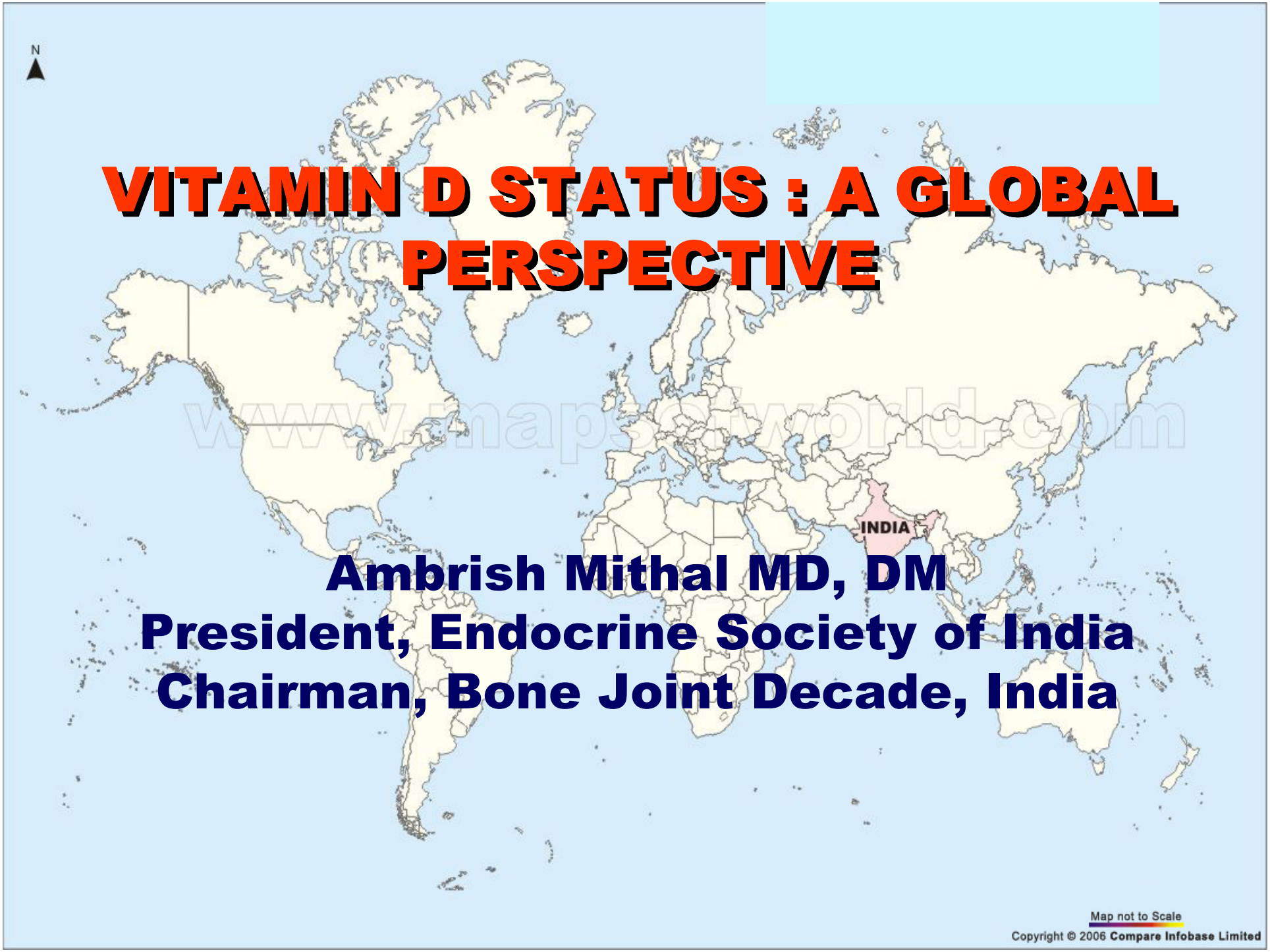


VITAMIN D STATUS : A GLOBAL PERSPECTIVE

Ambrish Mithal MD, DM
President, Endocrine Society of India
Chairman, Bone Joint Decade, India

What is normal vitamin D level – based on biological impact ?

1. Level below which PTH starts to rise

OR

2. Level at which fractional calcium absorption peaks

OR

3. Level at which bone density is optimal

OR

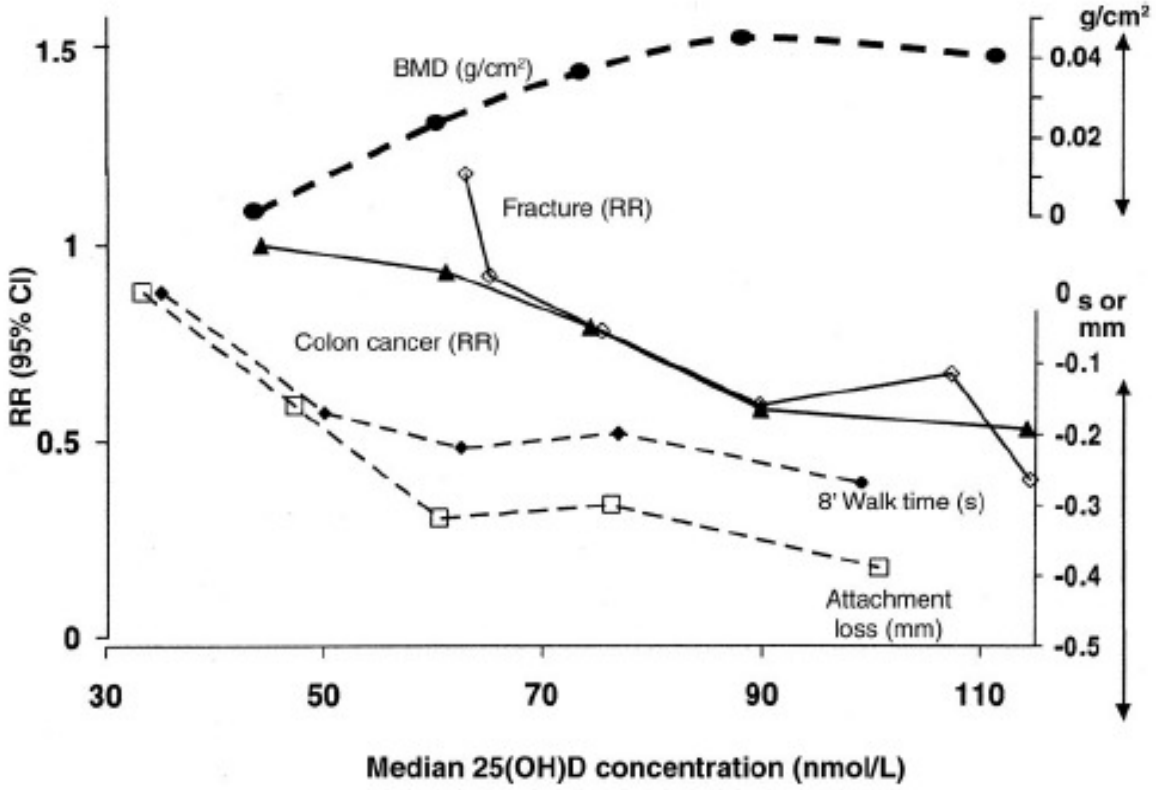
4. Level at which adverse clinical effects are reduced- fractures, falls, muscle strength.. Or non skeletal effects??

- ?ALL OF THE ABOVE

- Technical issues regarding 25(OH)D assays: mean between lab CV ~20-30%

Optimal Vitamin D for multiple health outcomes

- *Desirable 25(OH)D conc. for optimal health begins at 75 nmol/L; and the best conc. is 90-100 nmol/L*



Bischoff-Ferrari et al, 2004

Role of Vitamin D in human body- beyond bones!!

- Bone health
- Muscle power
- Immune system
- Cancer
- Skin
- Cardiovascular system
- Diabetes
- Neurological disorders/depression

Optimal 25(OH)D levels still controversial…

Vitamin D deficiency	<10ng/ml (<25nmol/l)
Vitamin D insufficiency	10-29ng/ml (25-74nmol/l)
Vitamin D sufficiency	>30ng/ml (>75nmol/l)

P Lips J of Steroid Biochem & Mol Biol 2007;103:620-625
Bischoff Ferrari HA et al Am J Clin Nutr 2006;84:18-28

Optimum 25 OHD level working definition

- IDEAL > 30 ng/ml (<75 nmol/l)

- ACCEPTABLE 20-29 ng/ml (50-74nmol/l)
- INSUFFICIENT 10-19 ng/ml (25-49nmol/l)
- DEFICIENT <10 ng/ml (<25 nmol/l)

United States

United States of America
25-41 °

United States

- ***Prevalence of vitamin D deficiency (<10ng/ml) was 1-3% across different age groups***.

Percentage of subjects with 25(OH)D <20ng/ml

Age	Males	Females
12-19yrs	13%	29%
40-59yrs	22%	39%
80&older	26%	37%

United States

- Prevalence of low serum 25(OH)D levels vary by race/ethnicity
- **Decline in 25(OH)D levels by 20%** in 2000-2004 NHANES survey as compared 1988-1994
- Reasons – increase in BMI, decrease in consumption of vitamin D fortified milk, widespread sunscreen use

Looker AC et al Bone 2002;30(5):771-777
Holick MF et al JCEM 2005;90(6):3215-24

Canada


Arctic Ocean
ARCTIC REGION
Arctic Ocean
NORTH AMERICA
EUROPE
ASIA
North Pacific Ocean
North Atlantic Ocean
North Pacific Ocean
MIDDLE EAST
CARIBBEAN
PACIFIC ISLANDS
CENTRAL AMERICA
AFRICA
SOUTH AMERICA
Indian Ocean
AUSTRALIA
South Pacific Ocean
South Atlantic Ocean
NEW ZEALAND
ANTARCTICA
Map View: Robinson Projection

Canada

- 93% healthy adults- 25(OH)D<30ng/ml

- *% of subjects with 25(OH)D <16ng/ml*
  - 22% of individuals with European ancestry
  - 78% of East Asian ancestry
  - 77% of South Asian ancestry
  - 25% of black women

Veith R et al Eur J Clin Nutr 2001;55:1092-1097

Canada

- Prevalence of low 25(OH)D levels is greatest during winter half of year
- Travel to lower latitudes (below 42°N) is associated with increase in 25(OH)D levels
- Increasing age associated with lower 25(OH)D levels
- Average serum 25(OH)D concentrations of Canadians are similar to those of Europeans

Latin America

Latin America
33°N to 55°S

Vitamin D status in Latin America

Country	Mean Age	25(OH)D ng/ml	% <30ng/ml
Argentina	71.3	17.6	87
Brazil	67.6	32.6	42.4
Chile	62.6	30.2	50.4
Mexico	65.6	26.2	67.1
Mexico	63.6	18.9	96.8
Mexico	65.8	31.2	50.6

Oliveri B et al Eur J Clin Nutr 2004;58:337-42J
Fradinger EE et al Medicina 1999;59:449-52

Latin America

- Latitude variation

  Mean 25(OH)D in elderly population from Argentina-
  - 20.7ng/ml(northern)
  - 14.2ng/ml(southern)

- Seasonal variation-

  Mean 25(OH)D in ambulatory women from Buenos Aires-
  - 25.3ng/ml(summers)
  - 21.3ng/ml(winters)

Oliveri B et al Eur J Clin Nutr 2004;58:337-42J
Fradinger EE et al Medicina 1999;59:449-52

Europe

Map View: Robinson Projection

Europe

Euronut Seneca Study:

- Southern Europe 8-12 ng/ml (20-30 nmol/l)
- Northern Europe 16-20 ng/ml (40-50 nmol/l)

MORE Study:

Decreasing level as we go South!!

Other studies:

Low levels in Greece, Spain, Italy as compared to the Netherlands

Lowest level in immigrants in the Netherlands- Turkish, Moroccan

Europe

- France: SUVIMAX study- age 35-65, men and women: results *as expected*

  – North France- 17.2 ng/ml (43 nmol/l)
  – Southwest France- 37.6 ng/ml (94 nmol/l)

  Low 25 OH D level predicted poor physical performance, falls and fractures.

Europe
Latitude/25OHD paradox

Possible reasons why North has better vitamin D status:

fatty fish intake- upto 400 iu/day

light skin colour

Sun seeking behaviour in the North vs
Sun fleeing in the South

Middle East

Middle East
(15-30°N)

Vitamin D status in the Middle East

Population group	25(OH)D<10ng/ml
Lebanese elderly men	37%
Lebanese elderly women	56%
Adolescents girls- Iran -Saudi Arabia -Lebanese	70% 80% 32%
Mothers	10-60%
Neonates	40-80%

Sedrani et al Am J Clin Nutr 1983;38(1):129-32
El Hajj Fuleihan et al Int Cong series Elsevier 2007;1297:92-108

Middle East

- Mean 25(OH)D is 4 to12ng/ml [university students and elderly, Saudi Arabia

- *Highest proportion of hypovitaminosis D is present in women with osteoporosis from Middle East (Lips 2006*)

No data from Africa available

South and East Asia

Map View: Robinson Projection

India

- *North India – 2 - 12 ng/ml (5 to 30 nmol/l)*
- *South India- 6 – 20 ng/ml (15 to 50 nmol/l)*

All ages deficient

Summer better than winter

South better than North

Rural better than urban

Paramilitary forces better

VITAMIN D STATUS IN OTHER COUNTRIES OF SOUTH EAST ASIA

VITAMIN D DEFICIENCY: A CONCERN IN PREMENOPAUSAL BANGLADESHI WOMEN OF TWO SOCIO-ECONOMIC GROUPS IN RURAL AND URBAN REGION

- Latitude 20°43' to 26°36'N and Longitude 88°3' to 92°40'E
- A cross-sectional study
- Two regions of Bangladesh. The Dhaka city area and west region of Nandail (Betagair Union), Mymensingh.
- Bangladeshi women aged 16-40 y
- Representative subjects of two groups
  - LSES (L), n=99
  - HSES (H) n=90

M Z Islam, et al. EJCN 2002 ;56 (1) : 51-56

RESULTS

	Group L	Group H
Prevalence of hypovitaminosis D	63%	46%
<10 ng/ml	17%	12%
< 15 ng/ml	50%	38%

HYPOVITAMINOSIS D IS COMMON IN BOTH VEILED AND NONVEILED BANGLADESHI WOMEN

		<10 ng/ml	<16ng/ml
Group A	Nonveiled Young Women	39%	78%
Group B	Veiled Young Women	30%	83%
Group C	Nonveiled Diabetic Women	38%	76%

Mean value of S-25-OHD was not significantly different in the groups

VITAMIN D STATUS OF BREASTFED PAKISTANI INFANTS

- 62 breastfed healthy infants and their nursing mothers belonging to the upper and lower socioeconomic classes
- The mean serum 25(OH)D – 13.8±10.6 ng/ml
- 25(OH)D levels <10 ng/ml – 55% (Infants)
  45% (Mothers)
- Significantly higher levels were found in infants of
  - Lower socioeconomic class ($p < 0:001$)
  - Living in mud houses ($p = 0:002$)
  - Infants > 6 months ($p < 0:001$).

Acta Paediatrica, 87, 737-740, 1998

SRI LANKA

Peak bone mass as measured by phalangeal bone mineral density and its association with nutritional status, socioeconomic status and physical activity

- **Total of 582 healthy females aged 30-39 years.**

Parameter	Mean	SD
PTH (pg/ml)	49.97	24.64
25(OH)D (ng/ml)	14.12	24.71
SAP (IU/L)	64.18	27.51

Extract from the PhD thesis by Dr M Rodrigo, Faculty of Medicine, Galle, Sri Lanka

VITAMIN D STATUS AMONG POSTMENOPAUSAL MALAYSIAN WOMEN (50-65 years)

	Malay women n=103	Chinese women n=173
Mean 25 (OH) D ng/ml	17.76±4.24	27.52±6.28
20-40 ng/mL	27%	87%
10-20 ng/mL	71%	11%

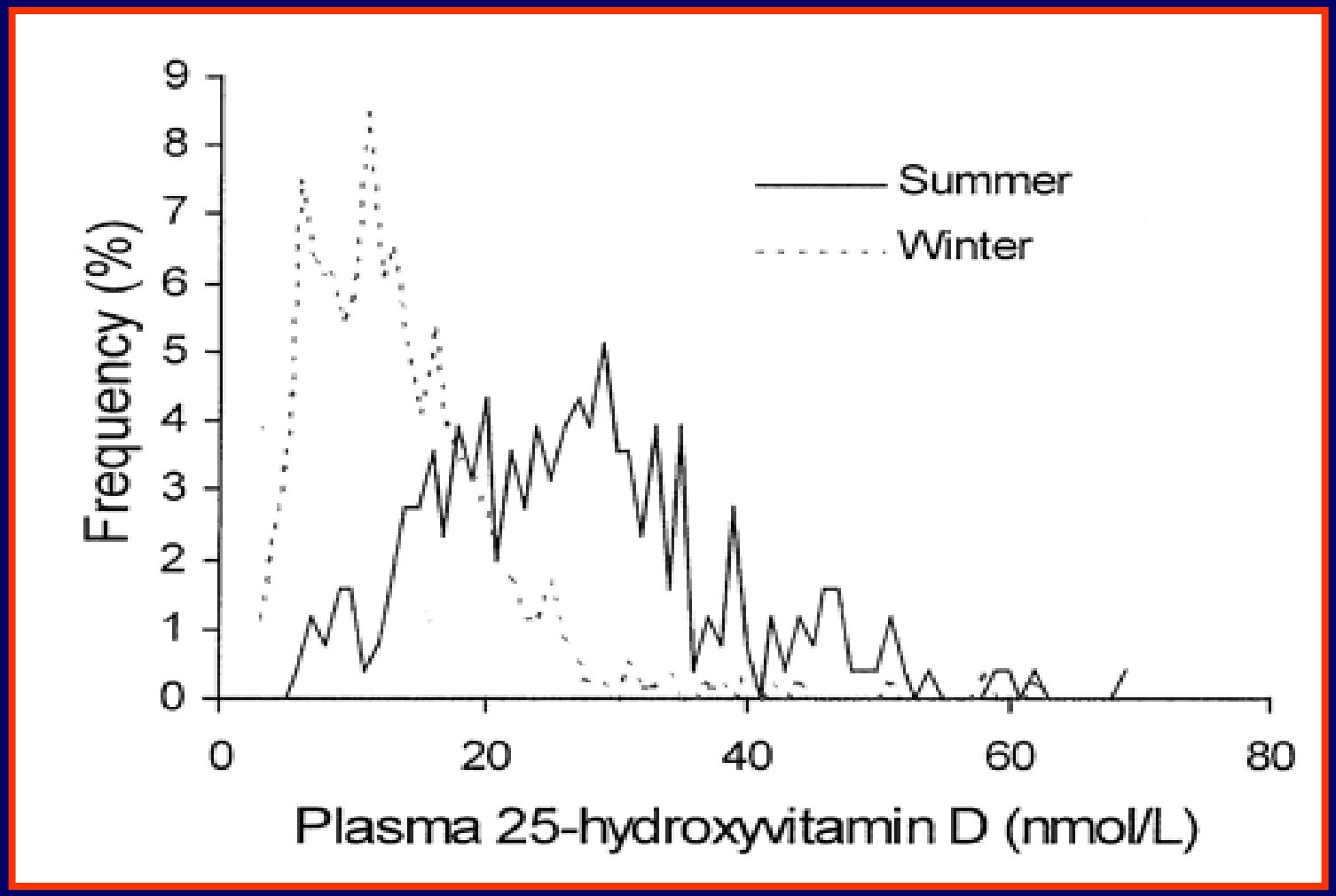
Suriah A Rahman, et al *Asia Pac J Clin Nutr 2004;13 (3):255-260*

VITAMIN D STATUS AND ITS ASSOCIATION WITH PARATHYROID HORMONE CONCENTRATIONS IN WOMEN OF CHILD-BEARING AGE LIVING IN JAKARTA AND KUALA LUMPUR

- A cross sectional study
- Sample of 504 non-pregnant women 18–40 years
- In two Asian cities, – Jakarta (6°S) and Kuala-Lumpur (2°N)
- Mean 25-hydroxyvitamin D -19.2 ng/ml
- 25 OH Vit D <7 ng/ml - Less than 1%
- 25 OH Vit D <20 ng/ml - 60%

T J Green et al *European Journal of Clinical Nutrition*,7 March 2007

DISTRIBUTION OF PLASMA 25-OHD CONCENTRATIONS IN GIRLS AGED 12–14 Y IN WINTER (*N* = 603) AND SUMMER (*N* = 254) IN THE BEIJING AREA (LATITUDE 40 °N).



PREVALENCE AND IMPACT OF VITAMIN D INSUFFICIENCY IN SOUTHERN CHINESE ADULTS

- 382 community dwelling Chinese adults >50 years
- Mean age - 69 ± 9 years.
- Mean 25(OH)D - 28.3 ± 10.8 ng/ml.
- 25(OH)D<30 ng/ml – 62.8%

- *Young women in HK 15 ng/ml vs 3.8 ng/ml in Beijing!*

W.Z.M. Wata, et al *Annals of Nutrition and Metabolism* 2007;51:59-64
Woo et al, BJN 2008;99, 1330-4

Japan

- Overall better than south/south east asia
- Common in inactive elderly
- Positively related to fish consumption
- ***Active elderly- 95% above 30 ng/ml !***

Nakamura K, J Bone Miner Metab, 2006

Oceania

Australia, New Zealand, New Guinea, Pacific islands 30°N-40°S

Vitamin D status in Australia

- *25(OH)D level <10ng/ml*
- Elderly – 68% men
- 86% women
- Pregnant women – 15%
- Neonates -11%
- *25(OH)D level <20ng/ml*
- Young adults (Queensland)- 23%
- *25(OH)D level <30ng/ml*
- Young athletes – 83%

Nowson C et al Proc Nut Soc Aust 2000;24:154
Inderjeeth et al NZ Med J 2007;120(1262):U2730
Brock K et al J Steriod Biochem Mol Biol2004;89-90:581-8

Australia

- Greater hisk in immigrants:
  middle eastern origin in Sydney- 4 fold risk;
  Vietnamese origin- 3 fold risk

Season appears to be more important determinant than latitude

- Risk factors - Greater disability, restricted sunlight exposure, dark skin color, cultural practices, prolonged breast feeding, younger maternal age, chronic medical conditions

New Zealand

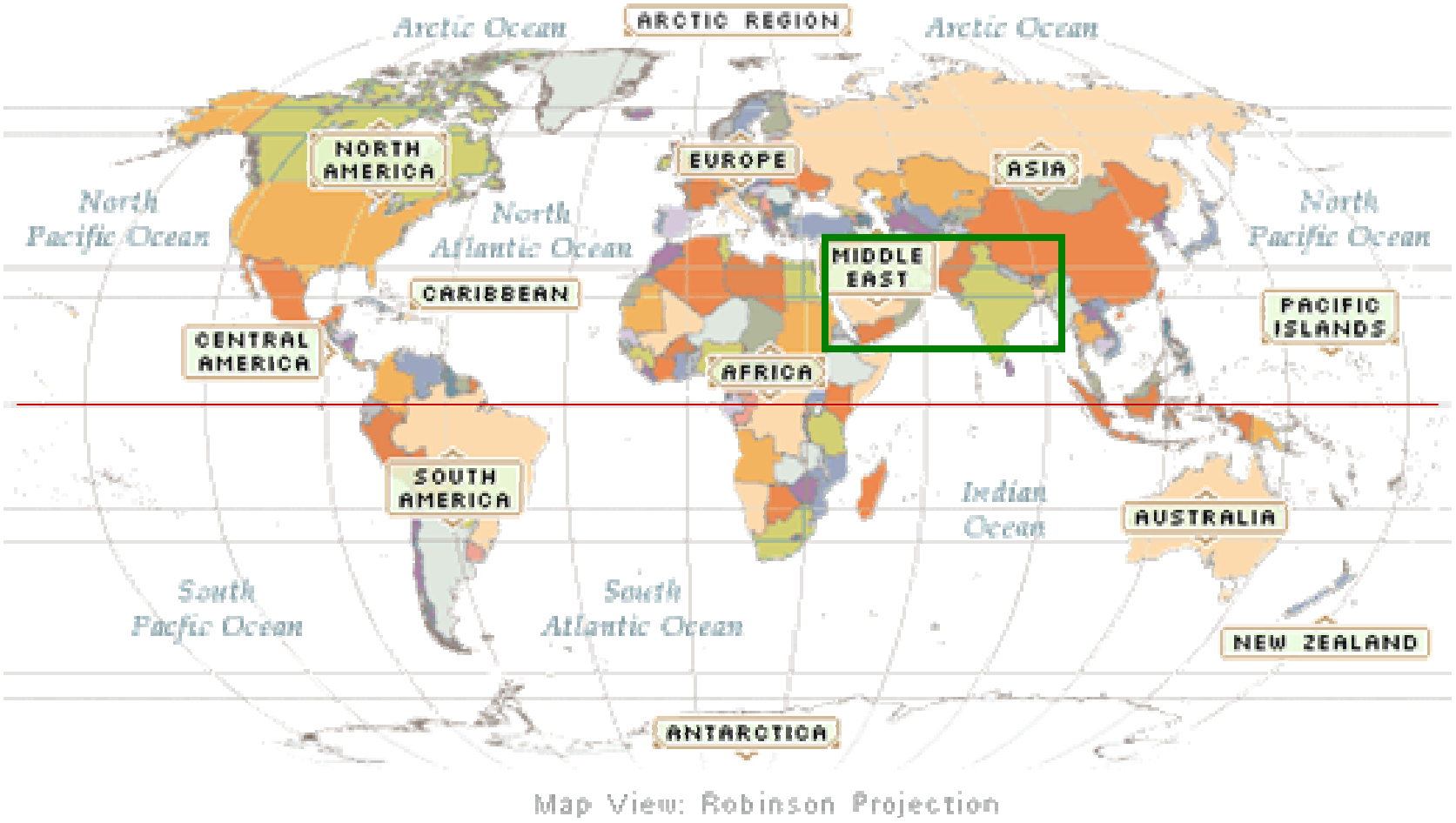
- *Mean 25(OH)D - 19ng/ml in women*
  21ng/ml in men
- Mean 25(OH)D of women in South Island of New Zealand was 2.4ng/ml lower than that in North Island.
- Pregnant women – 87% had 25(OH)D <20ng/ml
  - 61% had 25(OH)D <10ng/ml
- *Children - Prevalence of low 25(OH)D levels (<15ng/ml*)
  - 41% (Maori origin)
  - 59%(Pacific islander),
  - 25%(European)
- Determinants were age, ethnicity, obesity, latitude & season

Rockell JE et al Osteoporos Int 2006;17(9):1382-9
Judkins A et al NZ Med J 2006;119(1241):U2 144
Blok BH et al NZ Med J 2000;113(1117):374-6

Conclusions

- Vitamin D insufficiency common globally
- 25 (OH) D level of 30 ng/ml rarely seen!
- **South Asia and Middle East worst hit despite sun and favourable latitude!!**
- Key factors:
  - **Skin pigment/ethnicity,**
  - **outdoor exposure (age, cultural)**
  - **season**
  - **latitude**
- Fortification important in some areas

Global status



Osteoporos Int
DOI 10.1007/s00198-009-0954-6

REVIEW

Global vitamin D status and determinants of hypovitaminosis D

A. Mithal · D. A. Wahl · J.-P. Bonjour · P. Burckhardt · B. Dawson-Hughes · J. A. Eisman · G. El-Hajj Fuleihan · R. G. Josse · P. Lips · J. Morales-Torres · on behalf of the IOF Committee of Scientific Advisors (CSA) Nutrition Working Group

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Abstract
Summary This review describes the vitamin D status in different regions of the world with the objective of understanding the scope of hypovitaminosis D and the factors related to its prevalence that may contribute to the pathogenesis of osteoporosis and fragility fractures.
Introduction Vitamin D status has been linked to the pathogenesis of hip fractures as well as other skeletal and non-skeletal disorders. The purpose of this review is to provide a global perspective of vitamin D status across different regions of the world and to identify the common and significant determinants of hypovitaminosis D.
Methods Six regions of the world were reviewed—Asia, Europe, Middle East and Africa, Latin America, North America, and Oceania—through a survey of published literature.
Results The definition of vitamin D insufficiency and deficiency, as well as assay methodology for 25-hydroxyvitamin D or 25(OH)D, vary between studies. However, serum 25(OH)D levels below 75 nmol/L are

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