Vitamin D for Scotland

Could correcting deficiency mean helping the "*Sick man of Europe*"?

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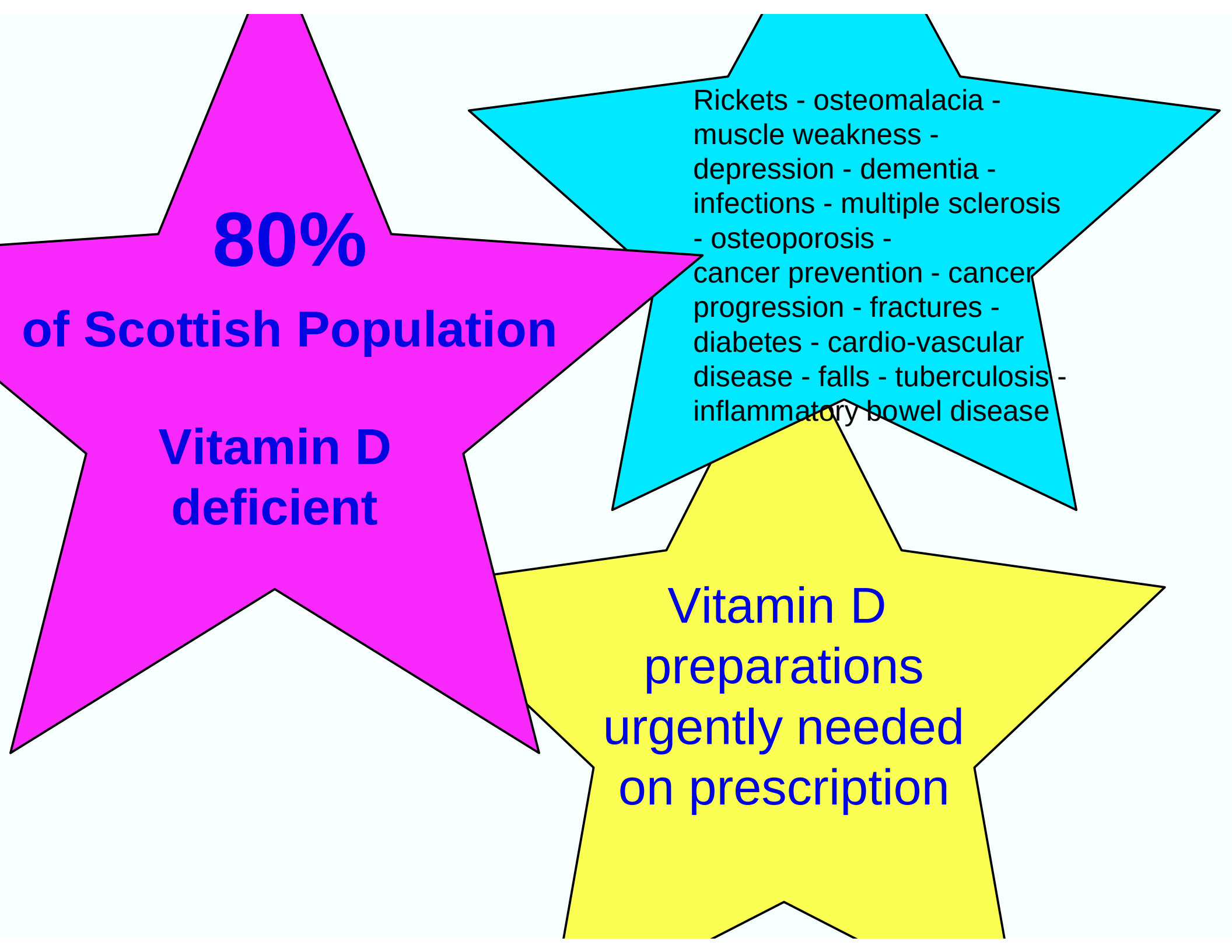
May 2012


80%
of Scottish Population
Vitamin D deficient
Rickets - osteomalacia - muscle weakness - depression - dementia - infections - multiple sclerosis - osteoporosis - cancer prevention - cancer progression - fractures - diabetes - cardio-vascular disease - falls - tuberculosis - inflammatory bowel disease
Vitamin D preparations urgently needed on prescription

First blood checks

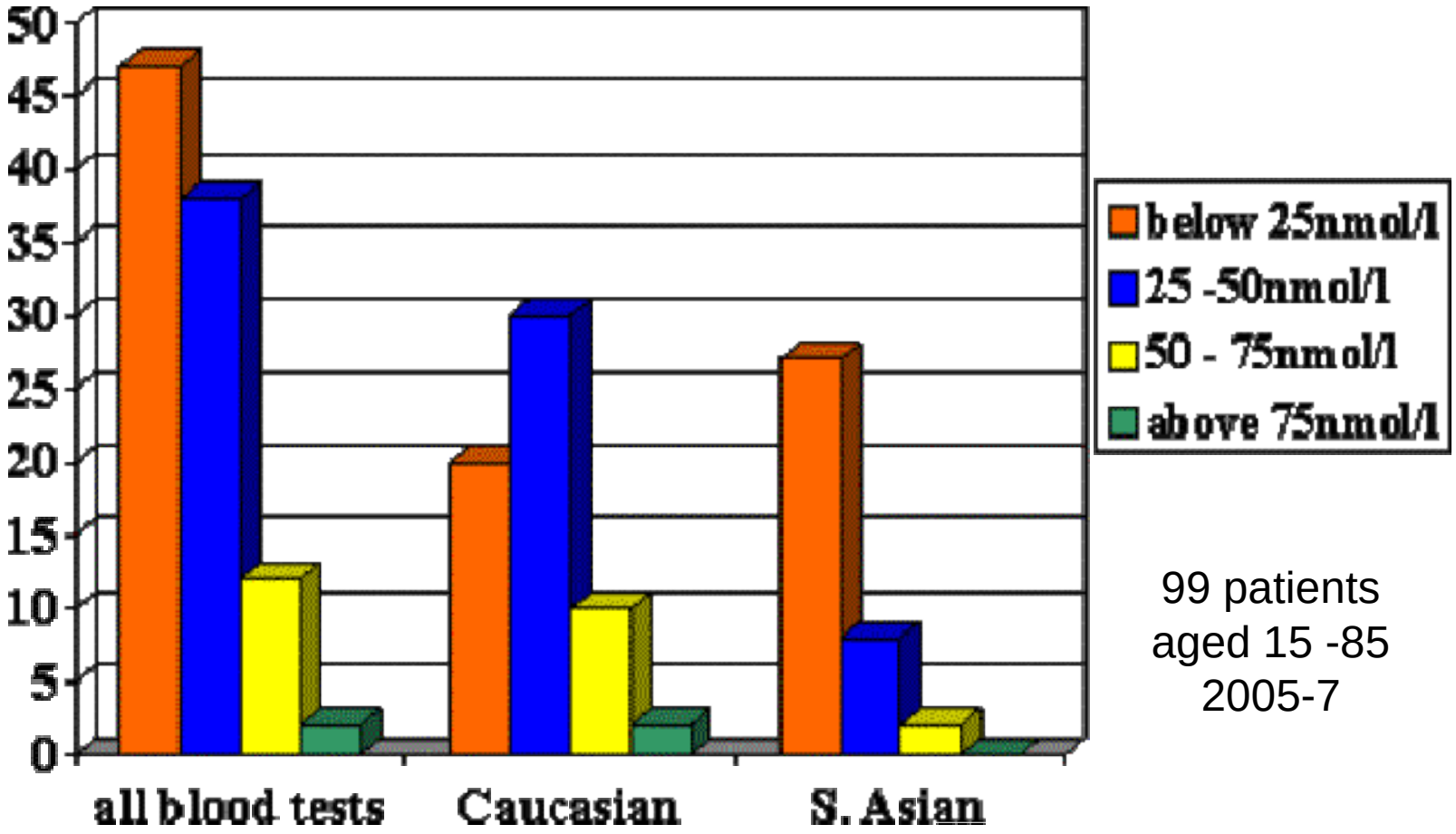
Why in our practice? Coincidence?

Anecdotes of dramatic improvements when severely deficient

25 -30% of us are severely deficient

In general:
fewer colds, **less aches and pains**
stronger muscles, **happier**

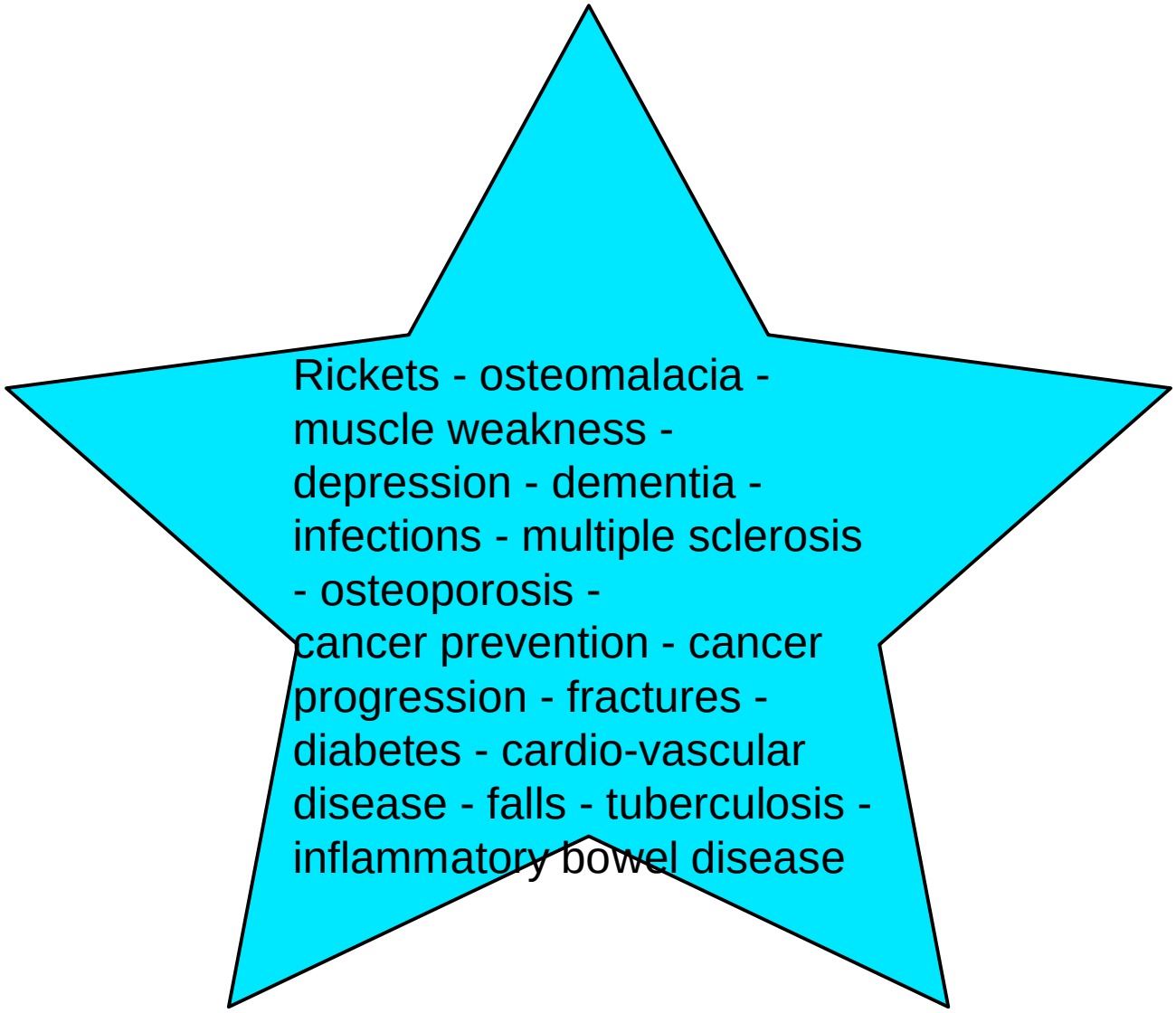
Serum 25(OH)D concentration in a general practice sample



99 patients
aged 15 -85
2005-7

Rhein, H. Vitamin D deficiency is widespread in Scotland. BMJ, letter 28 June 2008


Vitamin D
Vigantoletten 1000 I.E.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???

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Classical understanding:

- Calcium absorption - bone health
- blood level of 25 nmol/l is sufficient
- spoon of cod liver oil - 10 mcg is enough
- caution in UK due to over-enthusiastic fortification in 50's

Modern findings - last decade:

- transformation into a powerful hormone
- in addition to bone health: regulation of **immune system**, DNA repair, insulin production, influence on cancer cells...
- vitamin D receptor in every organ
- organs are only in best running order if sufficient vitamin D
- optimal levels around **100 nmol/l** or above
- toxicity only if above 500 nmol/l

Definition of deficiency?

Normal natural blood levels of out door workers: around 120 nmol/l

Barger-Lux, US, 120 nmol/l, 2002.
Binkley, Hawaian surfers, 80 nmol/l 2007,
Aydin, Turkish children, 180 nmol/l, 2010.
Rajasree, Indian fishermen 270 nmol/l, 1999.
Luxwolda, traditional living populations East Africa, 115 nmol/l 2012

Maximal PTH suppression: above 100 nmol/l

Ginde, 2011

Maximal calcium absorption: above 80-90 nmol/l

Heaney, 2005

	adequate blood level
NICE, SACN, DH, SIGN, FSA	deficiency≤25 new guidance awaited
Majority of vitamin D experts	75 - 200 nmol/l
WHO 2003, US Institute of Medicine 2010	50 nmol/l (for bone health)

as Edinburgh Royal Infirmary

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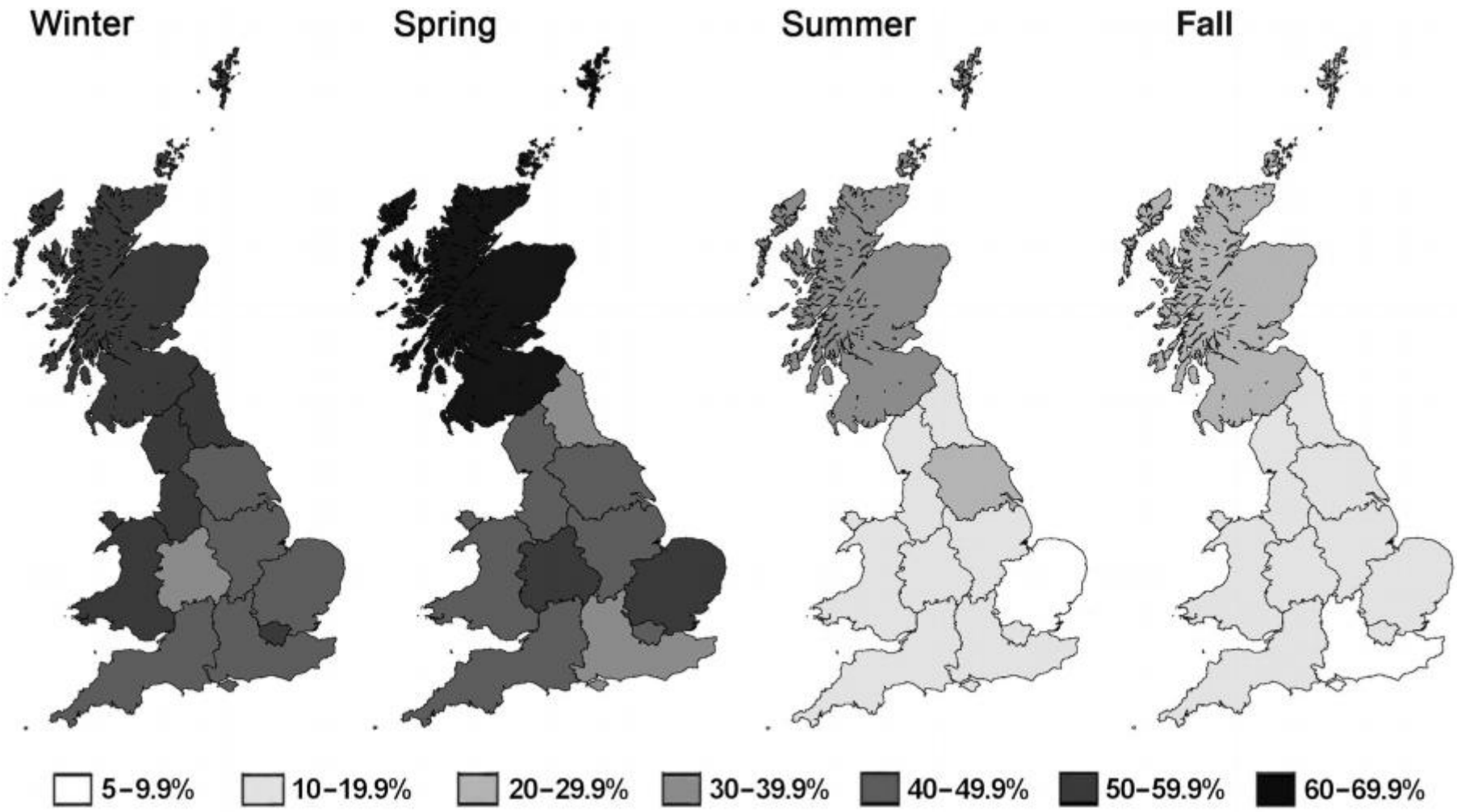
	adequate blood level	**daily supplements**
NICE, SACN, DH, SIGN, FSA	deficiency≤25 new guidance awaited	10 mcg for babies and adults at risk
Majority of vitamin D experts	75 - 200 nmol/l	Safe upper limit: 100 -250 mcg
WHO 2003, US Institute of Medicine 2010	50 nmol/l	Safe upper limit: 100 mcg

Levels in Scotland?

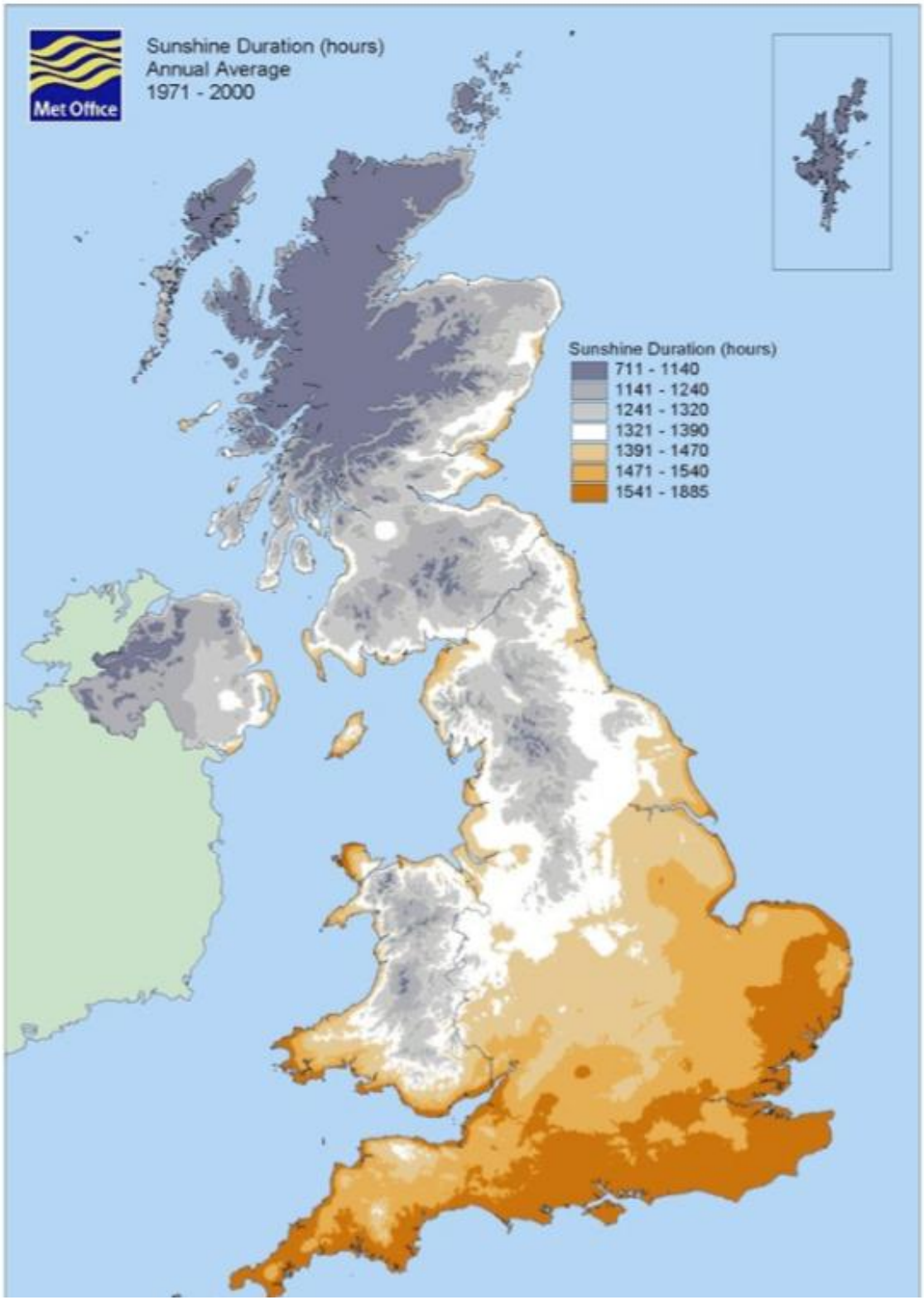
7437 participants, aged 45

The American Journal of Clinical Nutrition



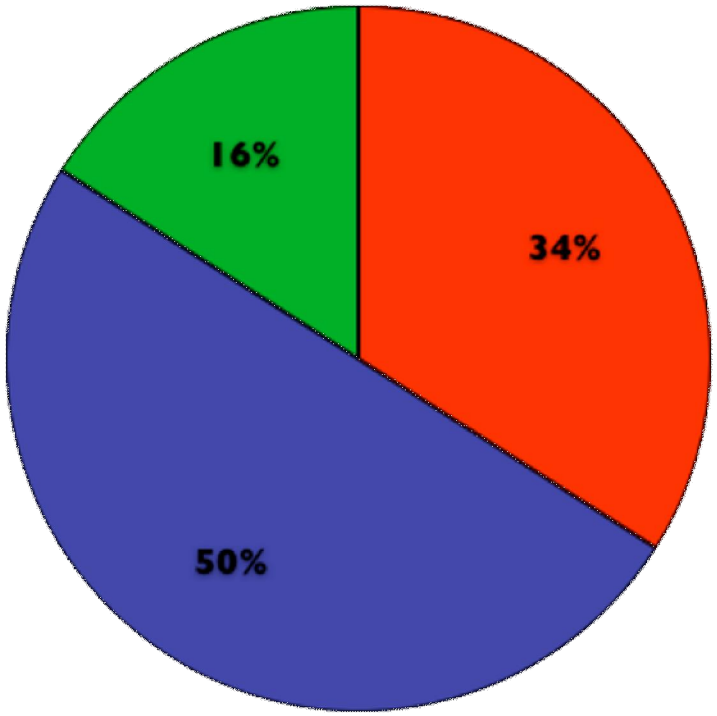
<40 nmol/L

Hyppönen et al 2007


Met Office
Sunshine Duration (hours)
Annual Average
1971 - 2000
Sunshine Duration (hours)
711 - 1140
1141 - 1240
1241 - 1320
1321 - 1390
1391 - 1470
1471 - 1540
1541 - 1885

Edinburgh University, 2011, Zgaga et al

Scotland-wide
2230 participants
age 21 - 80
July 2011

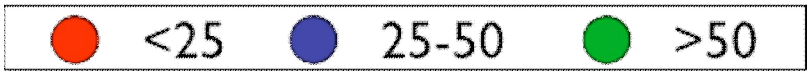


34% severe deficiency

red+ blue

84% deficiency

- defined as levels <50 nmol/l



Aberdeen, 338 Caucasian women, aged 55-70:
100% blood levels < 50 in all 4 seasons
MacDonald et al 2009

My own practice figures: of 350 tested, aged 16-85, 70 % levels <50 during 4 years, any season

Below 50 nmol/l:

US : 23% (men 50-70)
France: 54% (osteoporotic women 50 - 90)
Germany: 58% (aged 18 - 80)
Norway: 38% (aged 40 - 60)

Why such low level in Scotland?

Specifically Scottish Problems:

Northern latitude 55º - 60º

Clouds

Clothes

General modern life problems:

Sunscreen

Avoidance of midday sun

Evidence??

Stress fractures

a relatively common sports related injury

600 female navy recruits,
observed for 7 years,
double the risk of stress fractures if < 50 nmol/l compared to > 100 nmol/l

Burgi et al. 2011

6712 girls
aged 9-15, daughters of the women enrolled in the nurses health study,
for 5 years annual questionnaires self reported nutritional intake and sport activities
Highest **vitamin D intake** reduced stress fractures by **50%**
Neither calcium intake nor dairy intake was prospectively associated with stress fracture risk

Sonneville et al. 2012

Depression

- 12,594 Healthy adults: low vitamin D associated with depressive symptoms, especially in those with history of depression. cross sectional, 4 years. Hoang et al 2012

- 54 Depressed adolescents in a case-series were low in vitamin D and depression was ameliorated by vitamin D supplementation after 3 months. Base line 41nmol/l, after supplements 91 nmol/l. Högberg et al 2012

- 7,358 Cardio-vascular patients. Association of vitamin D levels with incident depression. lowest levels, below 37 nmol/l were nearly 3 times more likely compared to highest levels of above 125 nmol/l. May et al 2010

- Many more

Dementia:

- 492 late-onset AD cases, 496 controls, genetic association study. vitamin D treatment suppressed amyloid precursor protein confirming the observation that vitamin D insufficiency increases the risk of developing AD Wang et al 2011

- 318 participants, 50% higher prevalence of dementia among participants with 25(OH)D insufficiency (≤50 nmol/lL) Buell et al., 2010

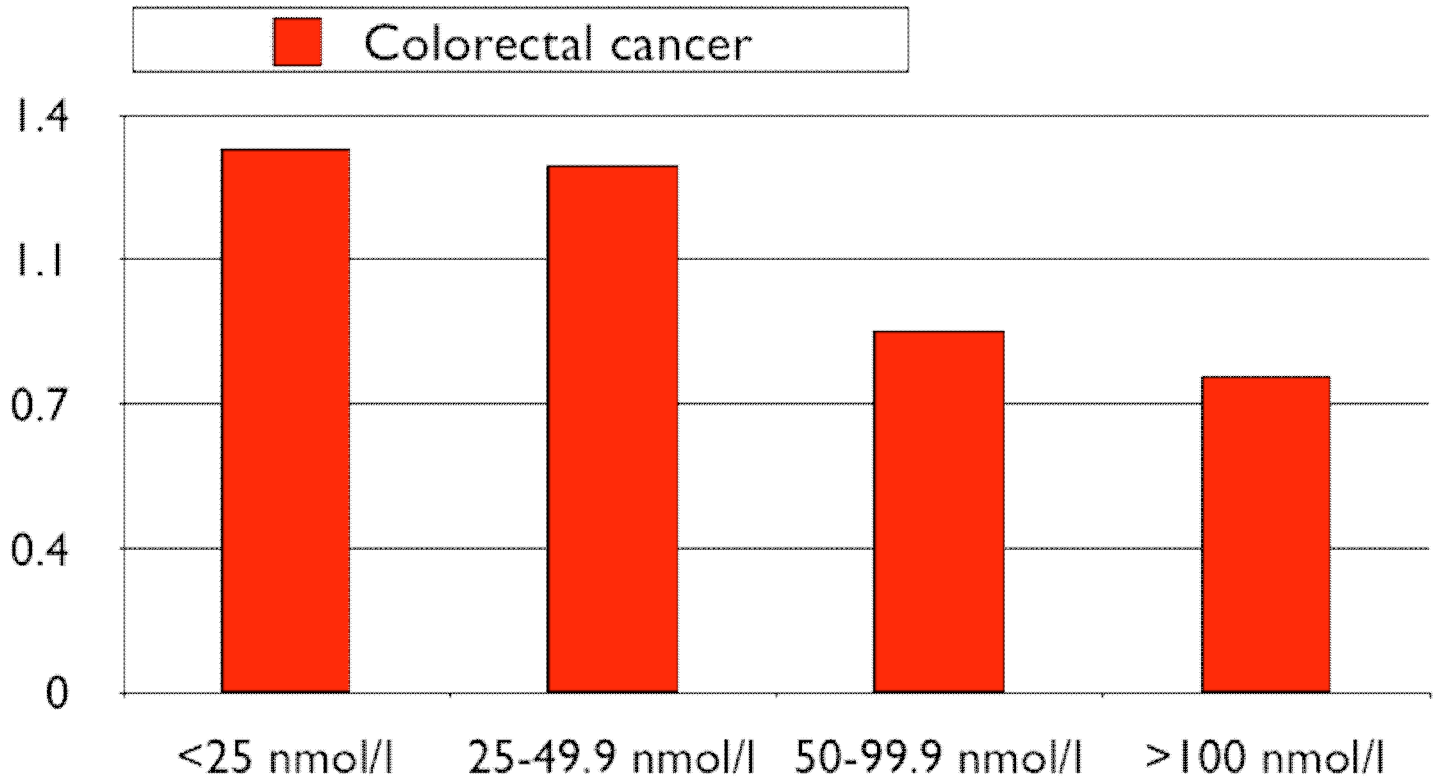
- Cognitive impairment -Annweiler et al., 2010; Oudshoorn et al., 2008; Przybelski and Binkley, 2007; Wilkins et al., 2006

- Lower serum vitamin D level at baseline predicates cognitive decline during the 4.6 years follow-up Slinin et al., 2010

- Many more

Jenar et al. BMJ 2010:
520 000 participants from 10 western European countries
1248 cases of incident colorectal cancer and 1248 controls

“.....patients in the highest quintile had a 40% lower risk of colorectal cancer than did those in the lowest quintile”



6789 participants
UK
45-year olds
July 2011

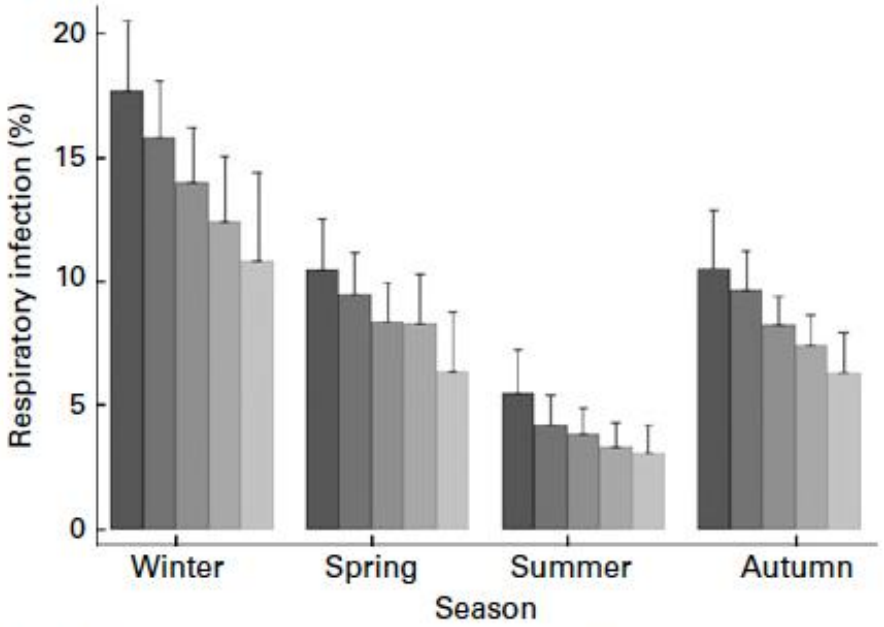


Fig. 2. Prevalence of respiratory infections with 95 % prediction intervals in the 25-hydroxyvitamin D categories of <25 nmol/l (■), 25–49·9 nmol/l (■), 50–74·9 nmol/l (■), 75–99·9 nmol/l (■) and >100 nmol/l (■) as predicted from a logistic regression model adjusted for factors of lifestyle, socio-economic position and adiposity, and season in the 1958 British birth cohort.

Berry et al, July 2011. Vitamin D status has a linear association with seasonal infections and lung function in British adults.
British Journal of Nutrition

Causal relationship?
or
Confounding?

Any evidence
for benefits of **taking**
supplements?

Animals:

UVB
transforms fatty secretions
into vitamin D

then ingested through licking and grooming

Sample of high quality randomised controlled trials:

22% reduction of fractures Trivedi 2003

7% reduction in mortality Meta-analysis of 18 RCTs, 57,000 participants - Autier 2007

70 % reduction in cancer Lappe 2007

39% reduction in influenza A in asthmatic children - Urashima 2010

83% reduction in asthma attacks in asthmatic children - Urashima 2010

significant improved respiratory muscle strength in COPD patients, 100,000 IU monthly - Hornixk 2011

6% reduction in mortality Cochrane Systematic Review. 50 RCTs, 94,148 participants - Bjelakovic 2011

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No negative outcomes in any trial

No harm done

Size of supplement?

One day in sunshine: 250 mcg

- IoM - safe: 100 mcg daily

- My personal recommendation to patients:

50-75 mcg daily or 500 mcg weekly. Some need more, especially when overweight.

Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, M. Murad H, Weaver CM. Evaluation, Treatment, and Prevention of Vitamin D Deficiency: an **Endocrine Society Clinical Practice Guideline.** J Clin Endocrinol Metab, July **2011**, 96(7)

10 mcg to all babies, starting after birth
15 - 25 mcg for children aged 1 to 18
37.5 - 50 mcg for all adults over 18
37.5 - 50 mcg for pregnant women (15 -25 mcg for pregnant women aged 14 -18)

10 mcg is not enough

in Scotland

except for babies

‘10 mcg is not enough’

Edinburgh University, 2011, Zgaga et al
2235 participants, aged 21-85, healthy controls in a study

	without suppl	with suppl
>50 nmol/l	16%	21%
25-50 nmol/l	43%	54%
<25 nmol/l	41%	25%

‘10 mcg is not enough’

400 IU is sufficient
for a baby

but not for a 20 - 30 times heavier adult

Pregnant women, new born babies-high risk group

Rickets in Scotland !

Ahmed et al 2011

described 160 cases
of childhood vitamin D deficiency

2002 - 8 increasing in these years

Yorkhill Hospital Glasgow

bowed legs, fits, pain, motor delay, fractures

Low vitamin D levels in pregnancy

pre-eclampsia
gestational diabetes mellitus
preterm delivery
low birth weight
birth length
bone mineral content

multiple sclerosis
type 1 diabetes mellitus
schizophrenia
adiposity

Present UK advise:

400 IU (=10 mcg) for pregnant women

Babies **only** to start at **6** months

‘10 mcg is not enough’

Belfast
Caucasian women: 120 pregnant women, 41 non pregnant
Holmes et al 2009

Antenatal vitamin D supplements raised levels but the **majority** had still levels below 50 nmol/l

ADC Online First, published on December 15, 2011 as 10.1136/archdischild-2011-301400

50 African or Pakistani mothers
more than 50 % did not take vitamin D during pregnancy
and during exclusively breast feeding

LETTER

Efficacy of vitamin D deficiency prevention strategies in Glasgow's maternity services

The publication by Ahmed *et al* illustrated the increasing burden of symptomatic vitamin D deficiency in Scotland, with cases presenting as young as two weeks of age.[1] In these infants maternal vitamin D levels and infant feeding practice would have undoubtedly played a role.

The Scottish Government adopted the National Institute for Health and Clinical Excellence 2008 guidelines in July 2009, recommending that all pregnant and breastfeeding women be advised about the benefits of vitamin D supplementation and assessed for eligibility to receive free vitamins through the Healthy Start scheme.[2] They suggest health professionals take particular care to ensure those at greatest risk follow this advice.

Our maternity hospital is within the catchment area of the Glasgow hospital in which Ahmed's study took place. We provide maternity services to many ethnic minority and asylum seeking women, who would be considered at high risk of vitamin D deficiency.

We performed an audit to assess how many of our high risk women recalled receiving advice antenatally, were taking vitamin D supplements as recommended and how many intended to give their children supplements. We identified these

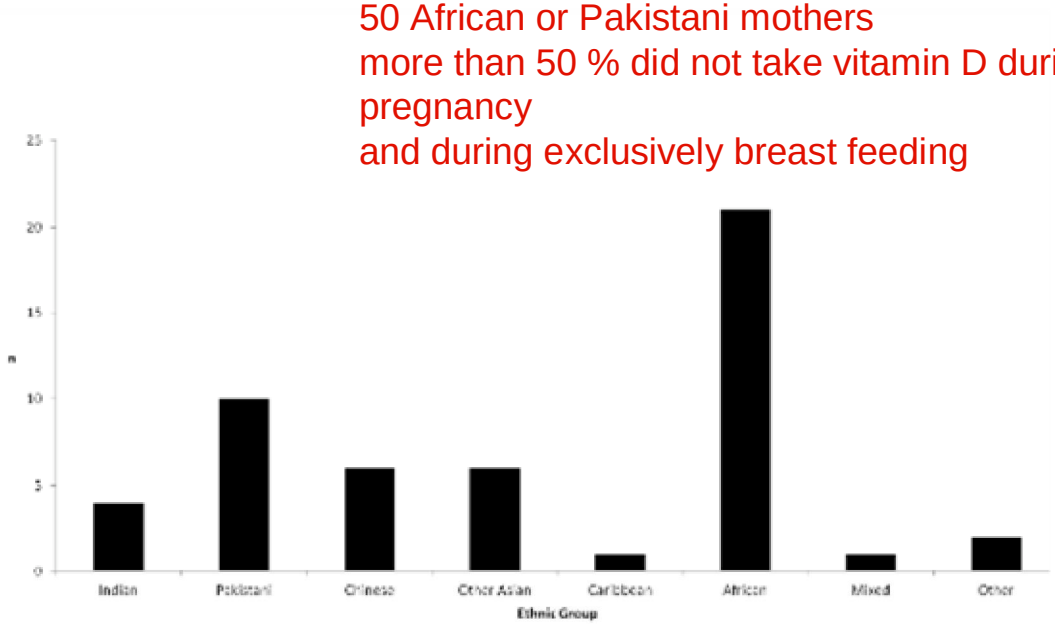

Figure 1 Ethnic group of mothers interviewed.

breast fed. Of this group, 14 (58%) recalled discussing vitamin supplementation, 6 (25%) took a vitamin D supplement, 6 (25%) were unsure which supplement they took and 12 (50%) either did not take any supplements or took a supplement that did not contain vitamin D.

Our audit has shown we are failing to convey the importance of vitamin D supplementation, with less than a quarter of this high risk group taking appropriate supplements during pregnancy. At least half of our exclusively breastfed infants are particularly vulnerable as their mothers have

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Contributors LL contributed to study design and was responsible for data collection, drafting and revising the article. KL was responsible for data collection and revision of the article. AJ was responsible for the study concept and revision of the article.

Competing interests None.

Ethics approval Women and Children Directorate, NHS Greater Glasgow and Clyde.

Provenance and peer review Not commissioned; externally peer reviewed.

In contrast to the UK:

Pregnant women:

Canadian Paediatric Society: 50 mcg daily

Endocrine Society Clinical Practice Guideline 2011: 37.5 - 50 mcg

Babies at birth:

European countries, US, Canada, WHO 2002: 10 - 12.5 mcg daily

Endocrine Society Clinical Practice Guideline 2011: 10 mcg daily

Our UK advice is

- too low in pregnancy
- too patchy - missing even those at highest risk
- non-existent for small babies

Proven bone health benefits > 50 nmol/l

Rickets

Confirmed widespread deficiency in Scotland

Reduced total mortality with supplements

and probably reduced rates of depression, cancers, colds....
and probably reduced rates of MS....

Relative safety of taking supplements

Proof of benefits to non-bone out comes?

U-shaped curve?

Advice from NICE, SACN - due 2014

Long-term damage of giving supplements??
Long-term damage of **not** giving supplements??

But

in Scotland:

No need to wait to replenish the deficient population

Vitamin D supplements

1. Scottish public - Right to be informed?

2. Urgent interim guidelines on supplementation

Suggest: Endocrine Society Clinical Practice Guideline 2011

3. Prescription

Vitamin D, low and high dosed, is in the WHO List of Essential Medicines

Inequalities in health

informed Times reader
level of education
little financial constraints
believe
individual health is priority
will accept own GP's advice

will accept prescription

VS.

many don't read
some cannot read
English
tight budgets
disengaged
health not top priority
it sounds like
complimentary medicine

will accept prescription

Colecalciferol tabs 12.5 mcg (Vigantoletten 500)-

1 daily, dissolve in few drops of water, then add to milk or food

1 pack of 90 = £10.60

Colecalciferol tabs 25 mcg (Vigantoletten 1000)

1 pack of 90 = £11.10

Colecalciferol caps 500 mcg (Dekristol)

1 bottle of 50 = £29.80

Scotland needs vitamin D!