

## Bone Health in Children with Medical Complexity

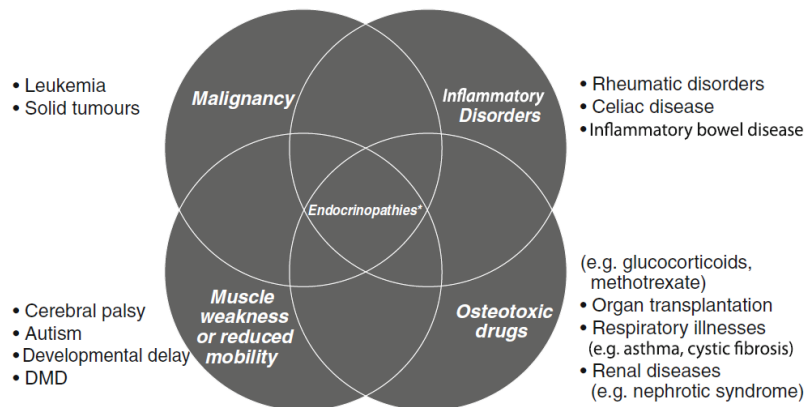
### DEFINITION:

Clinically Significant Fractures	Osteoporosis
<ul style="list-style-type: none"> <li>○ <b>2</b> or more long bone fractures by <b>10</b> years</li> <li>○ <b>3</b> or more long bone fractures by <b>19</b> years</li> <li>○ <b>1</b> or more vertebral compression fractures (loss of &gt;20% of vertebral body height) at <b>any age</b></li> </ul>	Clinically Significant Fracture Hx <b>AND</b> a DXA Z-score ≤ -2.0 SD adjusted for age, sex & height as appropriate

### ETIOLOGY:

<b>Primary osteoporosis</b>	Connective tissue disorders
<b>Secondary osteoporosis</b>	Reduced weight-bearing (e.g., CP, DMD), endocrine conditions (e.g., delayed puberty, GH deficiency), renal disease, malnutrition, inflammatory/infiltrative conditions, osteotoxic drugs (e.g., glucocorticoid, methotrexate)

#### Main Causes of Secondary Osteoporosis Associated with Fragility Fractures in Childhood



\*The endocrinopathies with potential to impact bone strength that are most frequently encountered in the chronic illness setting include delayed puberty, and growth hormone deficiency

### EPIDEMIOLOGY:

- Children with CP are at risk for osteoporosis and fragility fractures
- **70-80%** of fractures occur in the **distal femur** or **proximal tibia** following minimal trauma
- Children with CP are more likely to develop complications after a fracture, such as:
  - Further fractures, malunion, nonunion, and infections including pneumonia

#### Risk factors:

1. Decreased weight bearing	5. Delayed puberty
2. Inadequate calcium and vitamin D intake	6. Menstrual irregularity
3. Exposure to medications (e.g., anticonvulsants, PPIs)	7. Decreased sunlight exposure
4. Lean mass deficit	

- **Long-term enteral feeding + long-term PPI use → hypophosphatemia & negative bone health outcomes**

### CLINICAL FEATURES:

- **Asymptomatic – unless fractures occur, which then often cause pain/irritability and localized tenderness**
  - Should be considered in the non-verbal child with irritability NYD

**COMPLICATIONS:**

- Painful fractures
- Permanent deformity
- Premature loss of ambulation

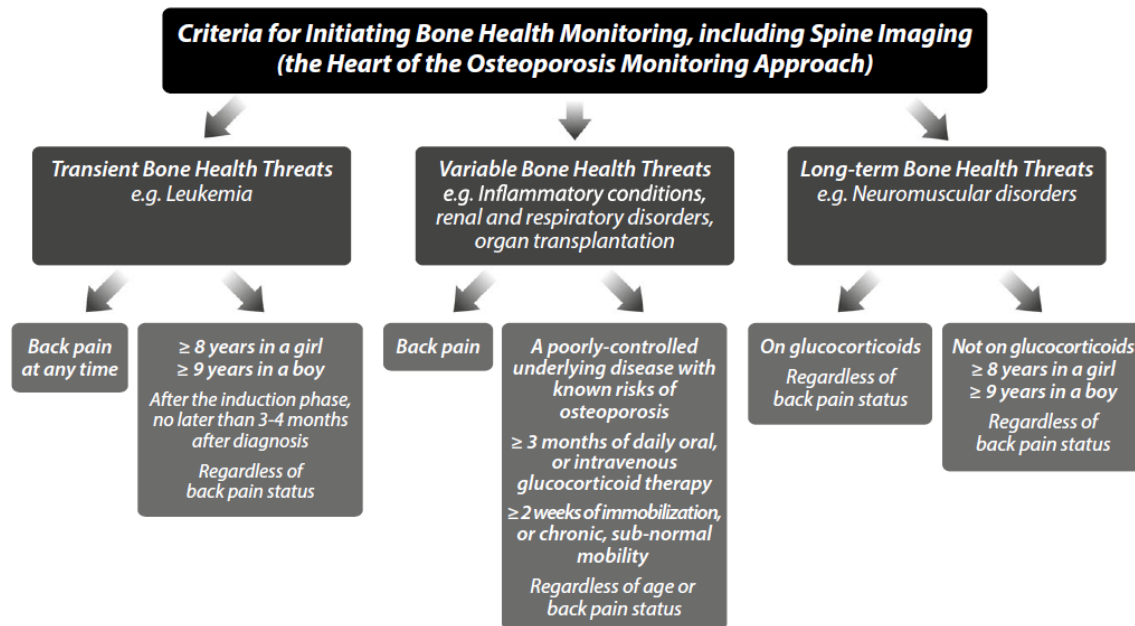
**DXA SCAN:**

- Preferred sites: Lumbar spine or whole body minus cranium (lateral distal femur if reference date available; correlate well with increased lower extremity fragility fracture risk in non-ambulatory children)
- Results to be adjusted for age, sex and height or bone age
  - **Z-score  $\geq -1$   $\rightarrow$  normal**
  - **Z-score  $< -1 > -2$   $\rightarrow$  osteopenia**
  - **Z-score  $\leq -2$   $\rightarrow$  osteoporosis**

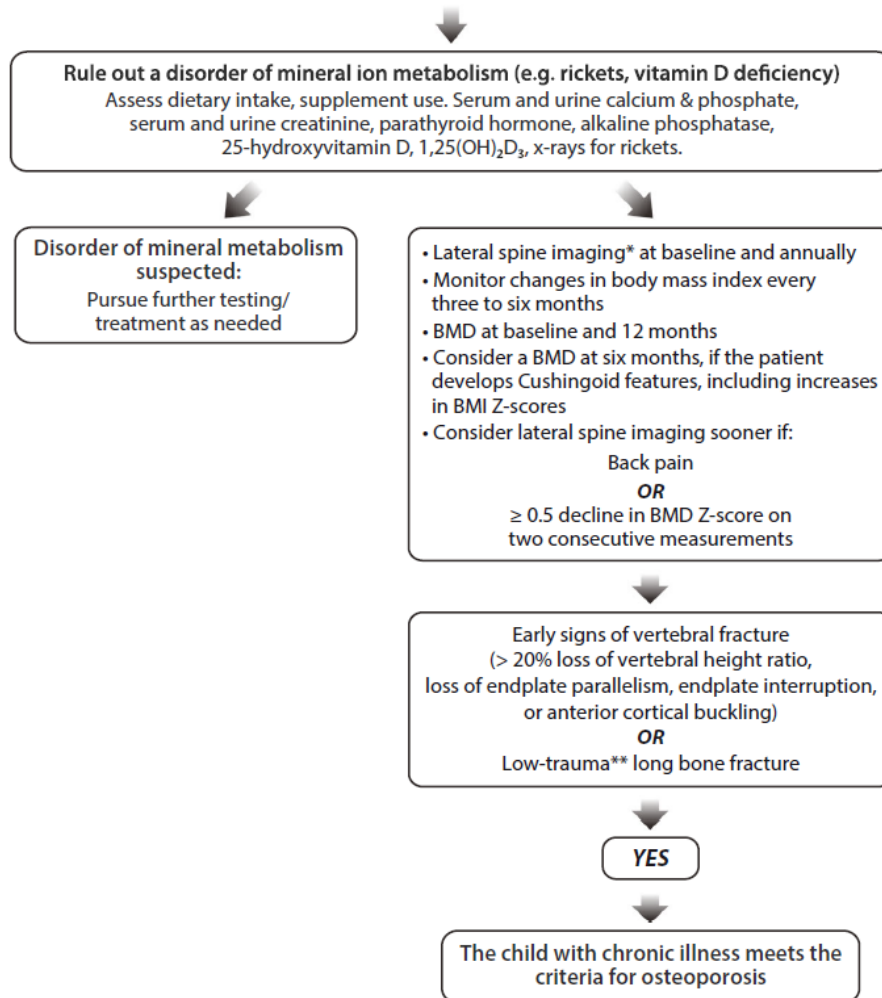
*In patients at risk for secondary bone disease, DXA should be performed when the patient may benefit from interventions to decrease their elevated risk of clinically significant fractures.*

**BONE HEALTH MONITORING & DIAGNOSIS OF OSTEOPOROSIS:**

**Criteria to initiate bone health monitoring, including spinal X-ray**



**Approach to the Monitoring and Diagnosis of Osteoporosis in Children with Chronic Illnesses After the Decision to Monitor the At-risk Child Has Been Made**



\* Spine imaging by lateral spine radiograph or “vertebral fracture assessment” (VFA) by DXA  
 \*\* Low trauma is defined as falling from a standing height or less, at no more than walking speed

**PREVENTATIVE MEASURES:**

1. Monitoring growth, puberty, and menstrual irregularities
2. Adequate **calcium** and **vitamin D** intake (via nutrition and/or supplementation)
3. Nutritional support
4. Promoting weight bearing activities

**PREVENTATIVE/TREATMENT SUPPLEMENTS AND MEDS:**

**VITAMIN D:**

Vitamin D intake:

Consider supplementing children with CP with vitamin D2/D3 (starting dose of **800-1000 IU/day**).

Age	RDA vitamin D (IU/day)	UL vitamin D (IU/day)
0-12 months	400	1500
1-3 years	600	2500
4-8 years	600	3000
9-18 years	6000	4000

Dietary sources of vitamin D	
Food	Vitamin D Content, IU
Fortified milk/infant formulas	400/ L
Fortified orange juice/soy milk/rice milk	400/ L
Yogurt (normal, low fat, or nonfat)	89/ 100 g
Cheddar cheese	12/100 g
Cereal fortified	40/ serving
Egg yolk	20-25 per yolk
Shrimp	152/100 g
Canned pink salmon with bones in oil	624/100 g
Cooked salmon/mackerel	345-360/100 g
Cod liver oil	175/g; 1360/ tablespoon

25-OH-vitamin D level:

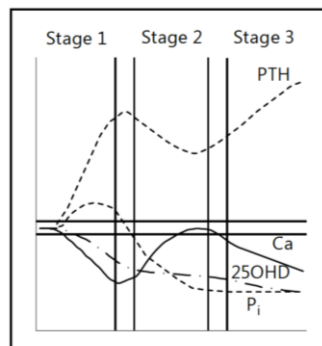
- Best available indicator of total body vitamin D status
- Half-life of 25-OH-vitamin D: 2-3 weeks
- Goal: **70-100 nmol/L**

Vitamin D deficiency/insufficiency definitions:

Canadian Pediatric Society (2007)	Pediatric Endocrine Society of North America (2008)	The Institute of Medicine (Health and Medicine Division of the National Academies, 2010)	The Endocrine Society (2011)
Deficiency: < 25 nmol/l	Deficiency: < 37.5 nmol/l	Deficiency: < 30 nmol/l	Deficiency: ≤ 50 nmol/l
Insufficiency: 25-75 nmol/l	Insufficiency: 37.5 - 50 nmol/l	Insufficiency: 30-50 nmol/l	Insufficiency: 52-72 nmol/l
Optimal: ≥ 75 nmol/l	Optimal: ≥ 50 nmol/l	Optimal: ≥ 50 nmol/l	Optimal: ≥ 72 nmol/l

IOM (Institute of Medicine). 2011 Dietary Reference Intakes for Calcium and Vitamin D. Washington DC: The National Academies Press  
 Holick MF et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2011; 96:1911-30  
 Canadian Pediatric Society Paediatr Child Health 2007;12:583-9

Stages of vitamin D deficiency:



Arnaud SB, Arnaud CD, Bordier PJ Vitamin D and Problems of Uremic Bone Disease. Berlin, de Gruyter, 1975, pp 397-416

Treatment of vitamin D deficiency:

- **0-1 Y/O:** 2,000 IU per day for 6-12 weeks to achieve a blood level 25(OH)D > 50 nmol/l, followed by maintenance therapy of 400-1,000 IU/day
- **1-18 Y/O:** 2,000 IU per day for 6-12 weeks or 50,000 IU once weekly for 6 weeks to achieve a blood level 25(OH)D > 50 nmol/l, followed by maintenance therapy of 600-1,000 IU/day

**PLUS, Ca supplement:** 500 mg/day elemental calcium (or 50-100 mg/kg/day divided BID or TID)

**CALCIUM:**Calcium intake:

Age	RDA vitamin D (mg/day)	UL (mg/day)
0-12 months	250	1500
1-3 years	700	2500
4-8 years	1000	2500
9-18 years	1300	3000

To maintain Ca intake, **increase dietary intake (1<sup>st</sup> option)**, and/or consider Ca supplementation, if required.

In children with **CP**, the following **daily Ca intake** is considered adequate:

- **1-3 y/O: 500 mg/day**
- **4-8 Y/O: 800 mg/day**
- **9-18 Y/O: 1300 mg/day**

**BISPHOSPHONATE:**

- Inhibits bone resorption (inhibits osteoclasts)
- Attaches to bones and remain in the skeleton for years
- In children with secondary osteoporosis, bisphosphonates improve BMD and decrease bone pain
- Paucity of long-term pediatric safety data
- Uncertainty about optimal dose, mode of administration, duration, and frequency
  - In pediatrics, **ONLY IV infusion formulations** are used (i.e., Pamidronate, Zoledronate)
- If required, consultation with an **endocrinologist** may be required
- Side effects:
  - Acute phase reaction:
    - Low-grade fever, myalgias, nausea/vomiting, bone pain, decreased lymphocyte counts
    - Usually within 48 hr of infusion
  - Transient hypocalcemia and hypophosphatemia
  - Atypical femoral fractures
  - Dental development
  - Osteonecrosis of the jaw (very rare)
- X-ray: Each cycle leaves a dense band at physis that migrates with growth

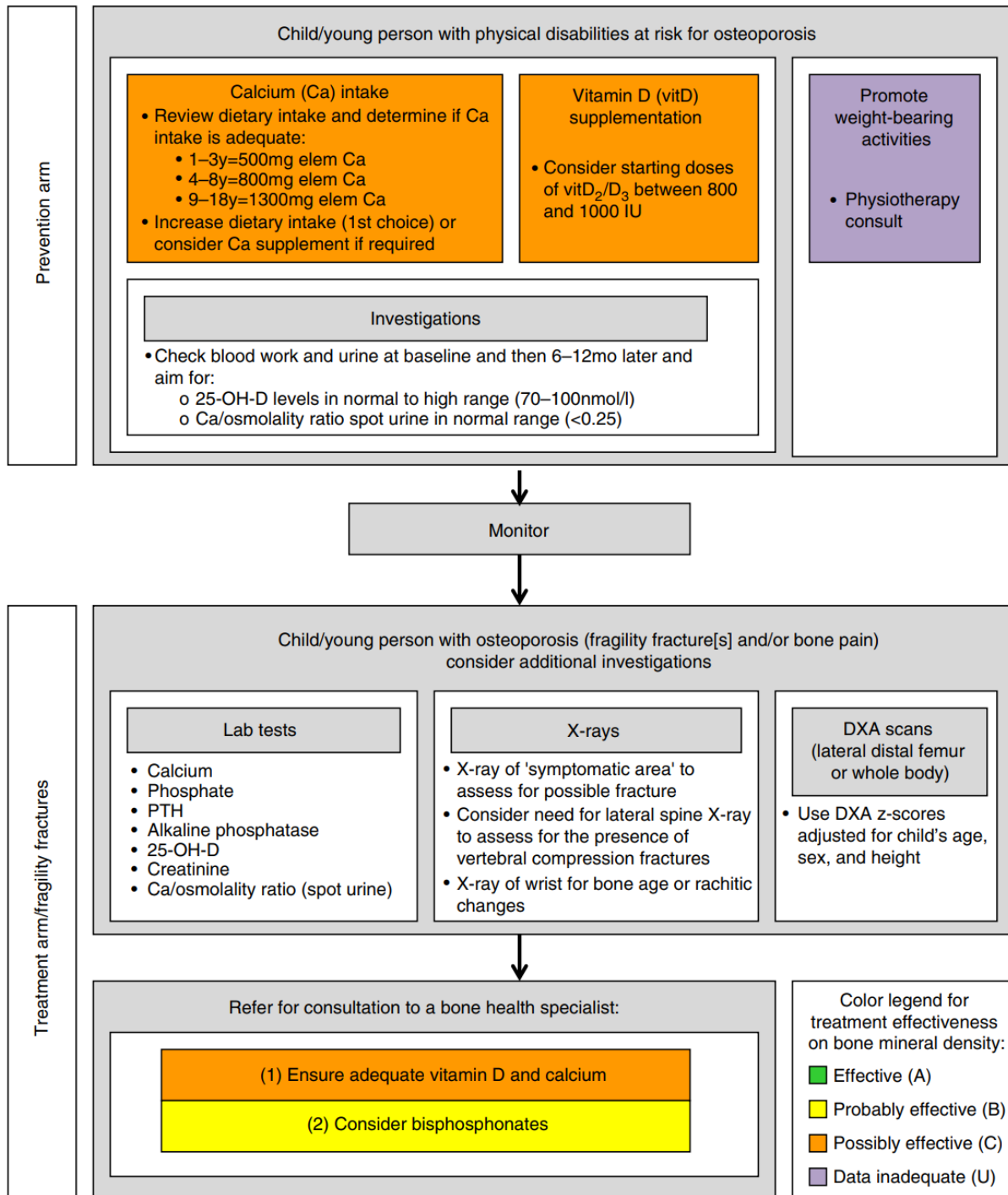
**INDICATIONS FOR CONSULTATION:**ENDOCRINE:

- (1) Vertebral compression fractures
- (2) Clinical features suggestive of primary osteoporosis
- (3) Secondary osteoporosis not responding to initial management (further fractures, BMD Z-Score worsening over time)

ORTHOPEDICS:

- (1) Any fragility fractures

**Osteoporosis clinical practice guidelines for children and young people with cerebral palsy**



**REFERENCES:**

- Ozel S, Switzer L, McIntosh A, Fehlings D. Informing evidence based clinical practice guidelines for children with cerebral palsy at risk for osteoporosis: an update Dev Med and Child Neurology. 2016; 918=923.
- Holick MF et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2011; 96:1911-30.
- IOM (Institute of Medicine). 2011 Dietary Reference Intakes for Calcium and Vitamin D. Washington DC: The National Academies Press.
- Leanne M. Ward. Part I: Which Child with a Chronic Disease Needs Bone Health Monitoring? Current Osteoporosis Reports (2021) 19:278–288.