

Women's Health in SMA

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Make today a breakthrough.

Common gynecologic problems in SMA

- recurrent urinary tract infections
- difficulty with pelvic exams
- possible suboptimal mammograms
- counseling regarding sexuality & contraception

Gynecologic needs

- annual gynecological exams
- cervical cancer screening
- breast exam
- STI screening
- evaluation and management of gynecologic infections and abnormal bleeding
- contraception counseling / family planning

ACOG recommends carrier screening

SMA carrier risk based on ethnicity

Caucasian	1:35
Ashkenazi Jewish	1:41
Asian	1:53
African American	1:66
Hispanic	1:117

ACOG Committee Opinion

- carrier screening either pre-conceptually or during pregnancy
- reproductive partner to be tested in carriers
- genetic counseling
- family notification in carriers

Options in SMA

- natural conception
- egg or sperm donation
- CVS
- Amniocentesis
- PGD

Common Obstetrical Problems

- progressive worsening pulmonary function
- worsening muscle weakness , pain and fatigue
- thrombotic events
- recurrent UTIs
- premature labor and delivery
- delayed postpartum recovery

Multidisciplinary Approach to Delivery

- Perinatology
- Pulmonary
- Anesthesia

SMA and pregnancy

pre-conceptual counseling

multidisciplinary team

post delivery assistance



Osteoporosis

Garey Noritz, MD

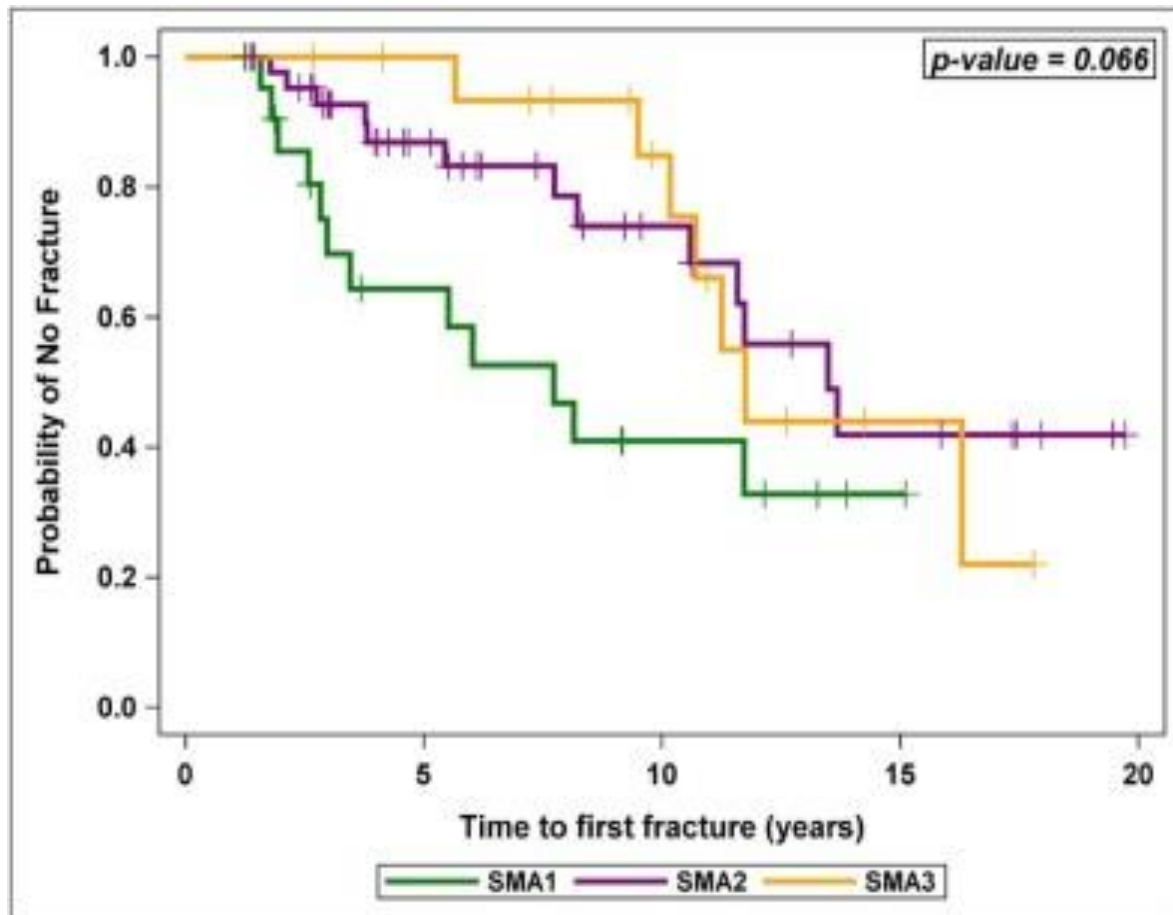
Internist and Pediatrician

Nationwide Children's Hospital



Make today a breakthrough.

Fracture Prevalence



85 patients under age 18
85% had low bone mineral density
38% had fractures

Fig. 2. Probability of remaining fracture free by SMA subtype.

Halley M. Wasserman, Lindsey N. Hornung, Peggy J. Stenger, Meilan M. Rutter, Brenda L. Wong, Irina Rybalsky, Jane C. Khoury, Heidi J. Kalkwarf

Low bone mineral density and fractures are highly prevalent in pediatric patients with spinal muscular atrophy regardless of disease severity

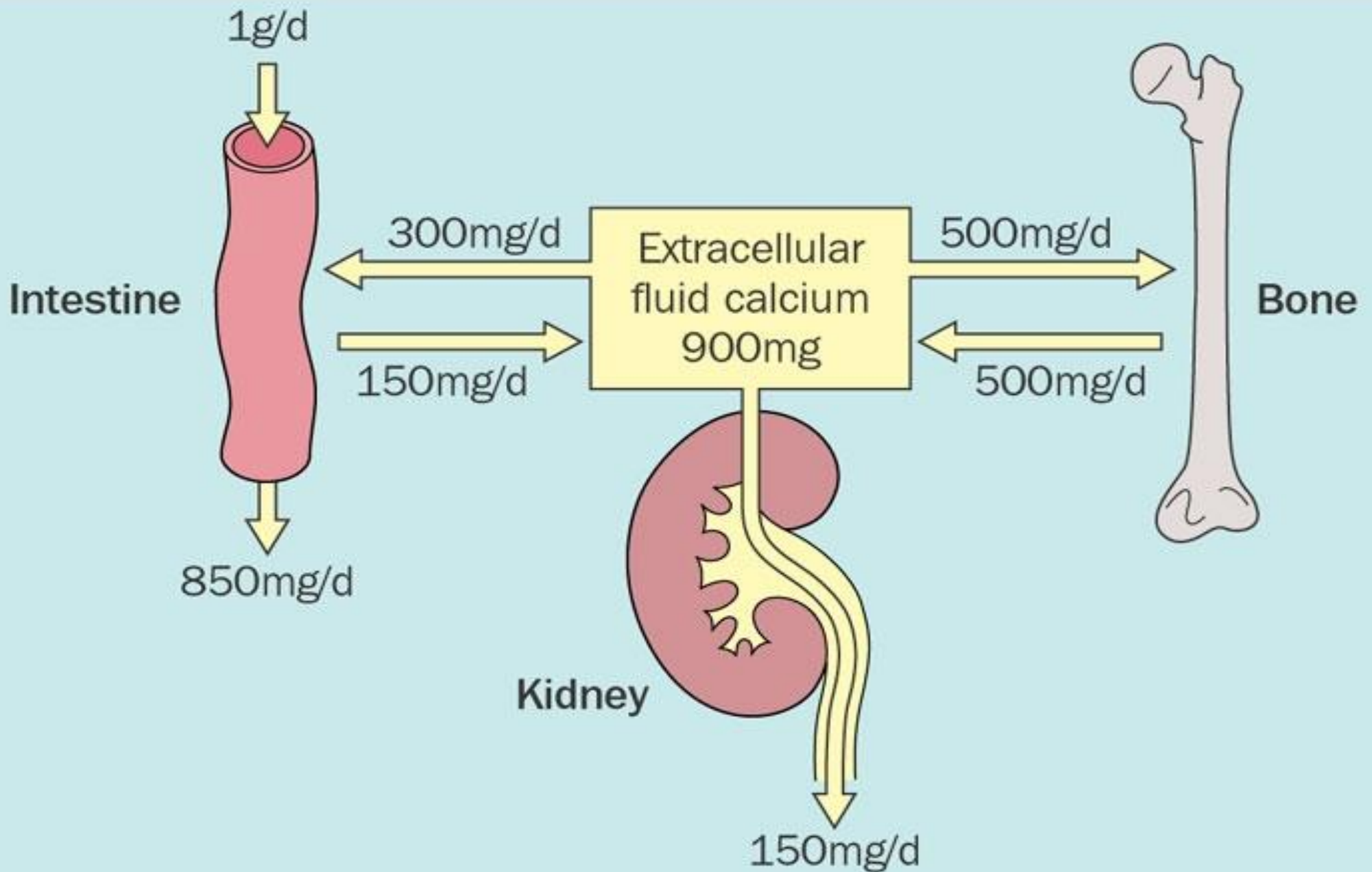
Neuromuscular Disorders, Volume 27, Issue 4, 2017, 331–337

<http://dx.doi.org/10.1016/j.nmd.2017.01.019>

Threats to Bone Health in SMA

- Putting stress on the bones by exercising stimulates formation of bone, which makes the bones thicker, while immobility stimulates resorption of bone, making bones thinner.
- Medications commonly taken by patients with SMA are associated with lower bone density
 - Corticosteroids (Prednisone), PPIs (Nexium, Prevacid), Valproic Acid, Depo-Provera
- Dysphagia can require nutritional supplementation.
- Patients with low bone density have greater needs for calcium and Vitamin D- and the typical American does not meet the recommended allowances.
- Low levels of sex hormones are associated with lower bone density, and these drop quickly at menopause

Calcium fluxes in a normal adult





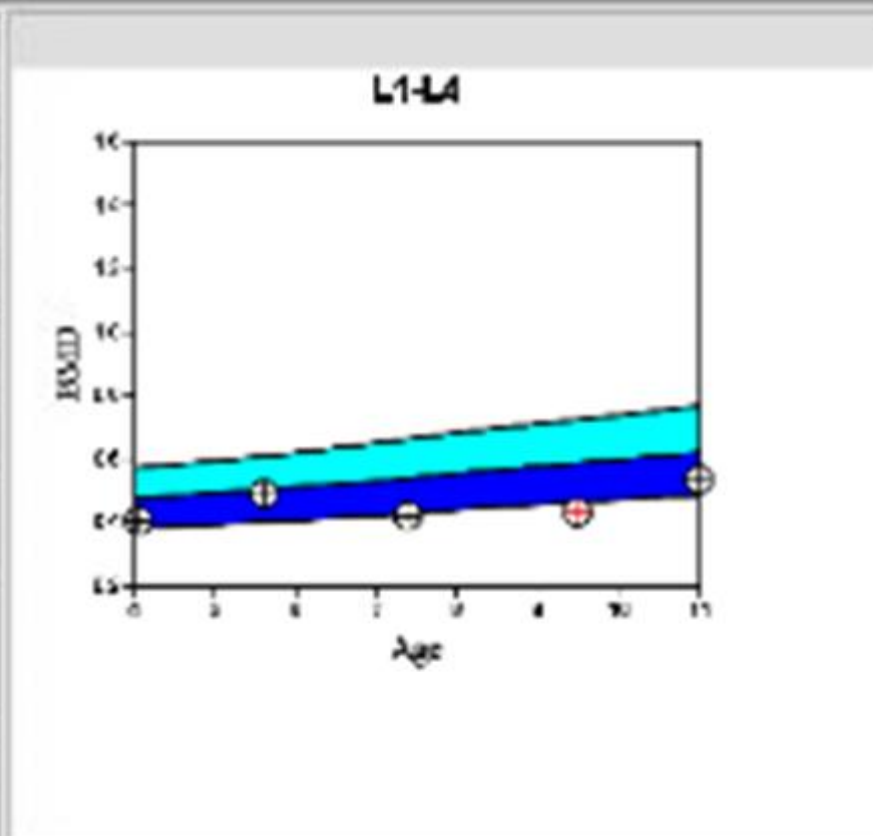
DXA Definitions

- In older adults, bone density is calculated and compared to a reference population (healthy young adult women) using “T-scores”. This is a measure of standard deviation from the mean; with 0 being equal to the mean bone density of the healthy controls
- A T-score more than 2.5 standard deviations below the mean ($T \leq -2.5$) is diagnostic of osteoporosis
- In children and young adults, the patient’s BMD can be compared to age and sex-matched controls using a “Z-score”. A Z-score < -2.0 is commonly used to define low bone mass.
- Osteoporosis = Low Bone Mass + Fragility Fracture



Images not for diagnostic use

117 x 105



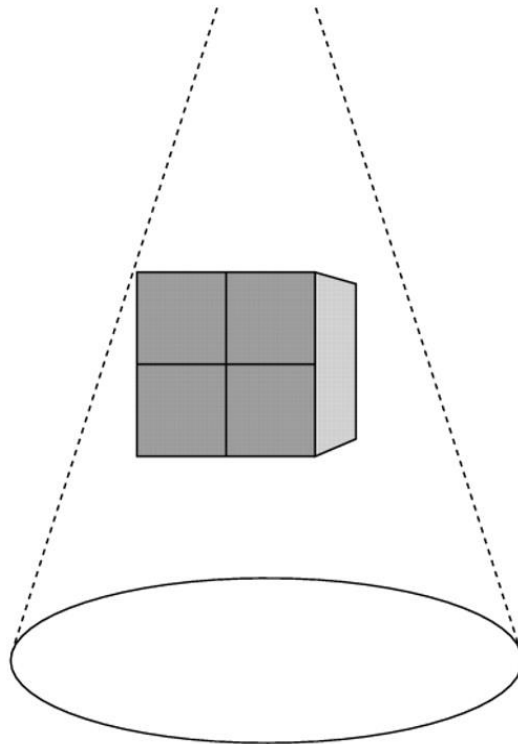
Tanaka vs. White Male; Z-score vs. White Male. Source: FO, DCQ, Holistic White Male.

Our Problems with DXA

- The bones of patients with SMA may be smaller, deformed, or surgically altered which can interfere with measurement.
- Contractures around joints can make positioning of the patient in the DXA machine difficult and lead to false readings.

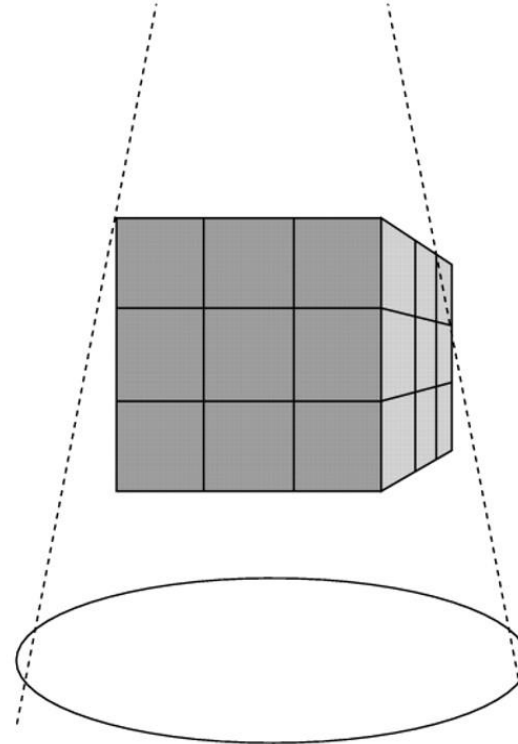
Volumetric vs. Areal Density

$2 \times 2 \times 2 \text{ cm}$



Mineral weight = 16 g
Volume = 8 cm^3
Projected area = 4 cm^2
Volumetric density = 2 g/cm^3
Areal density = 4 g/cm^2

$3 \times 3 \times 3 \text{ cm}$



Mineral weight = 54 g
Volume = 27 cm^3
Projected area = 9 cm^2
Volumetric density = 2 g/cm^3
Areal density = 6 g/cm^2

MY recommendations (part 1)

- All patients should have a diet history for adequate calcium intake (basically 3 servings of dairy daily):
- Blood for Vitamin D 25-OH, targeting >30 ng/mL
- Weight bearing exercise encouraged as able
- DXA every 1-2 years once school aged, or if there has been a fragility fracture
- Avoid Depo-Provera if possible, use oral contraceptive or low dose progesterone (Mirena, Nexplanon)

If DXA is low:

- Electrolytes, Calcium, Phosphorous, Liver, Blood count
- PTH
- TSH
- Celiac Panel
- Urine Calcium, How?
- Questionable:
 - Copper
 - Bone Markers (Osteocalcin, N-telopeptides)?

Treatment of Low Bone Density

- Nutritional
- Positional
- Pharmacologic
 - Bisphosphonates



Nutrition

TABLE 1 Selected Calcium and Vitamin D DRI Values for Children and Adolescents

Age	Calcium, mg/d		Vitamin D, IU/d	
	Recommended Intake*	Tolerable UL	Recommended Intake*	Tolerable UL
0-6 mo	200	1000	400	1000
6-12 mo	250	1500	400	1500
1-3 y	700	2500	600	2500
4-8 y	1000	2500	600	3000
9-18 y	1300	3000	600	4000

* Recommended intake values are the RDA values for children aged 1 year and older and AI values for infants younger than 1 year.

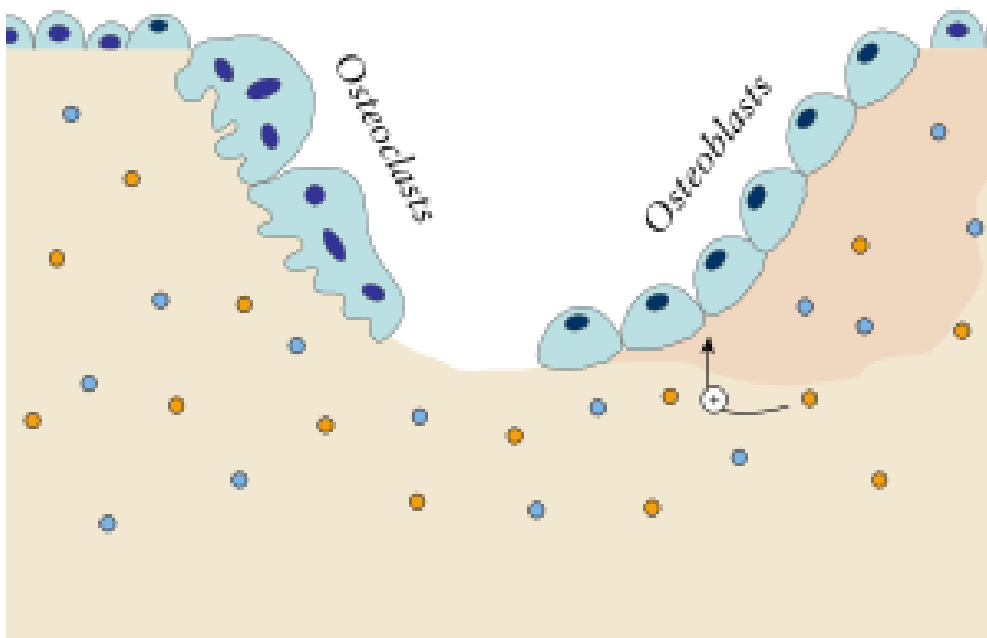


Positional Treatment of Low Bone Mass

- Supported Standing
- Vibrating platforms

Treatment of Low Bone Mass

- Bisphosphonates



- TGF- β , transforming growth factor Beta
- IGF, insulin-like growth factor



Figure 2
Sclerotic metaphyseal lines in distal tibia and fibula.

Bisphosphonates

- Oral- Daily, Weekly, or Monthly
- IV- q3 Months or Annually
- Side Effects:
 - With oral: esophagitis
 - With IV: flu-like symptoms
- Osteonecrosis of the Jaw?
- Atypical Femur Fractures?

MY Recommendations (part 2)

- I **recommend** bisphosphonate for patients with low BMD and an osteoporotic fracture.
- I **recommend** bisphosphonate for patients with an osteoporotic fracture.
- I **offer** bisphosphonate for patients with low BMD and no history of fracture.
- I **do not** think the evidence is strong enough to second-guess the patient/family's decision.