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SUNLIGHT-INDUCED VITAMIN D SYNTHESIS

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Skin-sunlight interface

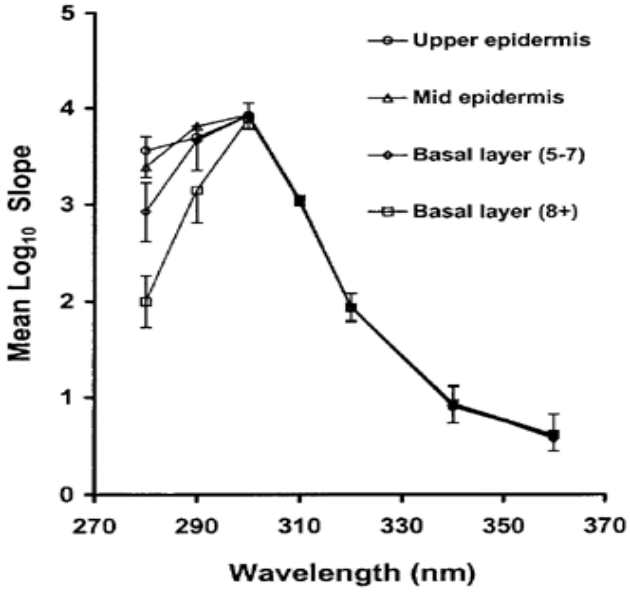
Solar UVR reaching
Earth's surface is ~95% UVA, 5% UVB

Penetration depth into skin

Epidermis

Dermis

Action spectrum



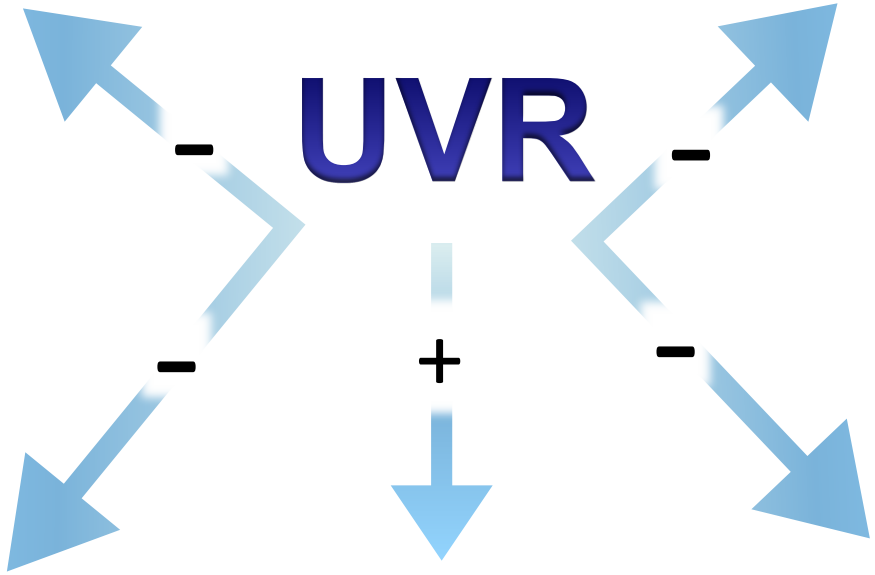
Young AR et al (1998) J Invest Dermatol

Skin-sunlight interface

Health outcomes

Sunburn

Immunosuppression
Skin cancers



Photoageing

Photosensitivity

Vitamin D synthesis

- VITAMIN D SYNTHESIS

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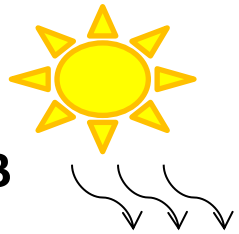
Vitamin D synthesis



UVB

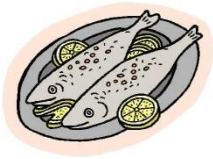
SKIN

7-dehydrocholestrol (Pro-vitamin D) → Previtamin D_3

Heat

Vitamin D_3

DIET



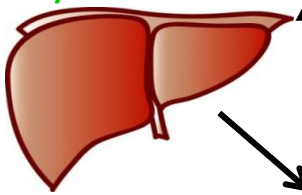
*Vitamin D_3

*Vitamin D_2

Liver 25-Hydroxylase (CYP27A1, CYP2R1, CYP3A4)

Bloodstream

LIVER

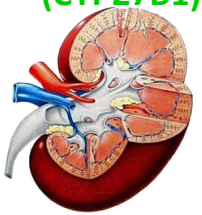


25 – Hydroxyvitamin D

Tissue Storage

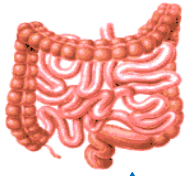
Kidney 1-Hydroxylase (CYP27B1)

KIDNEY



1,25 dihydroxyvitamin D_3

Calcium absorption



Calcium resorption

Cellular Functions
- Differentiation
- Proliferation

Inhibition of PTH production

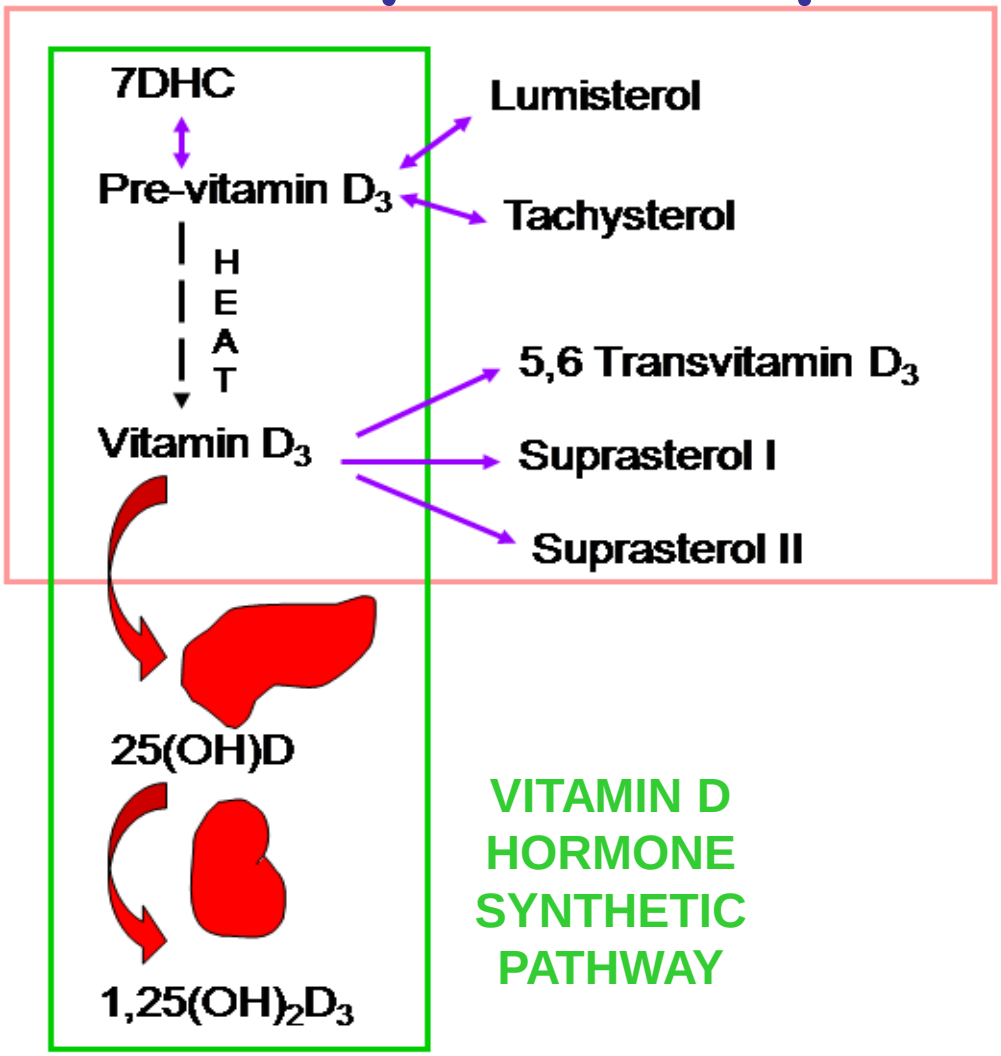
Vitamin D synthesis

- Most of the 7-DHC is present in the epidermis although there is a little in the dermis

- Within the epidermis, the cells in the lower layers (basal and stratum spinosum) are believed to contain most of the 7-DHC

Holick et al (1980) Science
MacLaughlin & Holick (1985) J Clin Invest

Biosynthetic pathway



SKIN REACTIONS

VITAMIN D HORMONE SYNTHETIC PATHWAY

Rhodes & Webb (2012) ESP Handbook;
Webb et al (1989) J Clin Endocrinol Metab

Cut-off Levels for Vitamin D status

Circulating 25(OH)D	Status
< *5* -10 ng/ml (*12.5* -25 nmol/L)	Deficient[1]
< 20 ng/ml (50 nmol/L)	Insufficient
≥ 20 ng/ml (50 nmol/L)	Sufficient[2]
< 32 ng/ml (80 nmol/L)	"Suboptimal"
≥ 32 ng/ml (80 nmol/L)	"Optimal"[3,4]

1. Dept of Health (1991, 1998); SACN 2007
2. Institute of Medicine (2011) Washington, DC.
3. Henry et al (2010) J Steroid Biochem Mol Biol
4. Dawson-Hughes et al (2005) Osteoporos Int

- MODIFIERS OF VITAMIN D STATUS

Solar source of vitamin D: external factors - predictable

Factors influencing solar zenith angle, UVR path-length:

- **Latitude** *(low)*
- **Season** *(summer)*
- **Time of day** *(solar noon)*

[UK latitudes (50-60°N) – insufficient ambient UVB in winter]

Solar source of vitamin D: external factors – more variable

Atmospheric conditions affecting UVR transmission:

- **Ozone** *(stronger absorber in UVB than UVA)*
- **Clouds** *(generally reduce all wavelengths)*
- **Aerosol pollutants** *(generally reduce all wavelengths)*

Earth's surface conditions - reflectivity

Solar source of vitamin D: personal factors - physiological

Skin pigmentation:

- Melanin is a broad UV-visible radiation absorber
- Melanin competes with the chromophore 7-DHC for absorption of UVB, thus making less available to 7-DHC.
- Darker skin reported to have same capacity for vitamin D synthesis but higher absolute UVR doses required.
- Experimental data conflicting. Situational.

Lo et al (1986) Am J Clin Nutr; Brazerol et al (1988) J Am Coll Nutr; Armas et al (2007) J Am Acad Dermatol; Bogh et al (2010) J Invest Dermatol; Farrar et al (2011, 2013) Am J Clin Nutr

Solar source of vitamin D: personal factors -physiological

Age:

- 7-DHC content in skin ↓ with age
- accompanied by ↓ability to photosynthesise pre-vitamin D_3 (ex vivo study of skin samples)

Tissue sink/storage:

- Fat, BMI
- Muscle

Genetic factors

McLaughlin & Holick (1985) J Clin Invest; Wang et al (2010) Lancet; Berry & Hypponen (2011) Curr Opinion Nephrol Hypertens

Solar source of vitamin D: personal factors - behavioural

Lifestyle:

- Time spent outdoors
- Time of day when outdoors
- Sunny holidays abroad

Webb et al (2010) Br J Dermatol;

Mavroeidi et al (2013) PLoS One

Solar source of vitamin D: personal factors - behavioural

Photoprotective measures:

- ***Use of shade***
- ***Clothing***
  - Usually confers high level of protection, though dependent on weave, colour, tight/loose fit
  - Surface area exposed: Reportedly important at low UVR doses (0.75 SED and 6 to 24% SA; without effect at 1.5 and 3 SED)
    Bogh et al (2011) Br J Dermatol

Solar source of vitamin D: personal factors - behavioural

Photoprotective measures:

- ***Sunscreens***
  - Increase in 25(OH)D occurred after UVR, except at sunscreen thickness of 2 mg/cm^2
  - Due to imperfect application methods, less impact in real life

Faurschou et al (2012) Br J Dermatol; Matsuoka et al (1988) Arch Dermatol; Norval & Wulf (2009) Br J Dermatol; Springbett et al (2010) J Photochem Photobiol B. Biol

- SUN EXPOSURE & PUBLIC HEALTH MESSAGES

National guidance on sun protection

SunSmart

CANCER RESEARCH UK

Department of Health

British Association of Dermatologists

- **Aimed at reducing excessive exposure** in summer - particularly evidenced by sunburn (also “sunbaking”)
- **Focuses on those at higher risk of skin cancer** particularly skin types I & II, multiple moles, freckles, h/o skin cancer
- **Vitamin D:** increasingly aware of need for messages allowing some “safe” exposure, and for more specific information for population sectors, incl. skin types V & VI.

Vitamin D from casual sun exposure at northerly (UK) latitudes

- ***Has been stated that brief, casual exposures to summer sunlight, several times per week, are sufficient for fulfilling vitamin D requirements in a light-skinned person*** ***NRPB Handbook (2002)***

- ***However:***
  - ***Previously based on estimates from v limited expts***
  - ***May not be appropriate based on re-evaluation of 25(OH)D cut off levels for vitamin D sufficiency***

- RESEARCH EXAMINING SUN-LIGHT EXPOSURE GUIDANCE & VITAMIN D

Studies in Manchester UK

245 white Caucasian adults

(A) Intervention study:
Course of simulated summer sunlight – mimicking casual exposures

(B) Field study: Measure personal natural sunlight exposure levels throughout the year

Relate resultant vitamin D to levels for deficiency, insufficiency & proposed "optimum"

Define amount & patterns of sun exposure sufficient to avoid low vitamin D in winter

Public health guidance on sunlight exposure

DH guidance on vitamin D supplements

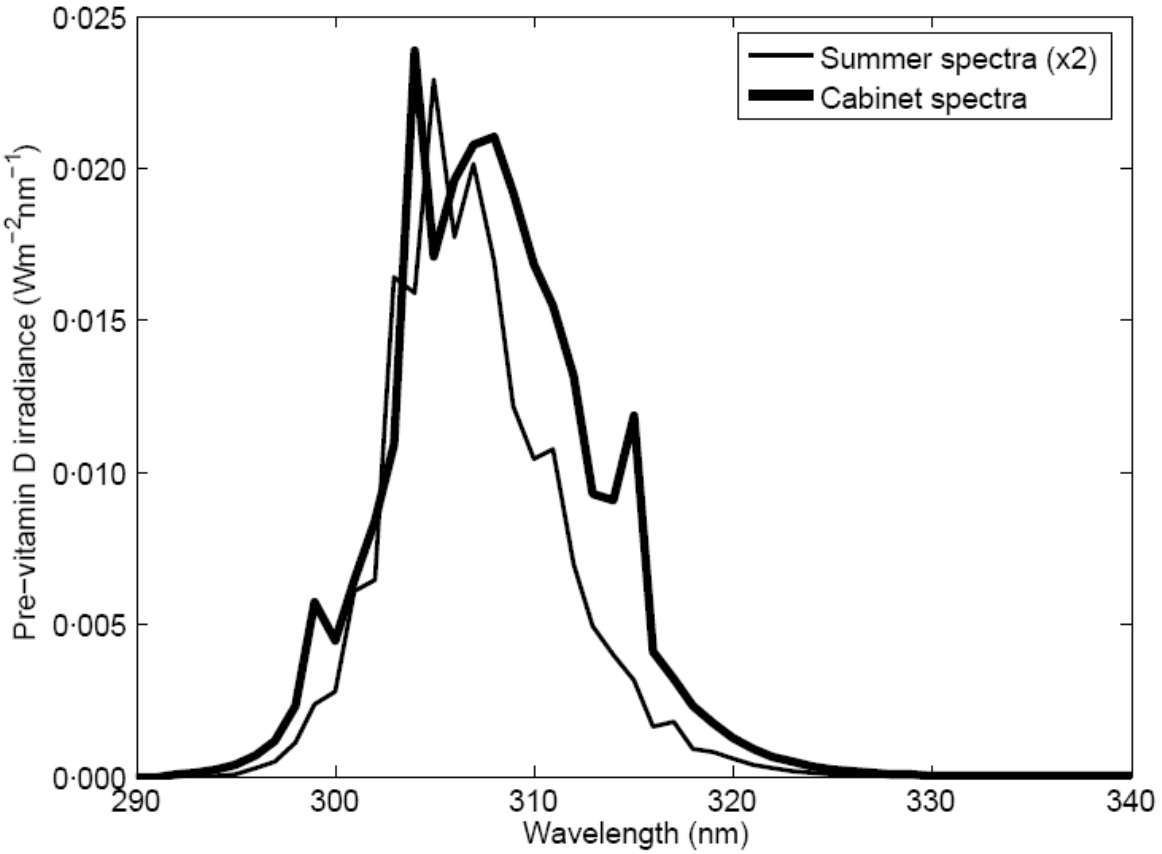
Rhodes et al (2010) J Invest Dermatol
Webb et al (2010) Br J Dermatol

Simulated summer sunlight exposures

- **N=120** white Cauc, 20-60y, phototypes I-IV, Manchester, UK
- **6-wk** course UVR - length of school summer holiday period
- **Jan - Feb** when ambient UVB is negligible at UK latitudes
- **Low dose** (1.3 SED, ~1.1 SED in sunlight) UVR x 3 weekly
- **Wearing T-shirts & knee-length shorts** - ~35% skin SA
- **95% UVA: 5% UVB** (Philips HB598 horizontal cabinet, irradiation of dorsal and ventral surfaces simultaneously, tubes replaced by Arimed B & Cleo Natural tubes).

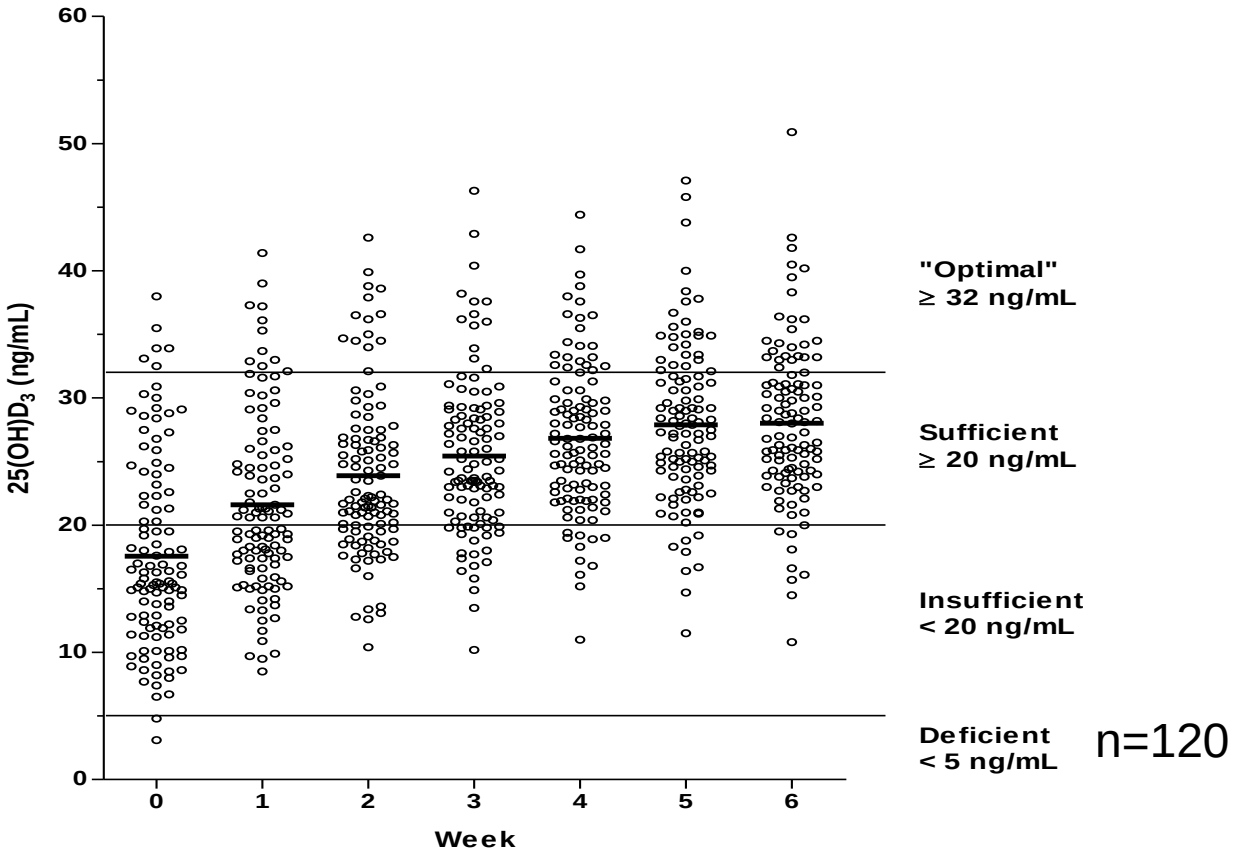
Rhodes et al (2010) J Invest Dermatol

Pre-Vitamin D irradiance



Rhodes et al (2010) J Invest Dermatol

Majority moved from insufficiency to sufficiency (IOM) after a simulated summer's casual sunlight exposures



Equivalent to 13 mins exposures, to 35% surface area, on a clear June midday in Manchester (53.5°N)

Approximate guide: how much time in the sun?

Lying flat:
Cabinet irradiates dorsal & ventral surfaces simultaneously. In sunlight, this would be sequential
= ~13 mins x 6/week

Standing up:
Radiative transfer modelling, Model SMARTS 2.95. Standing vertical with body sites randomly orientated to the sun
= ~17 mins x 6/week

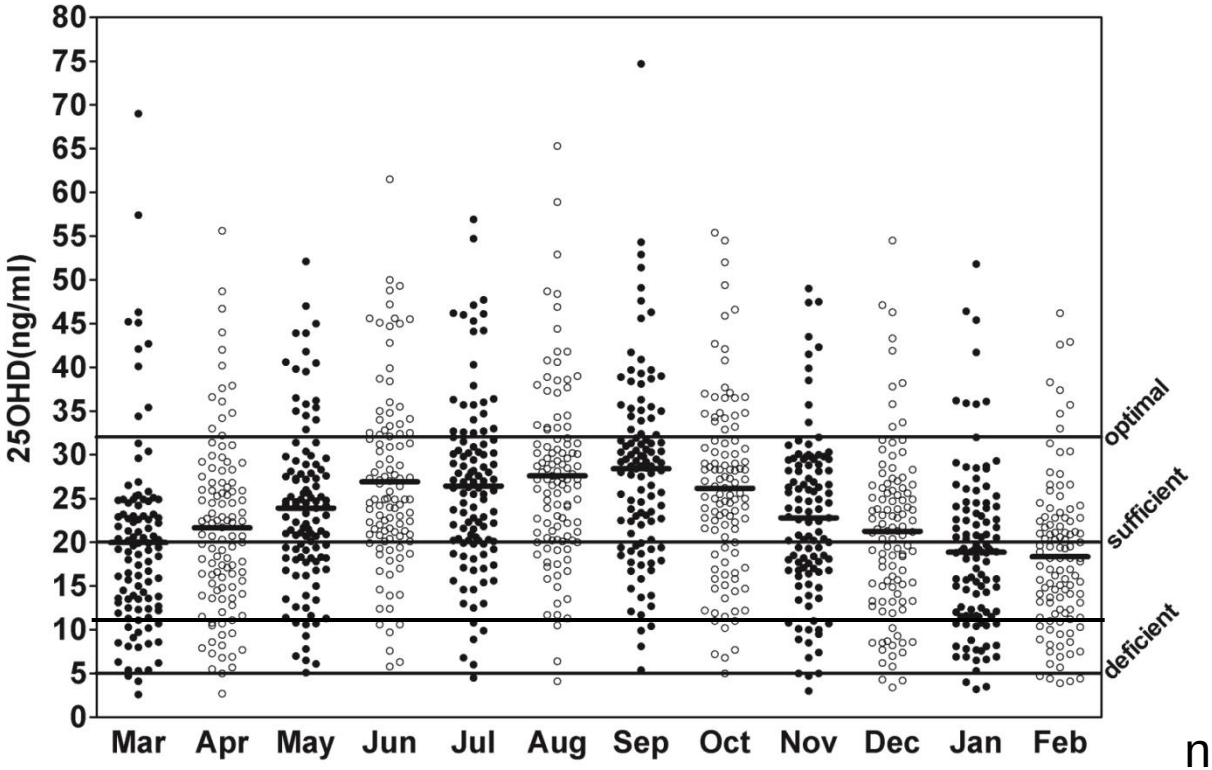
Webb et al (2011) Photochem Photobiol

Manchester, UK & other locations

Latitude	Solar elevation, midsummer, noon	Horizontal: ventral/dorsal sequentially (mins)*	Random vertical (mins)	Dates with noon solar elev > 45°
53.5° N Manchester	**60°**	**13**	**17**	**11Ap–31Aug**
30° N (Cairo, Austin)	83°	8	13	9 Feb – 2 Nov
40° N (Beijing, Philadelphia)	73°	10	14	8 Mar – 5 Oct
50° N (Frankfurt, Winnipeg,)	63°	12	15	2 Apr – 10 Sept
60° N (Oslo, Anchorage)	53°	16	19	1 May–1 Aug
Anywhere	solar elevation 45°	22	24	

*Approximate times based on 6 x weekly exposure. Other locations derived from UVR action spectra & local sunlight emission spectra. ***Webb et al (2011) Photochem Photobiol***

Manchester white Caucasian field study



n=125

Median solar exposures >3 SED/week in spring/summer vs 0.1 SED in winter
Clear seasonal pattern with late summer (Sep) peak and winter (Feb) trough
Mean noontime (11-00 to 13-00) mins outdoors = 9 mins (weekdays) & 18 mins (weekend days)

Webb et al (2010) Br J Dermatol

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Retaining sufficiency in winter?

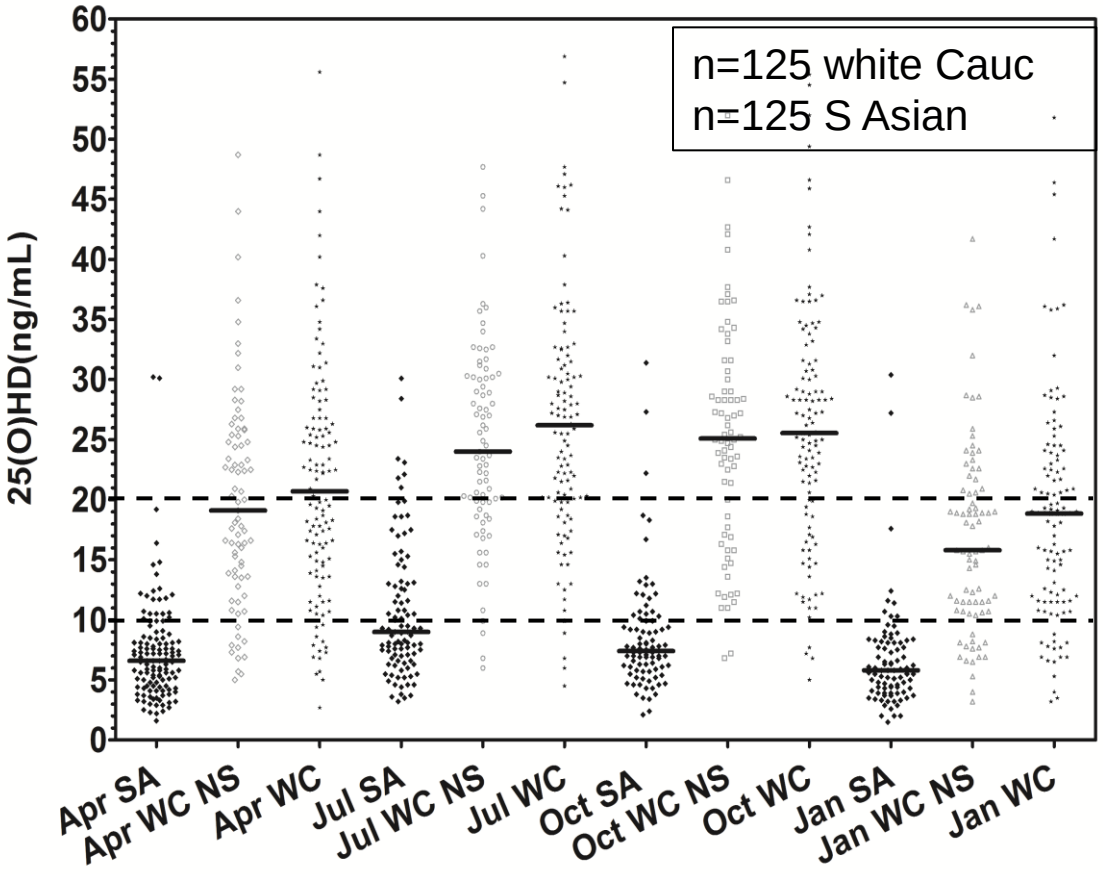
- Regression analysis in the field study indicates those (~25%) subjects reaching a summer-peak level of ~32 ng/mL, (80 nmol/l) retain >20 ng/mL (50 nmol/l) at winter trough (62% variance, $p<0.001$) ***Webb et al (2010) Br J Dermatol***

- If a year-round level of 20 ng/mL (50 nmol/l) is required, then current UK recommendations on sunlight exposure and oral vitamin D intake achieve this in a minority

- Further evaluation currently ongoing in larger data set with assessment against UK climate conditions

Department of Health

Darker skin types: field study

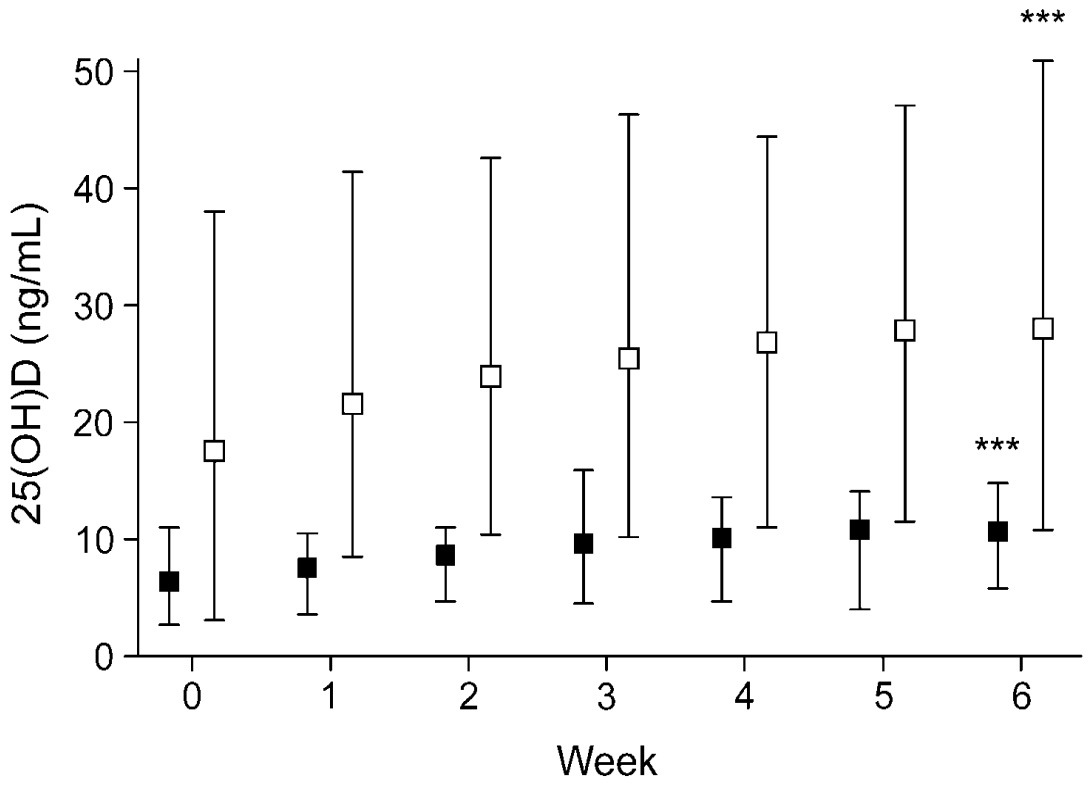


Complex of contributory factors in the field:

- Behavioural:
  - lower dietary vitamin D
  - virtually absent vitamin D supplement use
  - reduced skin exposure to when outdoors (diary cards vs UV badge data)
- Physiological:
  - darker skin

Kift et al (2013) Br J Dermatol; Mavroeidi et al (2010) J Steroid Biochem Mol Biol; Darling et al (2013) Osteoporos Int

Darker skin types: UVR intervention study (simulated summer)



Farrar et al (2011) Am J Clin Nutr

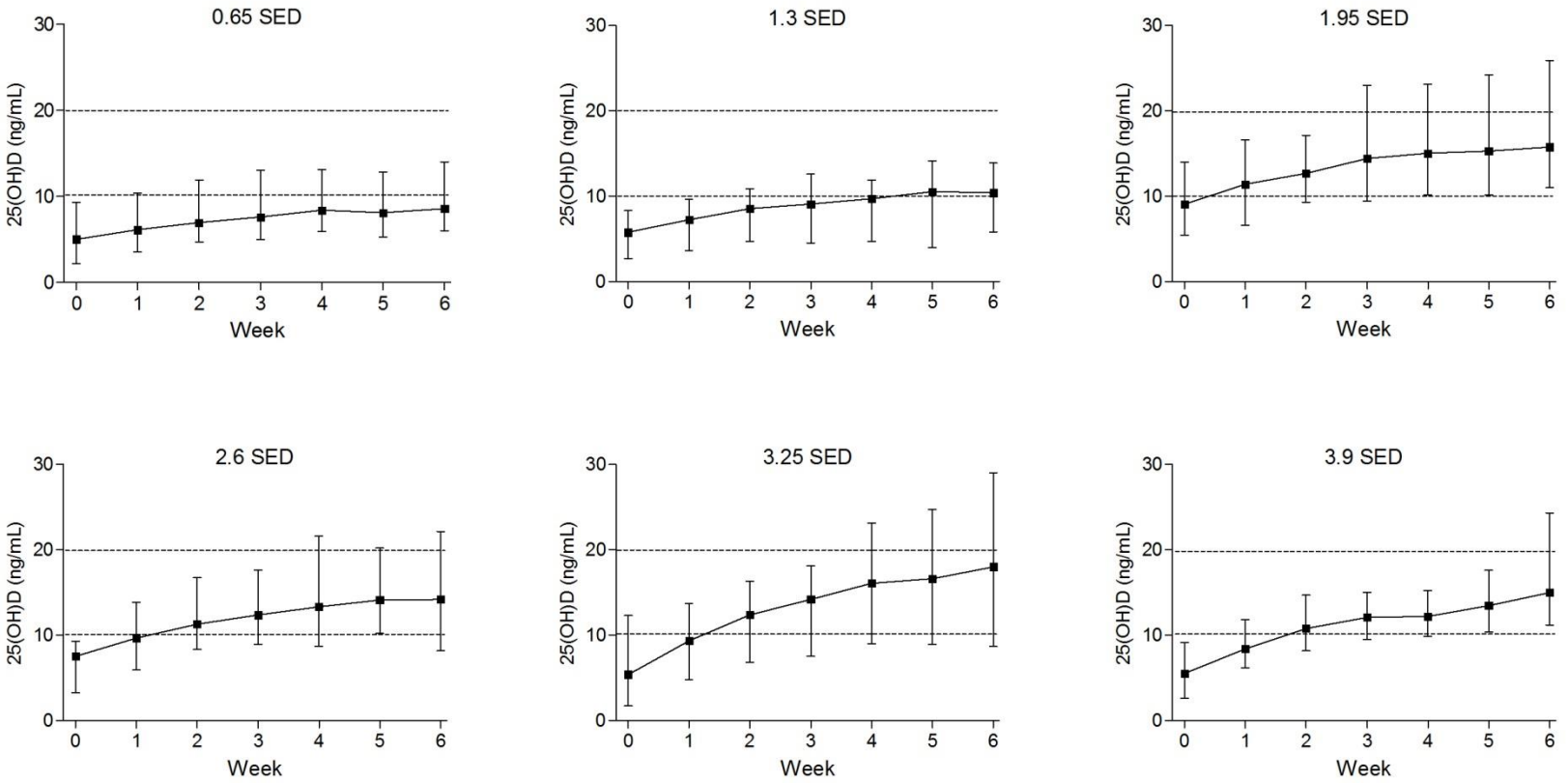
Identical UVR protocol

Commonly exposed skin sites; 35% SA

White square: white Cauc, n=120
Black square: S. Asians, n=15

***P<0.001

Darker skin types: S. Asian UVR-25(OH)D dose-response



n=10 per dose group. Those receiving ≥1.95 SED achieved >10 ng/ml (mean 25(OH)D 15.7ng/ml, ~40nmol/l)

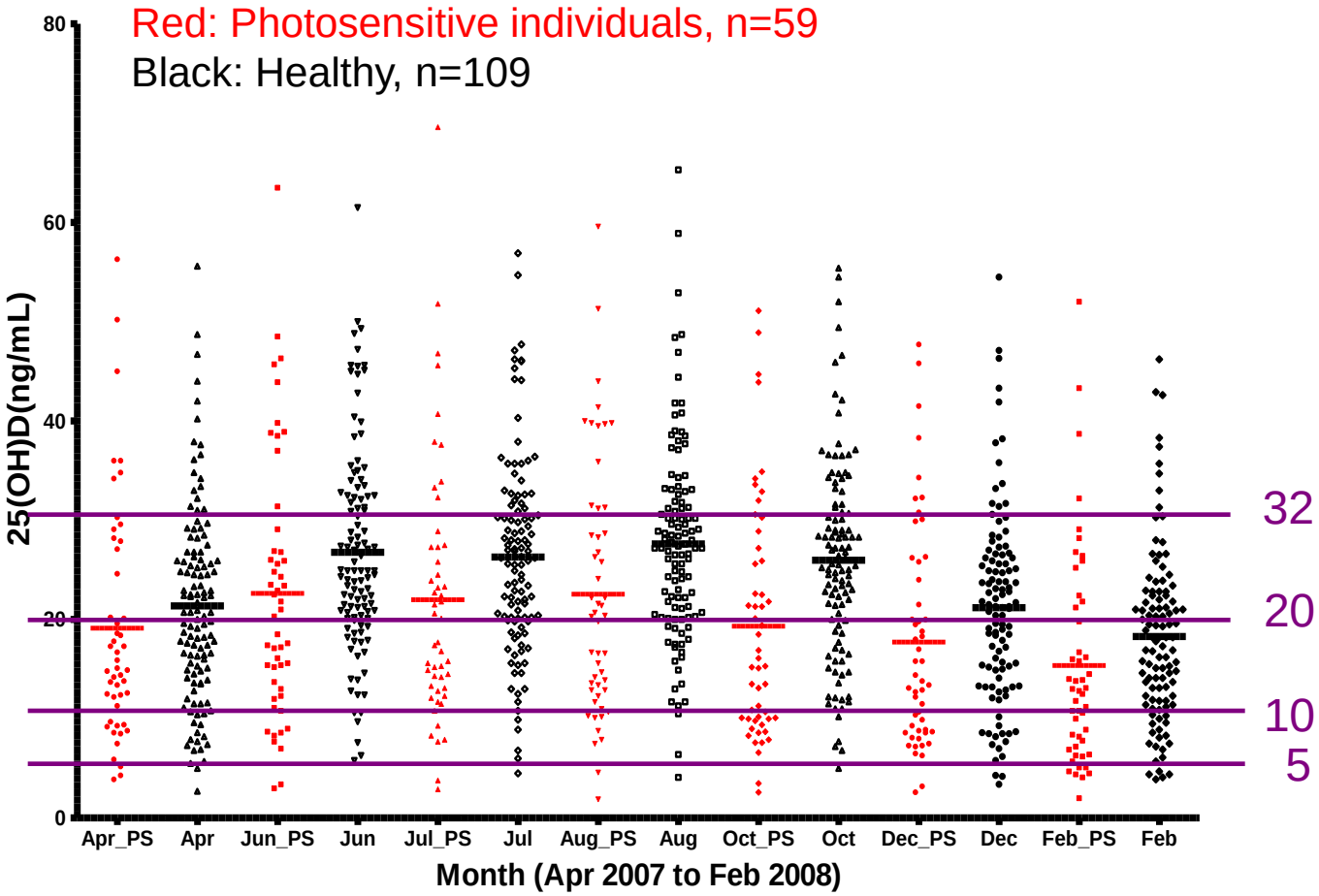
Farrar et al (2013) Am J Clin Nutr

Risk in photosensitivity conditions

- Large group of disorders where people show abnormal reactions to low doses of UV &/or visible radiation
- Aetiology: genetic, biochemical, immune, drug-induced
- Skin symptoms on sun exposure →
  - They avoid sunlight
  - Employ vigorous photoprotective measures
  - BUT: are no more likely to take vitamin D supplements

Stafford et al (2010) Br J Dermatol

Vitamin D status in photosensitive patients



Peak <20ng/ml (<10 ng/ml): **47% (9%)** photosensitive vs **17%** healthy subjects

Trough <20ng/ml: **73% (32%)** photosensitive vs **54%** healthy subjects

Rhodes et al (2014) Br J Dermatol;

Reid et al (2012) Photoderm Photoimmunol Photomed

Acknowledgements
(Greater Manchester studies)

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JL Berry

– Vitamin D Research Laboratory, Institute of Human Development

A Vail, JD Wilkinson

– Centre for Biostatistics, Institute of Population Health

Z Mughal, G Das, J Adams

- Paediatric Endocrinology & Clinical Radiology