Michael F Holick

Endocrine Diabetes and Nutrition Section
Department of Medicine

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RESEARCH INDUSTRY CLUB

Authors reiterated their view re D2 & D3 being the same

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D2D3

The D2-D3 Study:

Ergocalciferol (vitamin D2) vs. cholecalciferol (vitamin D3) food fortification: comparative efficiency in raising 25OHD status in Caucasian & South Asian women

Tripkovic L, Wilson LR, Hart K, Elliott R, Smith CP, Bucca G, Moller-Levet C, Penson S, Chope G, Johnsen S, Hyppönen E, Berry J, Lanham-New S

Grant No. BB/I006192/1
Grant Dates: April 2011 – March 2015

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Campden BRI
food and drink innovation

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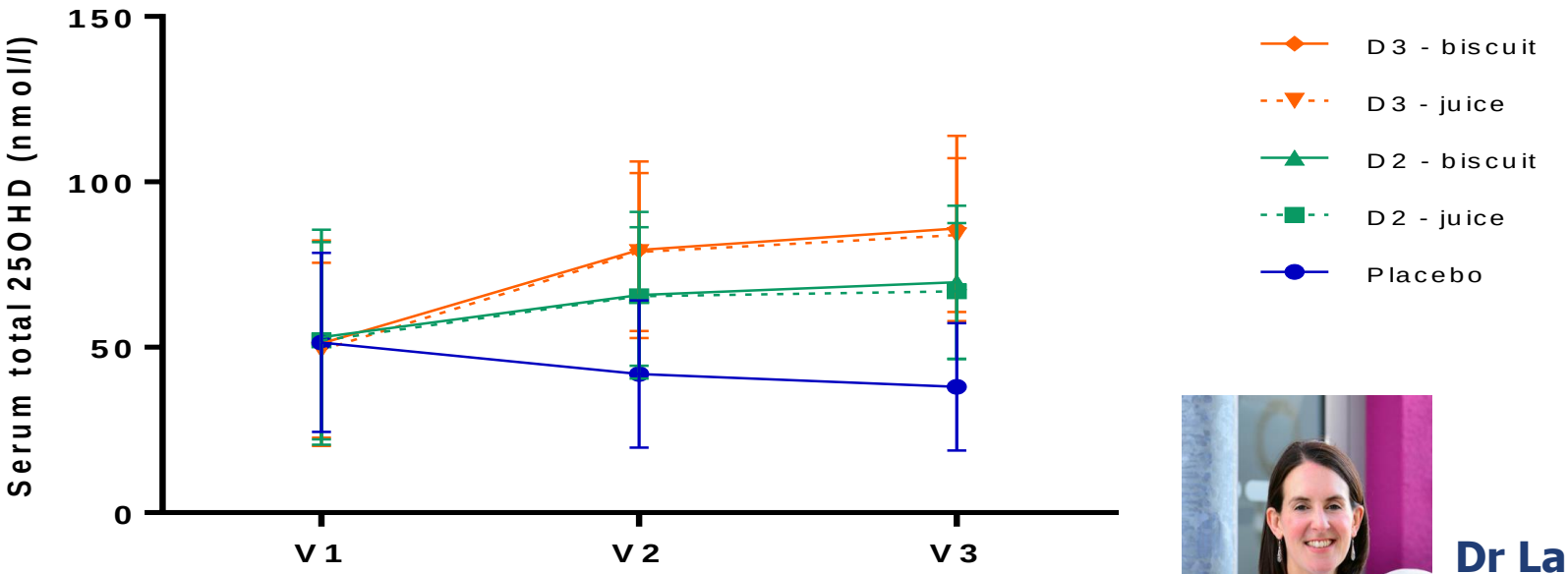
Serum total 25OHD levels per visit, taking into account the type of vitamin D consumed and the food matrix



Daily supplementation with 15 μg vitamin D_2 compared with vitamin D_3 to increase wintertime 25-hydroxyvitamin D status in healthy South Asian and white European women: a 12-wk randomized, placebo-controlled food-fortification trial

Laura Tripkovic,[1] Louise R Wilson,[1] Kathryn Hart,[1] Sig Johnsen,[2] Simon de Lusignan,[3] Colin P Smith,[4] Giselda Bucca,[4] Simon Penson,[5] Gemma Chope,[5] Ruan Elliott,[1] Elina Hyppönen,[6] Jacqueline L Berry,[7] and Susan A Lanham-New[1]

[1]Department of Nutritional Sciences, [2]Surrey Clinical Research Centre, and [3]Department of Clinical and Experimental Medicine, School of Biosciences and Medicine, Faculty of Health and Medical Sciences, University of Surrey, Guildford, United Kingdom; [4]School of Pharmacy and Biomolecular Sciences, University of Brighton, Brighton, United Kingdom; [5]Campden BRI, Chipping Campden, Gloucestershire, United Kingdom; [6]Division of Health Sciences, School of Population Health, University of South Australia, Adelaide, South Australia, Australia; and [7]Vitamin D Research Group, Department of Medicine, University of Manchester, Manchester, United Kingdom

The American Journal of CLINICAL NUTRITION

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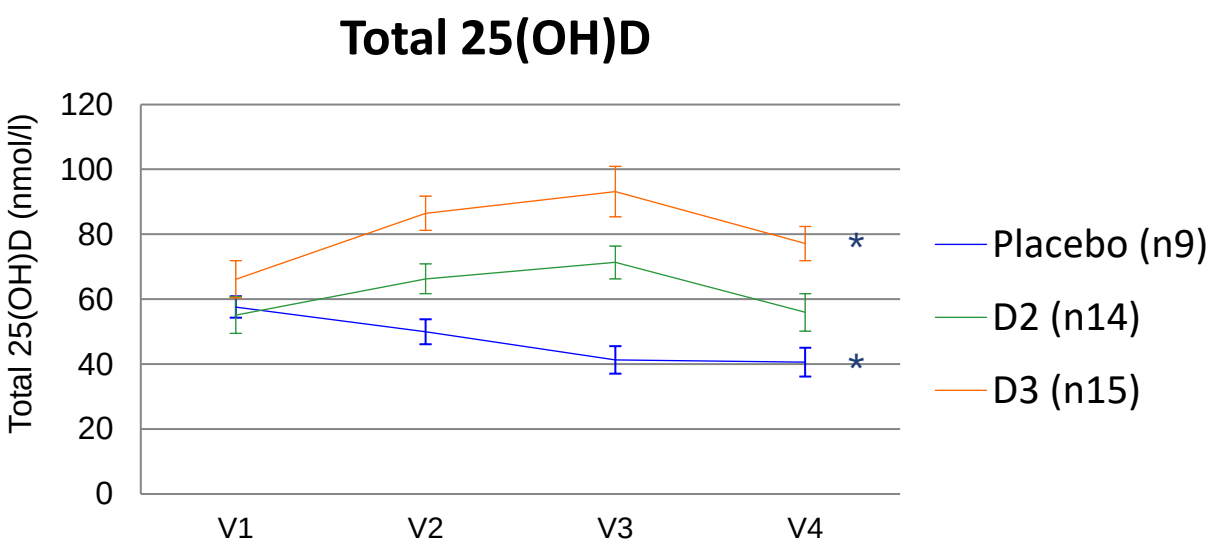
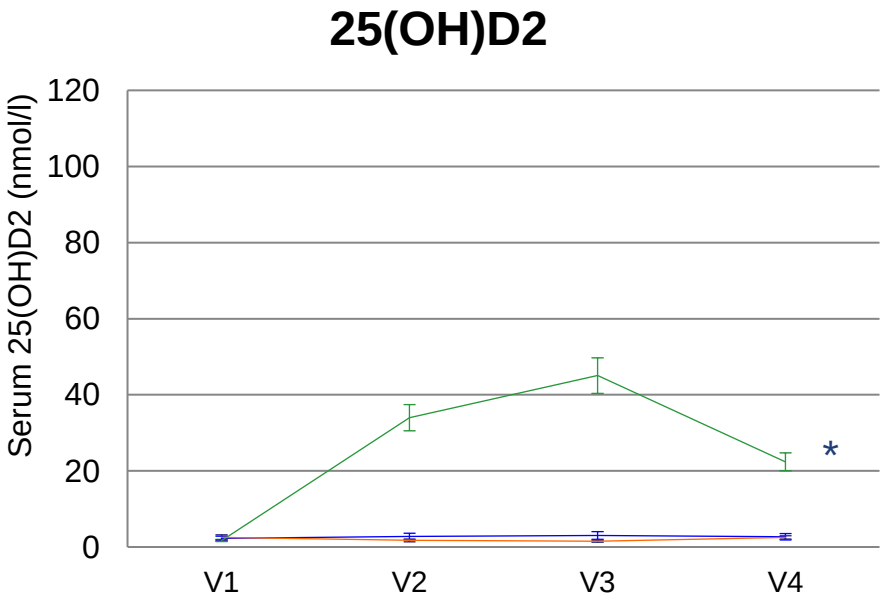
University of Brighton

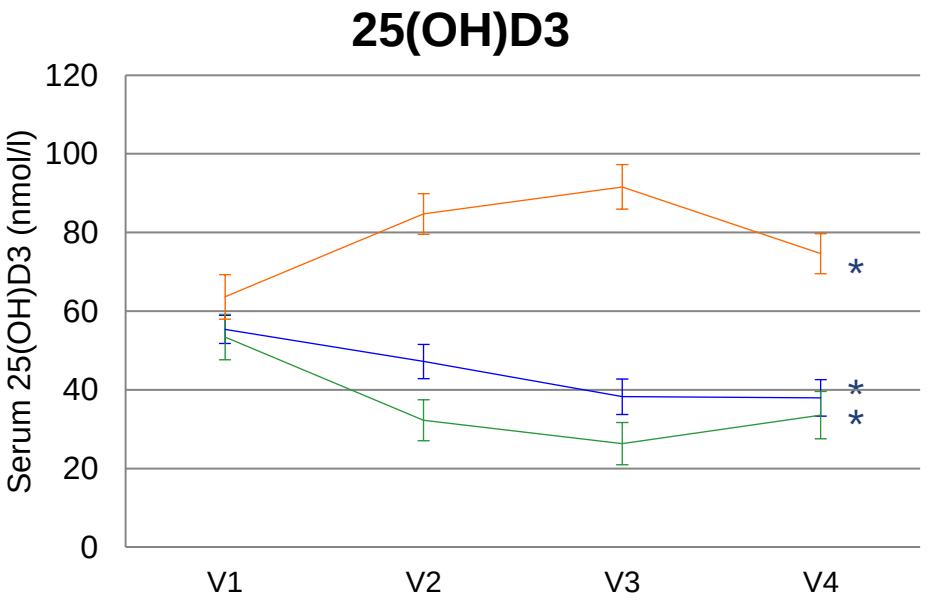
Dr Laura Tripkovic

Dr Louise Durrant

V4 Results: 4 Weeks Post-Intervention







*V4 significantly different to V1 ($p<0.021$)

Frontiers in
Immunology

IMPACT FACTOR 7.561
CITESCORE 8.1

Professor Colin Smith
Professor Functional Genomics
University of Brighton & Surrey

frontiers

Vitamins D2 and D3 have overlapping but different effects on the human immune system revealed through analysis of the blood transcriptome

Louise R. Durrant[1], Giselda Bucca[2], Andrew Hesketh[2], Carla Möller-Levet[1], Laura Tripkovic[1], Huihai Wu[1], Kathryn H. Hart[1], John C. Mathers[3], Ruan M. Elliott[1], Susan Lanham-New[1], Colin Smith[2*]

[1]University of Surrey, United Kingdom, [2]University of Brighton, United Kingdom, [3]Newcastle University, United Kingdom

Measuring Gene Expression in Humans

Most tissues: high frequency

sampling not possible

Whole Blood

'Bloodomics'

"An accessible window to the transcriptomic response of

Proc Natl Acad Sci U S A, **110**: E1132-E1141 (2013)

PNAS PLUS

Effects of insufficient sleep on circadian rhythmicity and expression amplitude of the human blood transcriptome

Carla S. Möller-Levet[1], Simon N. Archer[1], Giselda Bucca[1], Emma E. Laing, Ana Slak, Renata Kabiljo, June C. Y. Lo, Nayantara Santhi, Malcolm von Schantz, Colin P. Smith[1], and Derk-Jan Dijk[1,2]

Faculty of Health and Medical Sciences, University of Su

Proc Natl Acad Sci U S A **111**: E682-E691 (2014)

CrossMark click for updates

PNAS PLUS

Mistimed sleep disrupts circadian regulation of the human transcriptome

Simon N. Archer[1], Emma E. Laing[1], Carla S. Möller-Levet[1], Daan R. van der Veen, Giselda Bucca, Alpar S. Lazar, Nayantara Santhi, Ana Slak, Renata Kabiljo, Malcolm von Schantz, Colin P. Smith, and Derk-Jan Dijk[2]

D2-D3 Study: Transcriptomic Analysis

Tripkovic *et al* (2017) participants
n=335: WE n=245 , SA n=90

Selected 32 subjects from each of the D2 and D3 treatment groups, and 34 from the **placebo**

For D2 and D3, a range of serum [25OHD] responses to supplementation were chosen

Placebo subjects were chosen at random

Subjects for transcriptome analysis
n=98: WE n=67 , SA n=31

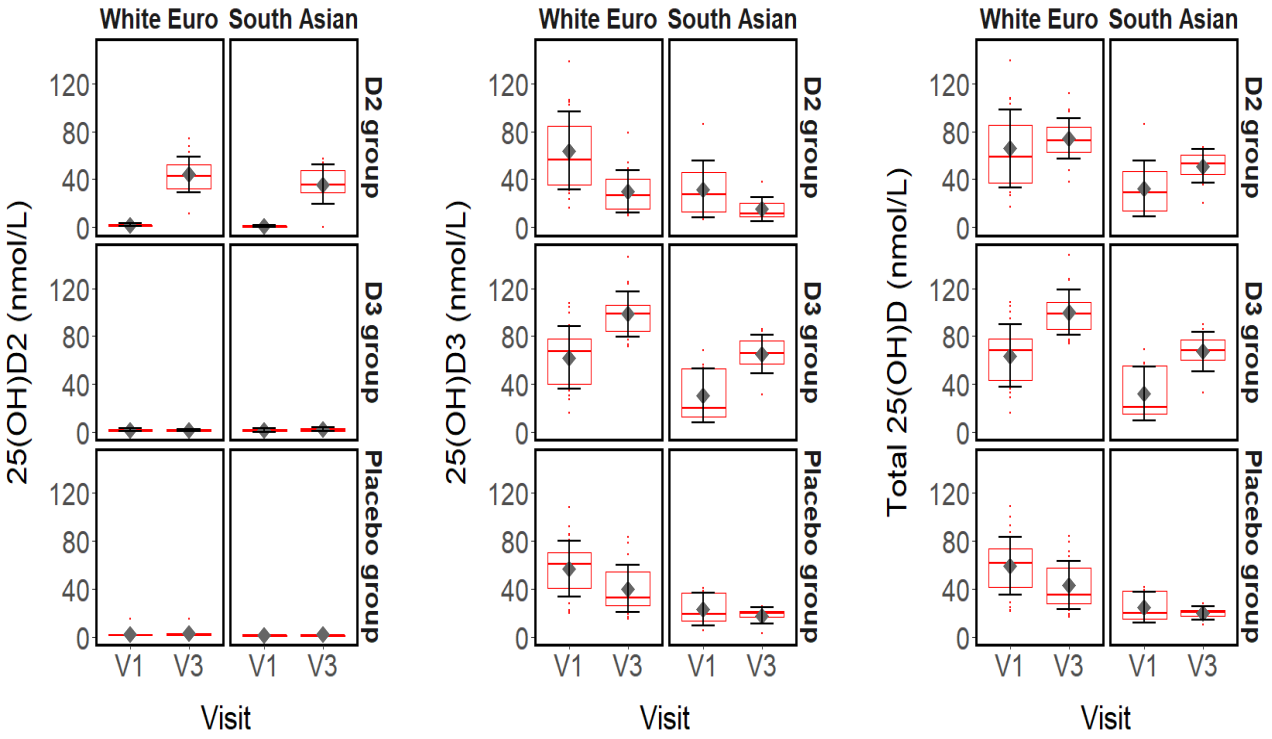
WE = white European
SA = South Asian

V1 = baseline visit; **V3** = sample at 12 weeks
Focused on determining changes at V3 versus V1

Ethnic groups and vitamin D metabolite levels (V1 and V3)

Group	WE (n)	SA (n)	Total (n)
D2	21	11	32
D3	21	11	32
Placebo	25	8	33

measurements $25(OH)D_2$ $25(OH)D_3$ Total 25(OH)D



Treatment

D2

D3

Placebo

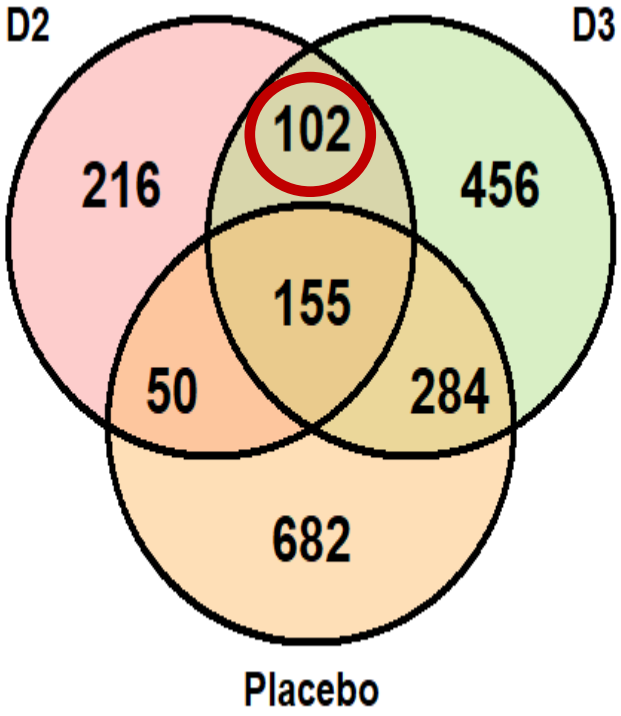
Transcriptome: differentially expressed genes

Comparison	**Sig. down** genes	**Sig. up** genes
WE D2 V3 v V1	498	350
WE D3 V3 v V1	**943**	**329**
WE P V3 v V1	1096	565
SA D2 V3 v V1	1	0
SA D3 V3 v V1	1	0
SA P V3 v V1	189	408
[WE D2 V3 v V1] v [WE P V3 v V1]	0	0
[WE D3 V3 v V1] v [WE P V3 v V1]	0	0
[WE D3 V3 v V1] v [WE D2 V3 v V1]	0	0
[SA D2 V3 v V1] v [SA P V3 v V1]	0	0
[SA D3 V3 v V1] v [SA P V3 v V1]	**2**	**3**
[SA D3 V3 v V1] v [SA D2 V3 v V1]	0	0

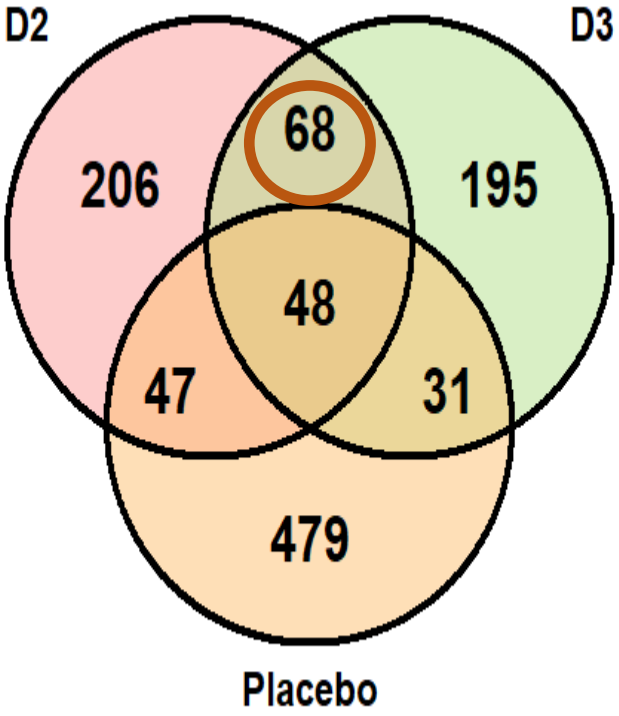
D3 & D2 do not have the same effect

More genes are down-regulated by D3 than D2 (*'paired' within group analysis)*

The placebo group helps us to distinguish D2-specific changes from D3 depletion



Down in WE V3 v V1



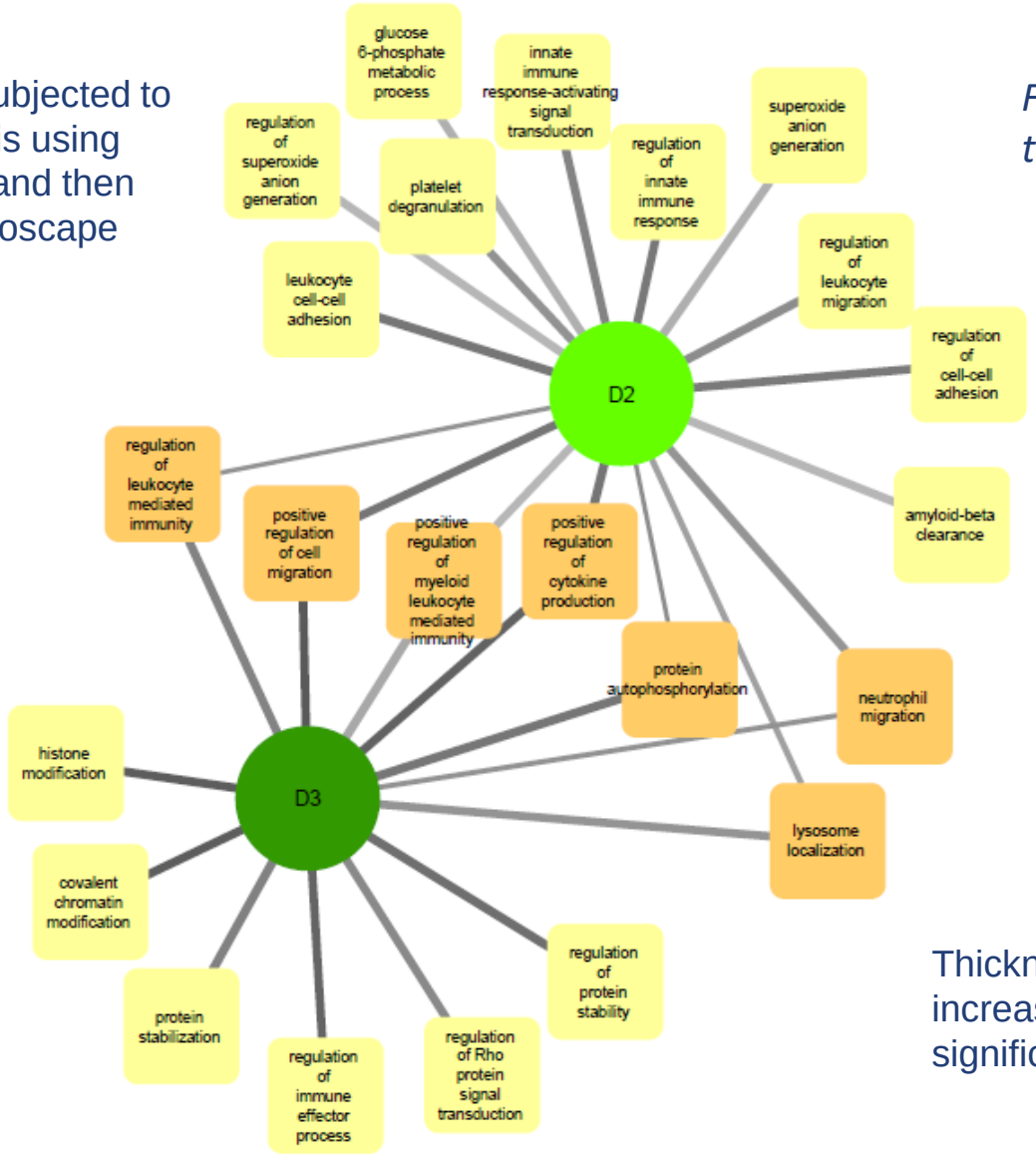
Up in WE V3 v V1

LIMMA-based differential expression analysis

Some pathways are influenced differently by vitamins D2 and D3 in the WE group

Significant GO Biological Pathway functional categories associated with **down-regulated** probes in the D2 or D3 treatment groups, but **not** the placebo

Gene products subjected to functional analysis using compareCluster and then imported into Cytoscape



*Focus on **pathways** rather than individual genes*

WE group

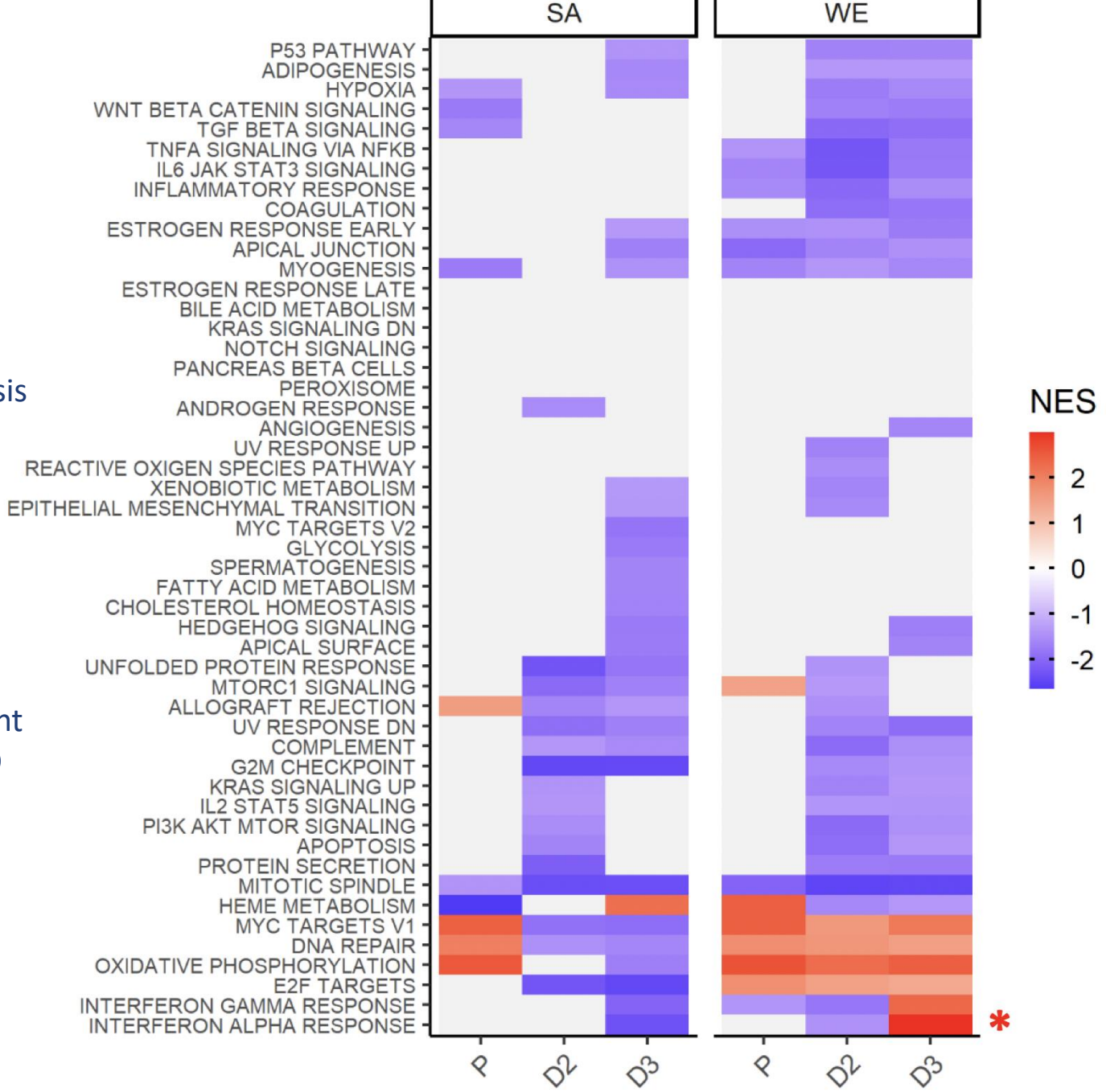
Thickness of lines connecting nodes increases with increasing statistical significance

Vitamin D_3 enhances interferon signaling while D_2 does not

Gene Set Enrichment Analysis (GSEA) using the 50 **Hallmark Gene Sets** from the Molecular Signatures Database (**MSigDB**).

Gene sets showing significant changes following vitamin D supplementation (time point V3 versus V1). Genes ranked by t-statistic.

NES: Normalized enrichment Score from the Gene Set Enrichment analysis



Key Pointers from this works I

Low vitamin D status remains a key public health concern globally.

Significant populations groups exhibit vitamin D deficiency **(as defined by a 25OHD status < 25nmol/l)**

Nutritional strategies to improve vitamin D status are urgently required

Darked-skinned population groups are at particular risk of severe vitamin D deficiency

From our novel transcriptome analysis, vitamin D2 does not appear to have the same physiological effect in humans as vitamin D3

Key Pointers from this Work II

Vitamin D supplementation (D3 much more so than D2) *suppresses* the activity of many pathways, including those of the immune system

Ethnic differences: South Asians may respond differently to vitamin D supplementation (*caveat*: low baseline measurements and different sample sizes)

This study has raised several interesting questions about D2 supplementation

Need for larger, properly powered, studies on the system-wide effects of vitamin D

Importance of vitamin D to the immune system II

Proceedings of the Nutrition Society (2012), **71**, 50–61
doi:10.1017/S0029665111001650
 First published online 18 August 2011

A meeting of the Nutrition Society hosted by the Irish Section jointly with the American Society for Nutrition was held at University College Cork, Republic of Ireland on 15–17 June 2011

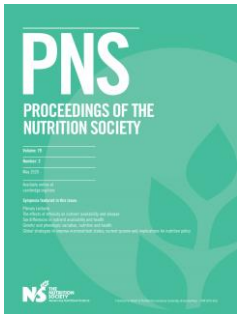
70th Anniversary Conference on 'Vitamins in early development and healthy aging: impact on infectious and chronic disease'

Symposium 3: Vitamin D and immune function: from pregnancy to adolescence
Vitamin D and immune function: an overview

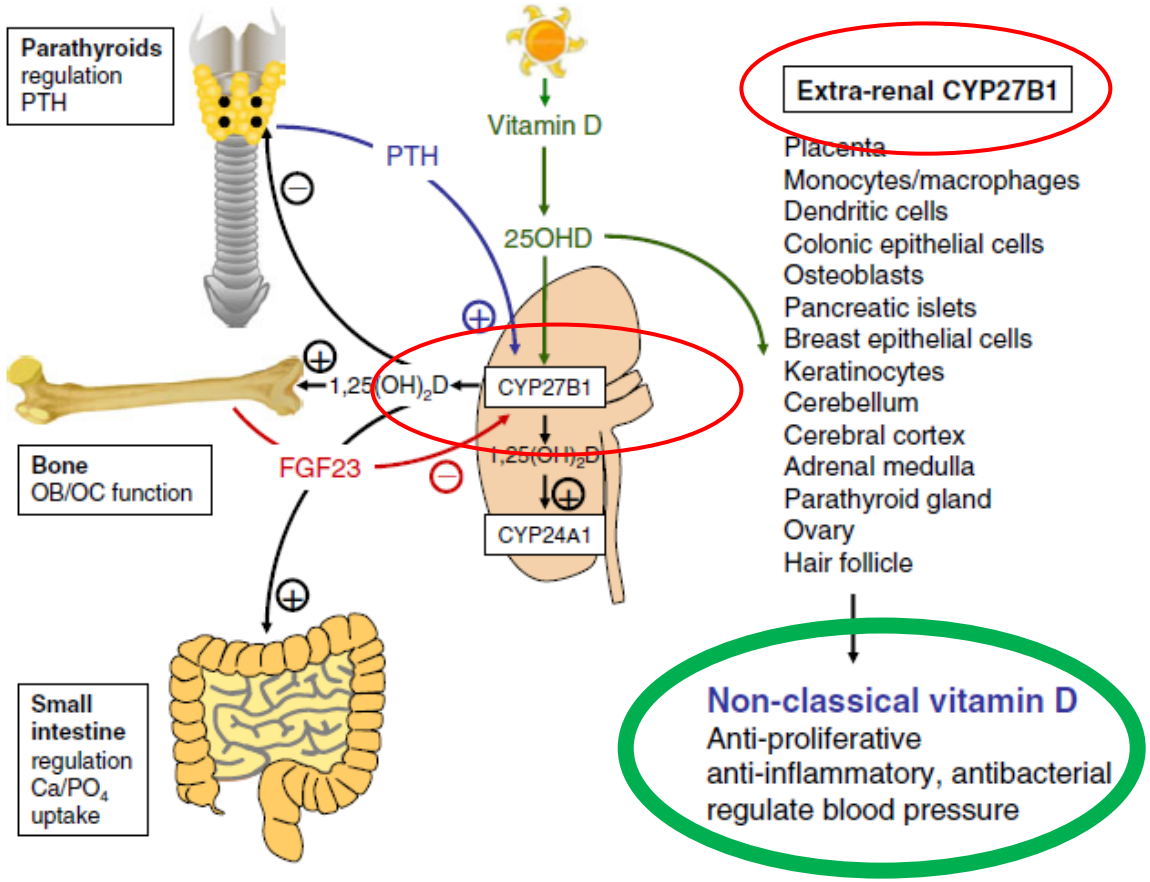
Martin Hewison
UCLA and Orthopaedic Hospital Department of Orthopaedic Surgery and the Orthopaedic Hospital Research Center, David Geffen School of Medicine at UCLA, 615 Charles E. Young, Los Angeles, CA 90095, USA

UNIVERSITY OF BIRMINGHAM

PNS's most highly cited paper on Vitamin D



Importance of vitamin D to the immune system III



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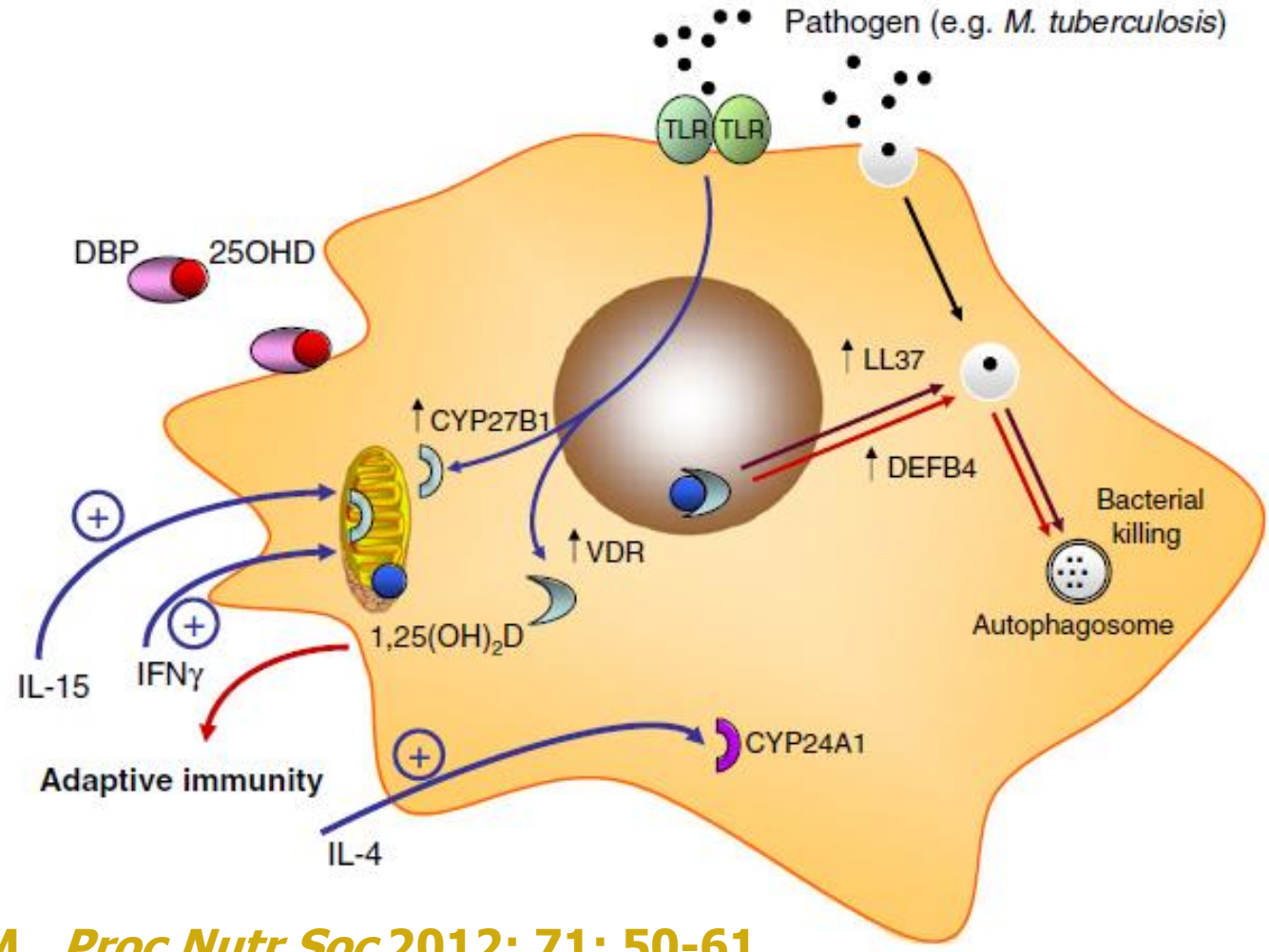
Hewison M. *Proc Nutr Soc* 2012; 71: 50-61

The importance of vitamin D to immune system IV



Hewison M. *Proc Nutr Soc* 2012; 71: 50-61

Vitamin D and Respiratory Health I

- It has been hypothesised that there is an association between seasonal upper respiratory tract infections and low vitamin D status because both occur in the winter months.

- However, controversy remains as to whether there is a direct link between the seasonality of influenza and vitamin D deficiency.

- Higher influenza incidence in winter may be due to behavioural reasons including the greater time spent indoors, which increases individuals' proximity and hence likely inter-personal transmission.

BMJ

N ACCESS

Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data

Adrian R Martineau,[1,2] David A Jolliffe,[1] Richard L Hooper,[1] Lauren Greenberg,[1] John F Aloia,[3] Peter Bergman,[4] Gal Dubnov-Raz,[5] Susanna Esposito,[6] Davaasambuu Ganmaa,[7] Adit A Ginde,[8] Emma C Goodall,[9] Cameron C Grant,[10] Christopher J Griffiths,[1,2,11] Wim Janssens,[12] Ilkka Laaksi,[13] Semira Manaseki-Holland,[14] David Mauger,[15] David R Murdoch,[16] Rachel Neale,[17] Judy R Rees,[18] Steve Simpson,Jr[19] Iwona Stelmach,[20] Geeta Trilok Kumar,[21] Mitsuyoshi Urashima,[22] Carlos A Camargo Jr[23]

For numbered affiliations see end of article.

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Additional material is published online only. To view please visit the journal online.

Cite this as: *BMJ* 2017;356:i6583
http://dx.doi.org/10.1136/bmj.i6583

Accepted: 01 December 2016

ABSTRACT

OBJECTIVES

To assess the overall effect of vitamin D supplementation on risk of acute respiratory tract infection, and to identify factors modifying this effect.

DESIGN

Systematic review and meta-analysis of individual participant data (IPD) from randomised controlled trials.

DATA SOURCES

Medline, Embase, the Cochrane Central Register of Controlled Trials, Web of Science, ClinicalTrials.gov, and the International Standard Randomised Controlled Trials Number registry from inception to December 2015.

ELIGIBILITY CRITERIA FOR STUDY SELECTION

Randomised, double blind, placebo controlled trials of supplementation with vitamin D_3 or vitamin D_2 of any duration were eligible for inclusion if they had been approved by a research ethics committee and if data on incidence of acute respiratory tract infection were collected prospectively and prespecified as an efficacy outcome.

RESULTS

25 eligible randomised controlled trials (total 11 321 participants, aged 0 to 95 years) were identified. IPD were obtained for 10 933 (96.6%) participants. Vitamin D supplementation reduced the risk of acute respiratory tract infection among all participants (adjusted odds ratio 0.88, 95% confidence interval 0.81 to 0.96; P for heterogeneity <0.001). In subgroup analysis, protective effects were seen in those receiving daily or weekly vitamin D without additional bolus doses (adjusted odds ratio 0.81, 0.72 to 0.91) but not in those receiving one or more bolus doses (adjusted odds ratio 0.97, 0.86 to 1.10; P for interaction=0.05). Among those receiving daily or weekly vitamin D, protective effects were stronger in those with baseline 25-hydroxyvitamin D levels <25 nmol/L (adjusted odds ratio 0.30, 0.17 to 0.53) than in those with baseline 25-hydroxyvitamin D levels ≥25 nmol/L (adjusted odds ratio 0.75, 0.60 to 0.95; P for interaction=0.006). Vitamin D did not influence the proportion of participants experiencing at least one serious adverse event (adjusted odds ratio 0.98, 0.80 to 1.20, P=0.83). The body of evidence contributing to these analyses was assessed as being of high quality.

CONCLUSIONS

Vitamin D supplementation was safe and it protected against acute respiratory tract infection overall. Patients who were very vitamin D deficient and those not receiving bolus doses experienced the most benefit.

SYSTEMATIC REVIEW REGISTRATION

PROSPERO CRD42014013953.

Vitamin D and Respiratory Health III

Limitations of meta-analysis/systematic review:

- High level of heterogeneity in the findings.
- Overall significant results in the meta-analysis of the 24 included trials was dependent on the inclusion of the two studies undertaken in developing countries: Mongolia and Afghanistan.
- These two trials had specific participants and the findings should not be extrapolated to populations from more developed countries.
- Furthermore, the specific clinical definitions of ARTI were varied across included studies, with many research participants with ARTI being self-diagnosed.

Hemilä H. Statistical problems in the vitamin D and respiratory infection meta-analysis. *BMJ* 2018;**356**:I658

McIndoe KS. Vitamin D supplementation to prevent acute respiratory tract infections. . *BMJ* 2017;**356** 1457

Vitamin D and Respiratory Health III

UNIVERSITY OF SURREY

BMJ

eLetter to BMJ

http://www.bmj.com/content/356/bmj.i6583/rr-3

Statistical problems in the vitamin D and respiratory infection meta-analysis

17 February 2017

Harri Hemilä
Adjunct professor
University of Helsinki
Tukholmankatu 8 B, Helsinki, Finland

The meta-analysis on vitamin D and respiratory infections by Martineau et al. [1] has two major problems: 1) the use of the odds ratio (OR) as the effect measure and 2) not exploring potential causes for the highly significant heterogeneity between the trials.

Vitamin D and Respiratory Health I

New meta-analysis from Professor Adrian Martineau's group. Now available on medRxiv server

Vitamin D supplementation to prevent acute respiratory infections: systematic review and meta-analysis of aggregate data from randomised controlled trials

Conclusions: Vitamin D supplementation was safe and reduced risk of ARI, despite evidence of significant heterogeneity across trials. The overall effect size may have been over-estimated due to publication bias. Protection was associated with administration of daily doses of 400-1000 IU vitamin D for up to 12 months. The relevance of these findings to COVID-19 is not known and requires investigation.

Systematic Review Registration: CRD42020190633

Vitamin D and RTI– Current Evidence I

PLOS ONE

RESEARCH ARTICLE

Effect of Vitamin D3 Supplementation on Respiratory Tract Infections in Healthy Individuals: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Danielle Vuichard Gysin[1], Dyda Dao[1], Christian Michael Gysin[2], Lyubov Lytvyn[3], Mark Loeb[1,4,5,6]*

1 Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario, Canada, 2 McMaster University, St. Joseph's Healthcare Hamilton, Hamilton, Ontario, Canada, 3 Department of Child Health and Evaluative Sciences, The Hospital for Sick Children, Toronto, Ontario, Canada, 4 Department of Pathology and Molecular Medicine, McMaster University, Hamilton, Ontario, Canada, 5 Department of Medicine, McMaster University, Hamilton, Ontario, Canada, 6 Institute for Infectious Diseases Research, McMaster University, Hamilton, Ontario, Canada

CrossMark click for updates

What the study found

- No difference in ARTI risk between vitamin D and comparator groups;
  - 14 RCTs, 6985 subjects
-
- No difference between groups in first laboratory confirmed ARTI;
  - 4 RCTs; 1392 subjects.

- Subgroup analyses: no differences were reported for participants with baseline 25(OH)D concentration <50 vs >50 nmol/L or those receiving daily/weekly vs monthly/3-monthly (6985 subjects)

Vitamin D and RTI– Current Evidence II

› Clin Infect Dis. 2019 Aug 17;ciz801. doi: 10.1093/cid/ciz801. Online ahead of print.

Effect of Monthly High-Dose Vitamin D Supplementation on Acute Respiratory Infections in Older Adults: A Randomized Controlled Trial

Carlos A Camargo [1], John Sluyter [2], Alistair W Stewart [2], Kay-Tee Khaw [3], Carlene M M Lawes [2], Les Toop [4], Debbie Waayer [2], Robert Scragg [2]

What the study did (2019):

Subjects: 5110 adults (mean age, 66 yrs); received vitamin D3 (initial bolus dose of 5000 µg then 2500 µg/month) or placebo. ARTIs were reported monthly through a mailed questionnaire.

What the study found:

.

There was no difference between groups in occurrence of at least 1 ARTI (adjusted HR for vitamin D vs placebo, 1.01; 95% CI, 0.94 to 1.07; p=0.85). In a subgroup analysis of participants with baseline 25(OH)D concentration <50 nmol/L, there was also no difference between groups in occurrence of ARTI (HR, 1.08; 95% CI, 0.95 to 1.23; p=0.27).

Vitamin D and RTI– Current Evidence III

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Vitamin D Supplements for Prevention of Tuberculosis Infection and Disease

D. Ganmaa, B. Uyanga, X. Zhou, G. Gantsetseg, B. Delgerekh, D. Enkhmaa, D. Khulan, S. Ariunzaya, E. Sumiya, B. Bolortuya, J. Yanjmaa, T. Enkhtsetseg, A. Munkhzaya, M. Tunsag, P. Khudyakov, J.A. Seddon, B.J. Marais, O. Batbayar, G. Erdenetuya, B. Amarsaikhan, D. Spiegelman, J. Tsolmon, and A.R. Martineau

What the study did (2020):

Subjects: 8851 children; received vitamin D3 (weekly dose of 14000IU) for 36 months or placebo. Primary outcome: positive QFT result; Secondary outcome: incidence of TB, ARTI, 25OHD status

What the study found:

There was no difference between Vitamin D and Placebo groups in occurrence of TB infection; TB disease or ARTI between vitamin D group and placebo.

September 2020

Vitamin D and RTI– Current Evidence II

Open Forum Infectious Diseases

MAJOR ARTICLE

Vitamin D and Acute Respiratory Infections—The PODA Trial

John F. Aloia, Shahidul Islam, and Mageda Mikhail

NYU Long Island School of Medicine, Mineola, New York

What the study did (2019):

African American women (mean: 68 yrs) received vitamin D3 (adjusted dose; 3 mths, maintain serum 25(OH)D >75 nmol/L: mean dose 87±37 µg/day) or placebo.

A questionnaire about ARTIs was administered by a research coordinator every 3 months.

What the study found:

There was no difference between groups in occurrence of ARTIs. Overall, the ARTI rate did not change significantly from baseline; there was no difference between groups over time.

Angiotensin-converting enzyme 2 (ACE2)

- Enzyme attached to the outer surface (cell membranes) of cells in the lungs, arteries, heart, kidney, and intestines. ACE2 lowers blood pressure by catalysing the hydrolysis of Angiotensin II (a vascoconstrictor peptide) into Angiotensin (1-7) (a vasodilator.

Mechanistic work re COVID-19/Vitamin D link:

- ACE2 is a key-player in the renin-angiotensin system (RAS) and its loss of function can lead to serious consequences - vitamin D is a negative endocrine regulator of RAS, and that normalization of vitamin D levels can lower RAS activity via transcriptional suppression of renin expression.

Vitamin D, SARS-CoV-2 Virus and COVID-19 Disease

Disclaimer: This is a preliminary study for early dissemination of results. Data are subject to changes.

Patterns of COVID-19 Mortality and Vitamin D: An Indonesian Study

Prabowo Raharusuna*, Sadiah Priambada, Cahni Budiarti, Erdie Agung, Cipta Budi

*Correspondence:

praboworaharusun@gmail.com

RSUD Kabupaten Sukamara

Kec. Sukamara, Kabupaten Sukamara,

Kalimantan Tengah 74171, Indonesia

April 26, 2020

- Article used more than 100,000 times
- Downloaded more that 17,000 times
- Used on social media more than 8000 times

Vitamin D, SARS-CoV-2 Virus and COVID-19 Disease

British Journal of Nutrition, page 1 of 2

Letter to the Editor

COVID-19 and misinformation: how an infodemic fuelled the prominence of vitamin D

In conclusion, we have taken several steps to investigate the identity and existence of the authors to no avail. As of the time this article was written (1 July 2020), a link to the Raharusuna *et al.* preprint at SSRN Electronic Journal cannot be accessed. However, the misinformation has been spread through various media and cited by several publications and believed by many to be true.

Joshua Henrina[1], Michael Anthonius Lim[2] and Raymond Pranata[3]

[1]*Siloam Heart Institute, Siloam Hospitals Kebon Jeruk, Jakarta, Indonesia*

[2]*Faculty of Medicine, Universitas Pelita Harapan, Tangerang, Indonesia*

[3]*Faculty of Medicine, Universitas Pelita Harapan, Tangerang, Indonesia*
email raymond_pranata@hotmail.com

doi:10.1017/S0007114520002950

British Journal of Nutrition
27th July 2020

COVID-19 and Vitamin D – Current Scientific Evidence III

Journal of Steroid Biochemistry and Molecular Biology 203 (2020) 105751

Contents lists available at ScienceDirect

Journal of Steroid Biochemistry and Molecular Biology

journal homepage: www.elsevier.com/locate/jsbmb

Check for updates

"Effect of calcifediol treatment and best available therapy versus best available therapy on intensive care unit admission and mortality among patients hospitalized for COVID-19: A pilot randomized clinical study"

Marta Entrenas Castillo [a], Luis Manuel Entrenas Costa [a,*], José Manuel Vaquero Barrios [a], Juan Francisco Alcalá Díaz [b], José López Miranda [b], Roger Bouillon [c], José Manuel Quesada Gomez [d]

- **Main Findings:**
- Study population – 76 patients hospitalized with COVID-19. All patients received best available treatment – hydroxychloroquine and azithromycin. Eligible patients were allocated through electronic randomisation to take oral calcifediol (0.532mg) or not. Groups not properly matched but results demonstrated a significantly reduced need for ICU treatment of patients requiring hospitalisation with COVID-19

Vitamin D - ARTI, SARS-CoV-2 Virus and COVID-19 Disease

NICE National Institute for Health and Care Excellence

Public Health England

NICE advice

COVID-19 rapid evidence summary: vitamin D for COVID-19

Evidence summary
Published: 29 June 2020
www.nice.org.uk/guidance/es28

SACN/post June 2020 paper 1

sacn
Scientific Advisory Committee on Nutrition

Rapid review:
Vitamin D and acute respiratory tract infections

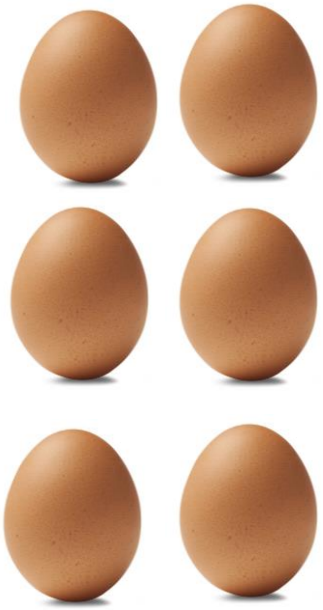
June 2020

BMJ Journals

Practical ways of increasing vitamin D intake I

Table 2 Dietary sources of vitamin D (PHE 2019)

	Vitamin D content (µg per 100 g/100 ml)
Fish and shellfish	
Grilled herring	16.1
Canned pink salmon in brine	13.6
Grilled salmon	7.8
Grilled kipper fillet	9.0
Baked rainbow trout fillet	8.2
Smoked mackerel	8.2
Tinned sardines in tomato sauce	3.3
Milk and milk products	
Build-up powdered sachet (shake)	1.7
Fortified soya milk	0.8
Skimmed milk, dried	0.8
Custard, confectioners'	0.8
Horlicks, powder	18.5
Animal products	
Lamb leg, roast	0.7
Beef, roast	0.8
Corned beef, canned	1.3
Grilled bacon back rashers	0.8
Grilled pork sausages	1.1
Fried lamb's liver	0.9
Chicken's egg, raw	3.2
Non-animal based products	
Fortified, low-fat spread, polyunsaturated	8.4
Baking fat/margarine	8.8
Bran type cereal, fortified	3.9
Breakfast cereal, cornflakes, fortified	4.7



Mushrooms

x 4 tins of sardines in tomato sauce (71g/ tin)

x 4 Bowls of fortified cereal (cornflakes; 30g)

1.33 litres of fortified dairy-free alternative milk

Slide courtesy of Dr Saskia Wilson-Barnes

Importance of avoiding vitamin D deficiency

Current evidence-based advice for the prevention of vitamin D deficiency includes:

1) Supplementation with vitamin D according to Government guidelines

- Supplementation with vitamin D is particularly important during times of self-isolation associated with limited sunlight exposure.

Press release

PHE publishes new advice on vitamin D

PHE is advising that 10 micrograms of vitamin D are needed daily to help keep healthy bones, teeth and muscles.

Public Health England

Vitamin D - ARTI, SARS-CoV-2 Virus and COVID-19 Disease

NICE National Institute for Health and Care Excellence

Public Health England

NICE advice

COVID-19 rapid evidence summary: vitamin D for COVID-19

SACN/post June 2020 paper 1

Evidence summary

Published: 29 June 2020

Updated 18th December 2020 and announced by Secretary of State
Watching brief for 2021 & 2022 onwards

Rapid review:
Vitamin D and acute respiratory tract infections

June 2020

BMJ Journals

Importance of avoiding vitamin D deficiency

Current evidence-based advice for the prevention of vitamin D deficiency includes:

1) Supplementation with vitamin D according to Government guidelines

Concluding Remarks

NDC Annual Lecture, University of Ulster at Coleraine. Wed 23rd Nov 2022

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- Vitamin D is essential for bone and muscle health. We now have enough scientific data to recommend vitamin D for the prevention upper or lower respiratory tract infections, influenza but not for COVID-19.
- Many people have low blood levels of vitamin D, especially in winter or if confined indoors, because summer sunshine is the main source of vitamin D for most people.
- Government vitamin D intake recommendations for the general population should be followed.
- Taking a daily supplement (400IU /d [10 µg/d] in the UK) and eating foods that provide vitamin D is particularly important for those self isolating with limited exposure to sunlight.
- Vitamin D intakes greater than the Upper Limit of 4000IU [100 µg] per day may be harmful and should be avoided.

https://www.nhs.uk/conditions/vitamins-and-minerals/vitamin-d/

Those to thank!

University of Surrey: Andrea Darling, Ruan Elliott, Kathryn Hart, Kourosh Ahmadi
University of Brighton: Colin Smith
University of Manchester: Jacqueline Berry
Newcastle University: John Mathers
University College London: Elina Hyppönen
Campden BRI: Simon Penson, Gemma Chope

Experimental genomics: Giselda Bucca and Louise Durrant
Bioinformatics: Andrew Hesketh and Carla Möller-Levet
PostDoc: Laura Tripkovic
PhD Students: Rebecca Vearing, Abigail Bournot

University of Brighton Innovation Seed Fund award
Philanthropists, Michael Chowen CBE DL and Maureen Chowen

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Food for thought

THE QUEEN'S ANNIVERSARY PRIZES
FOR HIGHER AND FURTHER EDUCATION
2017

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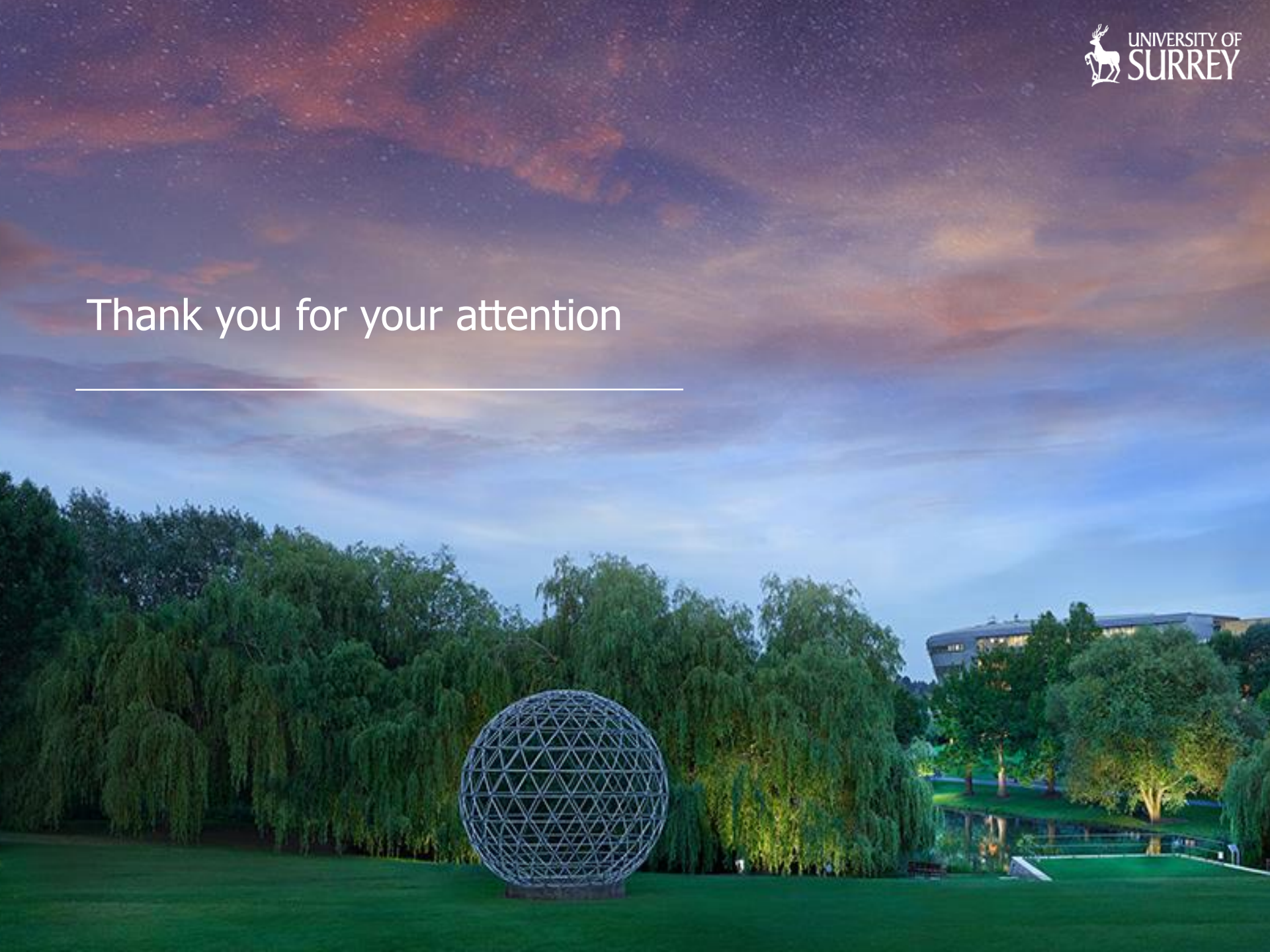
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Thank you for your attention