

Vitamin D in Metabolic Bone Diseases

Dr Thinn Thinn Hlaing
MBBS FRCP FRCPATH FHEA

Honorary Consultant in Chemical Pathology & Metabolic Medicine
Cambridge University Hospitals NHS Foundation Trust, UK

Outline

- Scale of vitamin D deficiency in Asia
- Case discussion
- Osteomalacia versus osteoporosis
- Vitamin D for bone health (analysis, interpretation and management of deficiency)
- Summary

Prevalence of Vitamin D in Asia

Country	Prevalence	Cut-off	Comment
South Korea	M 47% F65%	< 50 nmol/L	Sample size 6925
Malaysia	49%	< 75nmol/L	
Sri Lanka	40.5%	< 25nmol/L	
Bangladesh	38% - 50%	< 37.5 nmol/L	
India	70%	< 50 nmol/L	Population study
Singapore	M 9% F 18%	< 50 nmol/L	
China	69%	< 50nmol/L	Sample size 3262
Thailand	6%	< 50nmol/L	Sample size - 2641



120 women

31-60 years of age

Divided:

Pre-menopausal and Post-menopausal

Age: 31-40, 41-50 and 51-60 years

Findings:

serum 25(OH)D3 level
(108.52±40.77, 113.48±46.57,
54.57±12.66 nmol/L)

BMD T score (-1.67 ±0.69, -
1.93±0.64, -2.74±0.76)

Ei Ei Hlaing et al. Myanmar Health Sciences
Research Journal 2015

TTM, 40 year old female

- 2008 - twin delivery , breast fed for one year
- 2009 - **Fell** on back, sustained spinal fracture T9
- Gradually **poor mobility** , difficult to stand up, **proximal myopathy**
- 2011 and until now - joint pain / further back pain
- Limited mobility due to back pain

Key Laboratory Investigations

- Calcium 1.98 ↓
- Phosphate 0.11 ↓
 - ALP 322 ↑

Radiological Investigations

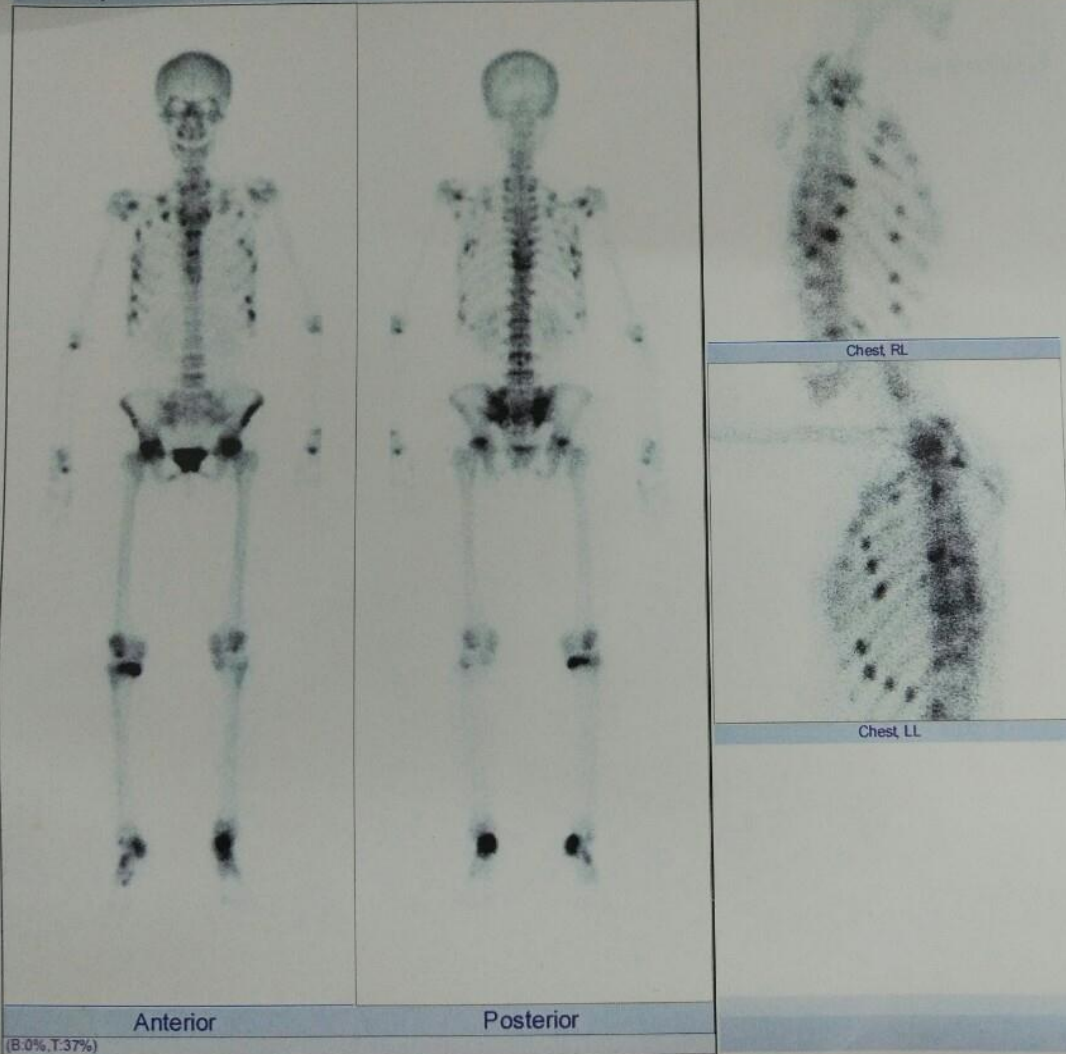
- Spine Xray (2009): anterior wedge collapse of T9



**December 2012 T1 weighted MRI:
T9 osteoporotic compressed fracture**

Whole Body Bone Scintigram 1/5/2012

Spot Views 1/5/2012



Technetium scan (2012): Increased uptake in T9-10 +
high uptake in hip, ankle, right knee



15.8.2015: Multiple compressed #
of the thoracolumbar spine
(L3, T9,10,11,12 #)



13.8.2016: Marked kyphosis
- L1 sub endplate #
- L3, T 9,10, 11,12 #



7.2.2015 Foot X Ray:
Justa-articular osteopenia of metatarsal and phalangeal bones

Drugs She Was On...

- Osteofos 10 mg (2011-2012)
- S/c calcitonin (2012 Jan / April)
- Fosteo (**September 2012** , 4 injections)
- Protelos (Protos) (**June 2012** uptil 2016 June)
- IV zolendronate (**2012 June** / 2013 Jan / Nov 2013 / Jan 2014)
- Prednisolone 5 mg/day (May 2013 to 2016)
- Vit D3 1 BD
- Bon Max since March 2016

Investigations in Our Clinic (4.9.2016)

- TSH - 1.38 IU/L
- ESR - 12 mmol/1st hr
- CRP - 1.86 mg/l
- RA - negative
- Urine BJP - not detected

- Calcium - 2.17mmol/L
- Phosphate - 0.15 mmol/L
- ALKP - 386 IU/L , ALT 10 IU/L
- PTH - 91.28 pg/ml ,
- Vit D <3 nmol/L

DXA Scan

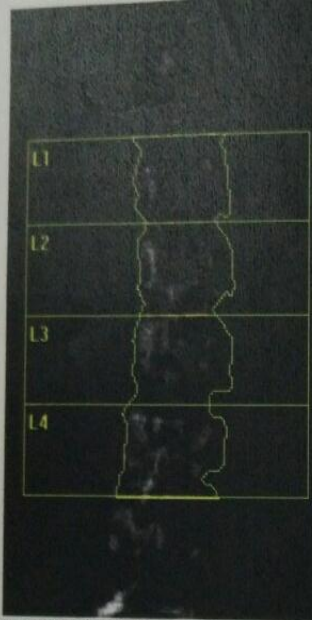


Image not for diagnostic use
116 x 118

Scan Date: August 19, 2016 ID: A08191605
 Scan Type: x Lumbar Spine
 Analysis: August 19, 2016 09:45 Version 13.4.2
 Spine (auto low density)
 Operator:
 Model: Discovery W (S/N 87994)
 Comment:

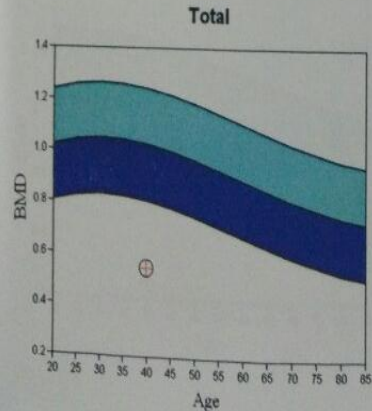
DXA Results Summary:

Region	Area (cm ²)	BMC (g)	BMD (g/cm ²)	T-score	PR (%)	Z-score	AM (%)
L1	10.35	5.55	0.537			-3.9	55
L2	10.72	6.13	0.572			-3.9	57
L3	10.95	5.63	0.515			-5.0	49
L4	12.14	6.87	0.566			-4.3	55
Total	44.15	24.19	0.548			-4.3	53

Total BMD CV 1.0%

Within the range - 1.8 - 1.9

Spine Z-score (-4.3)



Comment: Osteoporosis and high risk of fracture

Referring Physician:

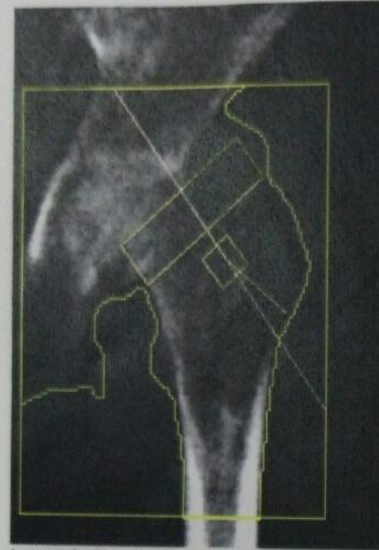


Image not for diagnostic use
102 x 122
NECK: 49 x 15

Scan Information:

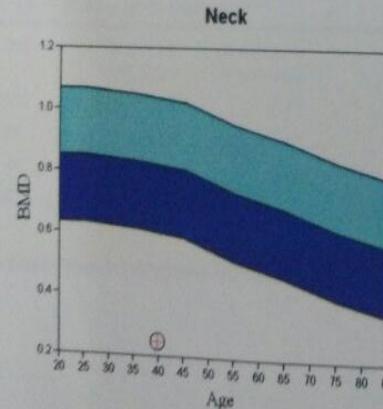
Scan Date: August 19, 2016 ID:
 Scan Type: x Left Hip
 Analysis: August 19, 2016 09:49 Versi
 Hip (low density)
 Operator:
 Model: Discovery W (S/N 87994)
 Comment:

DXA Results Summary:

Region	Area (cm ²)	BMC (g)	BMD (g/cm ²)	T-score
Neck	7.38	1.83	0.248	
Total	79.56	33.03	0.415	

Total BMD CV 1.0%

Hip Z-score (-4.2)



Comment: Osteoporosis and

Points to Ponder

- Osteomalacia or osteoporosis or both
- Challenges in BMD interpretation in patients with osteomalacia
- Vitamin D treatment in severe deficiency patients
- Use of anti-resorptive therapies in vit D deficient patients
 - Safety points to consider

Osteomalacia vs Osteoporosis

- Osteomalacia: Bone disorder characterized by **impairment of mineralization**, causing accumulation of unmineralized matrix or osteoid in the skeleton
- Osteoporosis: Bone disorder characterized by **low bone mass** and **microarchitectural deterioration** of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk



Normal
Normal Structure,
Fully Mineralized



Osteomalacia
Normal Structure,
Under-Mineralized



Osteoporosis
Structurally Degraded,
Fully Mineralized

Osteomalacia versus Osteoporosis

	Osteomalacia	Osteoporosis
Clinical Features	Mild - no symptoms Severe: proximal muscle weakness and myalgia Insufficiency fractures	Usually no symptoms (exception: back pain if vertebral fractures present)
Biochemical Changes	Low Ca, Low PO ₄ , high ALP, low vitamin D, high PTH	No biochemical changes
Radiological changes	X-ray changes (++) DXA: osteopenic to osteoporosis T-score changes	X-ray: osteopenic changes DXA: low T-scores

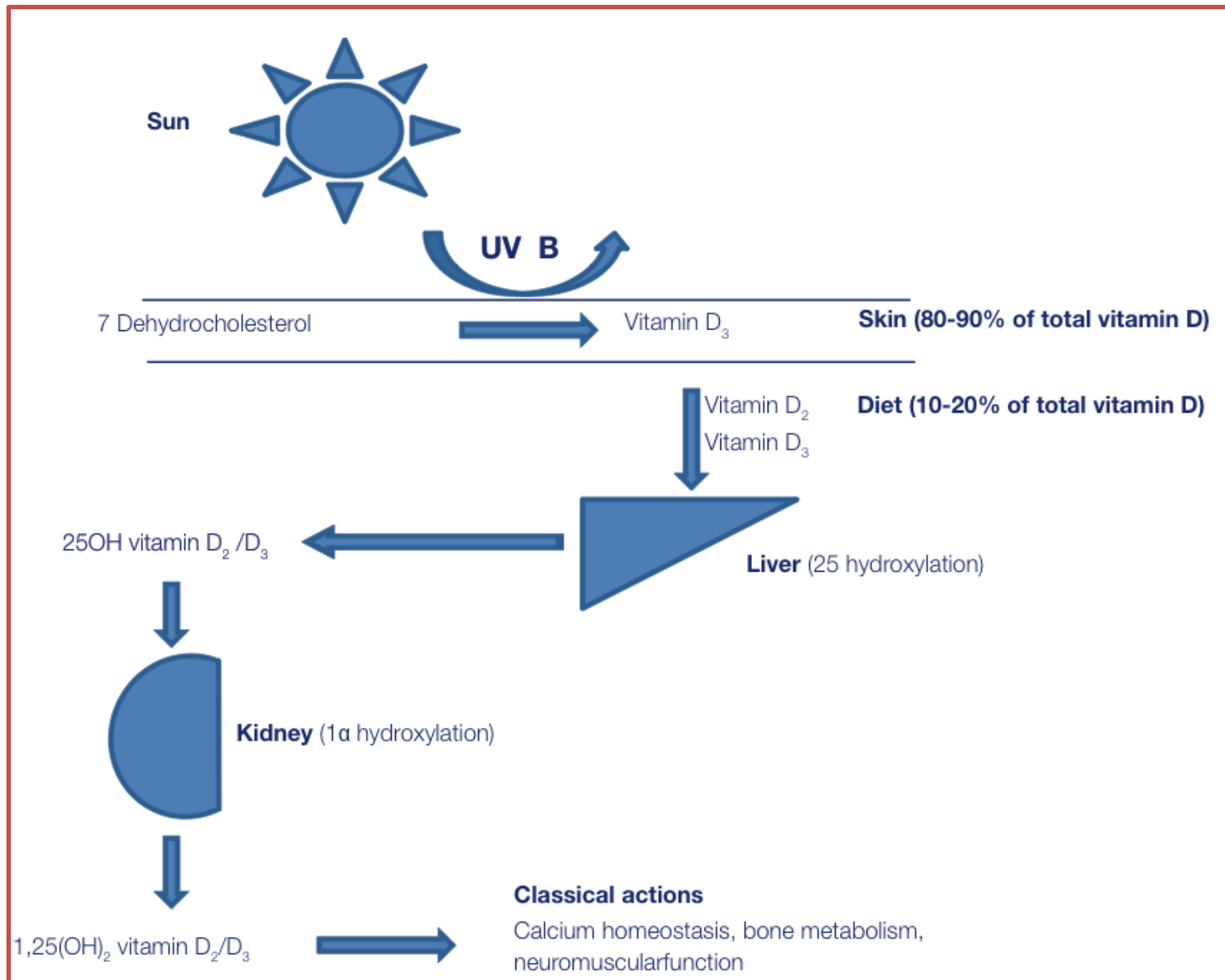
BMD changes in Osteomalacia

Comparison of T-scores of bone densitometry in our patients with osteomalacia and healthy individuals.

Parameters	Osteomalacia cases	Healthy cases	P Value
No. Investigated	20	28	--
Female/Male	16/4	23/5	0.99
Age range year &(mean)	20-60 (39±14.27)	20-60 (39.27±13.09)	0.94
Lumbar spine (L2-L4) T score range & (mean)	-0.8 to -5.2 (-3.005±1.28)	+2.7 to -1.3 (+0.265±1.08)	0.001
Femoral Neck T score range & (mean)	-1.0 to -5.4 (-3.009±1.34)	+2.1 to -1.7 (+0.225±0.89)	0.001

- Low BMD in the region of osteoporosis results by bone densitometry may be detected in **up to 70%** of patients with osteomalacia
- It is important to distinguish between primary osteoporosis and secondary osteoporosis due to osteomalacia
- Management and following its effects is different in these two conditions.

Vitamin D Synthesis



Vitamin D in Bone Health

Without vitamin D...



With vitamin D...



Institute of Medicine (IOM) 2014 suggested:

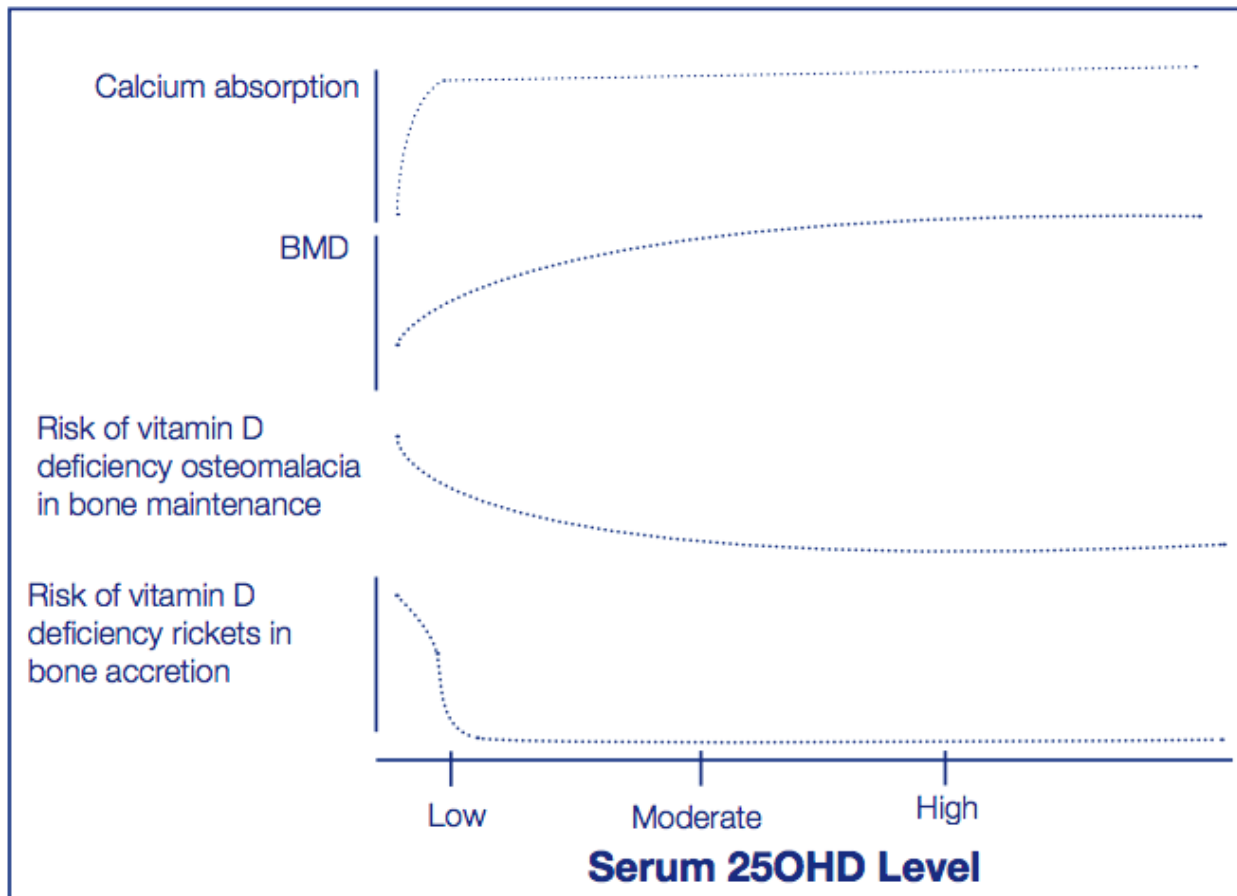
(1) PTH (secondary hyperparathyroidism occurs vit D < 30nmol/L)

(2) BMD & fragility fractures

(Combined Calcium & vit D supplementation reduces the risk of hip and other #)

(3) Falls (vit D supplementation of 800IU/day improves physical performance)

Relationship between Serum Vitamin D & Bone Health Outcomes



Serum 25 (OH) vitamin D of **> 50 nmol/L** is
adequate for entire population

Vitamin D in Bone Health

- When to assess its status on whom?
 - everyone?
- What to request?
- How to interpret the results?
 - Optimum vs deficient
- What to replace?
 - how much and how long?

Indications of Vitamin D Testing

- (1) Patients with **bone diseases** (a) that may be improved with vitamin D treatment or (b) where correcting vitamin D deficiency prior to specific treatment would be appropriate
- (2) Patients with **musculoskeletal symptoms** that could be attributed to vitamin D deficiency

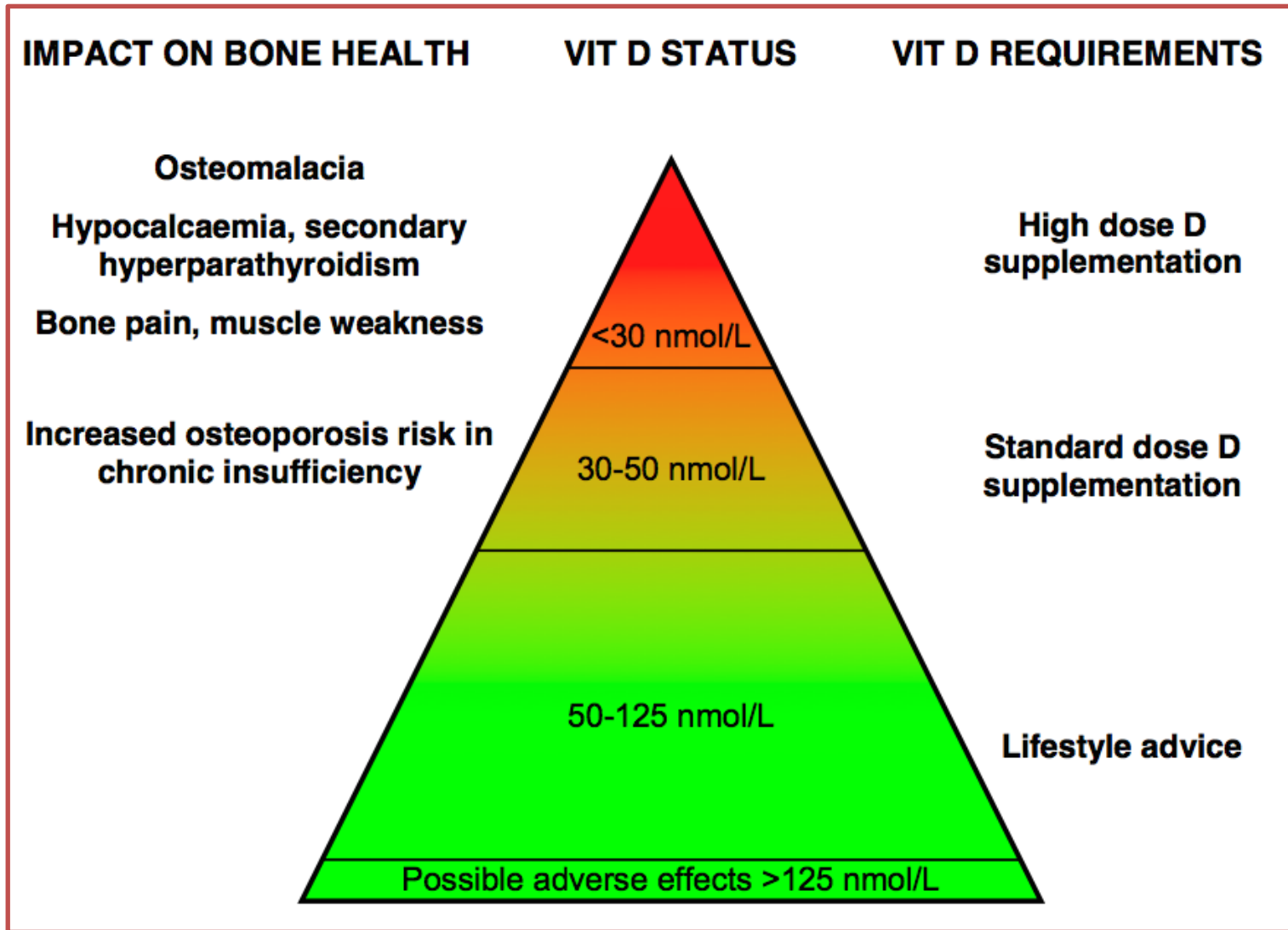
Do Not Routinely check vitamin D in following group

- (1) Asymptomatic individuals at **higher risk of vitamin D deficiency (consider replacement 400 IU/day individual cases)**
 - all pregnant and breastfeeding women, esp teenagers and young women
 - older people, aged 65 years and over
 - people who have low or no exposure to the sun
 - people who have darker skin, for example people of African, African-Caribbean or South Asian origin, because their bodies are not able to make as much vitamin D
- (2) Asymptomatic healthy individuals

Vitamin D Testing & Interpretation

- What to request?
 - 25 hydroxy (OH) vitamin D (either measured by LC-MS or Immunoassays)
- How to interpret the results?
 - Serum 25OHD < 30 nmol/L is deficient.
 - Serum 25OHD of 30–50 nmol/L may be inadequate in some people.
 - Serum 25OHD > 50 nmol/L is sufficient for almost the whole population.

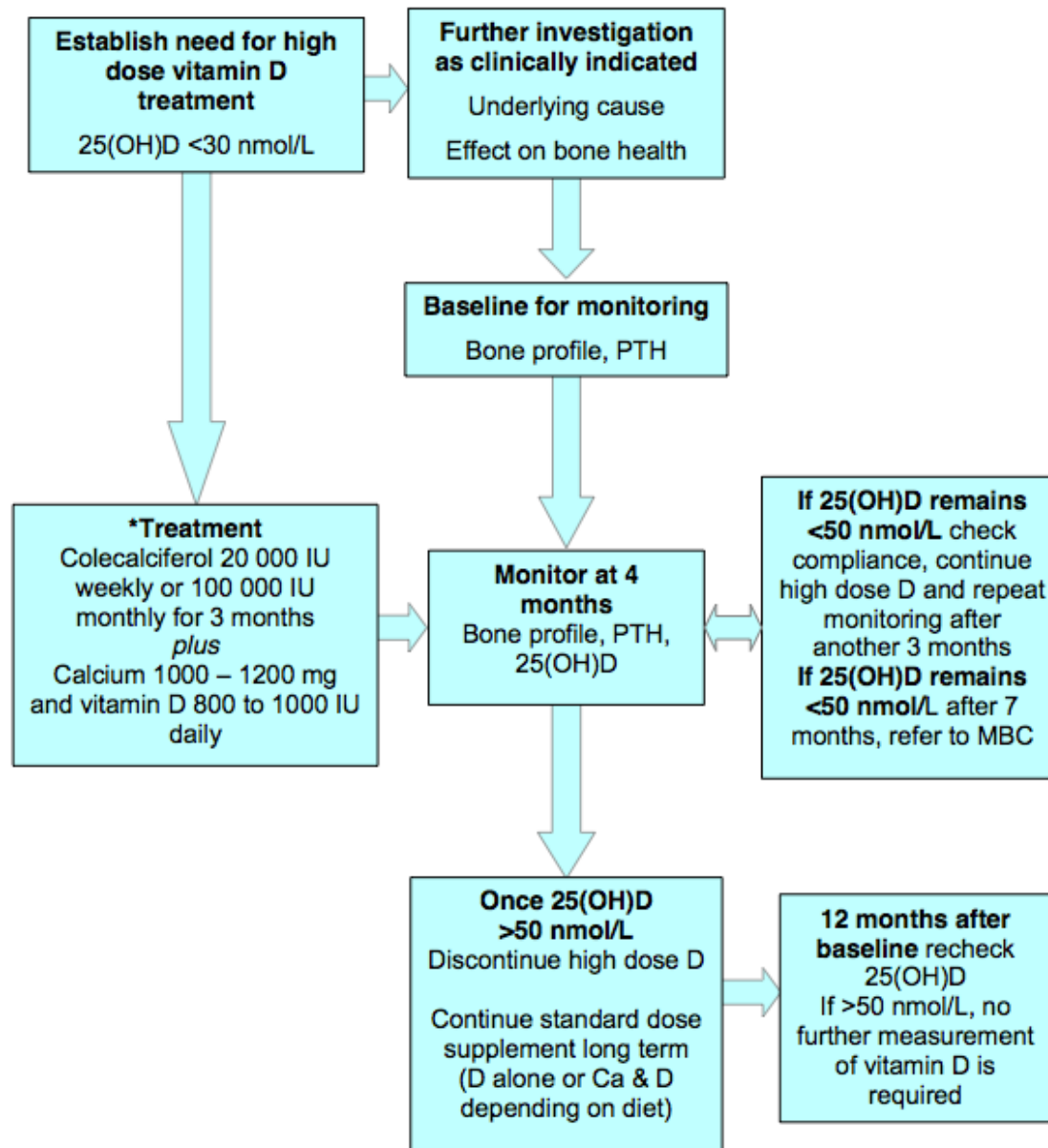
Management of Vitamin D Deficiency



Management of Vitamin D Deficiency

- What to replace - D2 (Ergocalciferol) or D3 (Cholecalciferol)
 - D3 is the preferred choice
- Oral or IM - oral is preferred
- For standard dose replacement (vit D 30-50nmol/L)
 - Kalplus D Forte (400 IU vitD/500mg Cal) twice a day or
 - 1000 D plus 2 tablets of calcivita forte
- For high dose vitamin D replacement - refer to a specialist or refer to the guidelines

High Dose Vitamin D Supplementation & Monitoring



Diagnosis of Our Patient

- Osteomalacia
- Severe Vitamin D deficiency
 - Spine fractures

Management

- Stop Prednisolone, Bon Max, Proteolos
- 5000 IU Vit D OD x 3/12
- Calcichew D3 1 BD
- Muscol
- Omeprazole if dyspepsia symptoms +
- Follow up vitamin D measurement in 3 months

Summary

- Vitamin D deficiency is highly prevalent globally
- Associated with severe bone health outcomes - osteomalacia, increased fracture risk and falls
- 25 (OH) vitamin D testing must be done in patients with metabolic bone diseases or with muscle symptoms
- Optimum serum vitamin D for bone health for 97% of population is > 50 nmol/L (IOM report)
- Replete vitamin D status if found deficient is a requirement prior to starting anti-resorptive therapies for osteoporosis
- Severe deficiency < 30 nmol/L must be replaced with high dose vitamin D (20000IU/week for 3 months)



Let's Shed Some Light on Ourselves!