Osteoporosis in Duchenne Muscular Dystrophy

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Division of Endocrinology
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• Background: Bone Basics & Osteoporosis
• Bone Changes and Fracture Risk in Individuals with Duchenne Muscular Dystrophy
• Impact of Glucocorticoid Therapy on Bone in Individuals with Duchenne Muscular Dystrophy
• DMD Care Guidelines 2018 - Screening of Bone Mineral Density and Fractures in Individuals with Duchenne Muscular Dystrophy
• Treatment of Osteoporosis in Individuals with Duchenne Muscular Dystrophy
Bone Basics: Important Cell Types

Osteoclast: Breaks down bone
Osteoblast: Builds bone

Bone Growth: More Osteoblast Activity

Activity of Osteoblast: Increasing Bone Mineral Density
Activity of Osteoclast: Maintenance of Bone Mineral Density

Bone Loss: More Osteoclast Activity

Activity of Osteoblast: Decreasing Bone Mineral Density
Activity of Osteoclast: Decreasing Bone Mineral Density

Bone Basics: Bone Structure

Bone is made up of mainly collagen, calcium phosphate crystals

- Bone mass, can be reported as bone mineral content (BMC, g) or areal Bone Mineral Density (BMD (g/cm²)).
- Peak bone mass is achieved in the second or third decade, depending on the skeletal site

2 main types of Bone microarchitectures: Trabecular and Cortical Bone

Trabecular bone is found in multiple areas including the Hip, Femoral neck, Vertebral body of spine

Cortical bone is found in areas including the dense outer shafts of long bones

Screening for Osteoporosis in Muscular Dystrophy

• Progressive myopathy, a key risk factor for reduced bone strength

Bone Basics: Osteoporosis

- Osteoporosis has been defined by the World Health Organization as a systemic disease characterized by
  - Diffuse Bone loss with increased fracture risk
  - Low Bone Mineral Density (BMD) can be detected
    - Increased osteoclast activity,
    - Decreased osteoblast activity
  - Deterioration of bone micro architecture seen in trabecular bone, cortical bone, and or both
  - This leads to increased Skeletal fragility → Increased fracture risk
Bone Basics: Osteoporosis - Osteoporosis in children

- Osteoporosis in children:
  - Low Z score < -2 and significant fracture history (2 or more long bone fractures before 10 years of age or 3 or more long bone fractures before 19 years of age)
  - One or more vertebral fractures occurring in the absence of local disease or high-energy trauma
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Bone Mineral Density (BMD) Decreases in those with Muscular Dystrophy

QUS Bone Health Data: Control vs Muscular Dystrophy

• Bone Density decreases in those with muscular dystrophy vs control;

Bone Mineral Density (BMD) without Glucocorticoid Treatment

BMD is lower in DMD even without glucocorticoid treatment

- Decreased Muscle tension
- Increased The inflammatory response (e.g. increased IL-6, IL-11, inhibin-βA and transforming growth factor-β, TNF alpha were increased.)
- Increased activation of osteoclastogenesis by altered metabolism in the muscle (for example, activation of nuclear factor of NF κB pathways);
Bone Mineral Density (BMD) Decreases in Both Ambulatory and in Non Ambulatory

Lumbar BMD Decreases in both ambulatory and in non ambulatory

Femur BMD Decreases in both ambulatory and in non ambulatory

BMD Z score decreases more as individuals become non ambulatory (in Non Steroid and Steroid Exposed Patients)

Bone Mineral Density (BMD) Decreases in Non Ambulatory > Ambulatory

QUS Bone Health Data: Ambulatory vs Non Ambulatory

- Bone Density is worse in individuals with muscular dystrophy who become non ambulatory

Fracture Risk in DMD

Fracture risk increase with Loss of Ambulation

Mean age of loss of ambulation (11.2 yrs)

Increased Fracture Probability

Fractures can happen in the long bones or spine and risk increases with age

Long Bones

Vertebrae

Developmental Medicine & Child Neurology 2002, 44: 695–698
Journal of Child Neurology 2016, Vol. 31(9) 1181-1187
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Time to Ambulation Improves with Glucocorticoid Therapy

- On steroids
- No steroids;
- No steroids; but used briefly in past
Spinal Alignment/Scoliosis Improves with Glucocorticoid Therapy

<table>
<thead>
<tr>
<th>Reference</th>
<th>Treatment</th>
<th>Mean age at end of study, y</th>
<th>Untreated group</th>
<th>Treated group</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td>Prednisolone 0.75 mg/kg/qod</td>
<td>10.8 (SD 1.2)</td>
<td>7/77 (9%)</td>
<td>0/66 (0%)</td>
<td>0.02 (0.00-0.38)</td>
</tr>
<tr>
<td>14</td>
<td>Deflazacort (0.6 or 0.9 mg/kg/d)</td>
<td>&gt;13</td>
<td>90%</td>
<td>30/34 (90%)</td>
<td>Could not be calculated</td>
</tr>
<tr>
<td>12</td>
<td>Deflazacort</td>
<td>16 (range 15-18)</td>
<td>16/21 (76%)</td>
<td>5/29 (17%)</td>
<td>0.23 (0.10-0.52)</td>
</tr>
<tr>
<td>5</td>
<td>Deflazacort</td>
<td>13.8 (SD 1.6)</td>
<td>30/34 (90%)</td>
<td>4/40 (10%)</td>
<td>0.03 (0.00-0.48)</td>
</tr>
</tbody>
</table>

Abbreviations: CI = confidence interval; RR = relative rate.

<table>
<thead>
<tr>
<th></th>
<th>Montreal</th>
<th>Toronto</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Treated</td>
<td>Control</td>
</tr>
<tr>
<td>Scoliosis</td>
<td>28/42 (67%)</td>
<td>10/37 (27%)</td>
</tr>
<tr>
<td>Scoliosis surgery</td>
<td>12</td>
<td>0</td>
</tr>
</tbody>
</table>


Glucocorticoids decrease Osteoblast function and increase Osteoclast action
Prolonged Glucocorticoid therapy

• Prednisone: 0.75 mg/kg/day

• Deflazacort: 0.9 mg/kg/day

• Daily vs Intermittent therapy

Despite Steroid therapy, there are continued changes to the bone.
Glucocorticoid (Steroid) Induced Osteoporosis

Glucocorticoid use can lead to the development of decreased BMD

![Graph showing BMD](image)

Glucocorticoid use can lead to the development of increased fracture risk

![Graph showing Z Scores](image)

Fracture Risk
- High Fracture Risk: With Steroids & Prior Fractures
- Moderate Fracture Risk: With Steroids
- Low Fracture Risk

DMD: Risk of Low Trauma Fractures

• Low-trauma fractures are defined as those occurring from a standing height or less.

• A vertebral fracture that occurs without major trauma is an important indication of abnormal bone fragility.

• A Long fracture that occurs without major trauma is an important indication of abnormal bone fragility.
DMD: Risk of Fractures

• A large % with DMD have low-trauma extremity fractures (usually the distal femur, tibia, or fibula), while up to 30% develop symptomatic vertebral fractures

• Boys with glucocorticoid-treated DMD frequently develop osteoporosis, which manifests as low-trauma vertebral or long-bone fractures

DMD: Risk of Fractures

• DMD and Osteoporosis –
  • ~20–60% of boys with DMD have low-trauma extremity fractures (usually the distal femur, tibia, or fibula),
    • Death due to fat embolism syndrome after long-bone fractures has also been reported in boys with DMD

• Vertebral Fractures: true prevalence is probably higher than existing reports suggest (? Up to 40 to 50%?)
  • ~30% develop symptomatic vertebral fractures
  • Vertebral fractures are frequently asymptomatic

Fracture Risk in DMD with and without Glucocorticoid Treatment

Glucocorticoid Tx increases long bone fracture risk but lowers vertebral fracture risk; however risk for vertebral fractures is still high with glucocorticoid therapy.

20 to 30% by ages to 10 to 11

Fracture Risk in DMD with Glucocorticoid Treatment

<table>
<thead>
<tr>
<th>Table 2. Incidents and Age at Time of Long Bone and Vertebral Fractures.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Number of patients (n, %)</strong></td>
</tr>
<tr>
<td>Long bone</td>
</tr>
<tr>
<td>13 (27)%</td>
</tr>
<tr>
<td><strong>Number of incidents (n)</strong></td>
</tr>
<tr>
<td>19</td>
</tr>
<tr>
<td><strong>Mean age at time of fracture</strong> (years, months ± 1 SD)</td>
</tr>
<tr>
<td>11.0 ± 3.10</td>
</tr>
<tr>
<td><strong>Range of ages at time of fracture</strong> (years, months)</td>
</tr>
<tr>
<td>4.0-17.6</td>
</tr>
<tr>
<td><strong>Length of time on corticosteroids</strong> (years, months ± 1 SD)</td>
</tr>
<tr>
<td>4.10 ± 3.10</td>
</tr>
</tbody>
</table>

*3 patients had both long bone and vertebral fractures. *P < .05.

Avg time of fracture on glucocorticoids
Long bone: 4 yrs 10 mo
Vertebral: 6 yrs 7 mo

Risk of fracture Long bone > Vertebral bone; But Risk nearly equivalent by age 12

Fracture Risk in DMD with Glucocorticoid Treatment also Increased in Non Ambulatory

• A Retrospective Study of patients with wheel chair use
  • 33% had at least 1 fracture
    • 249 of 747 cases.
  • Full-time wheelchair use increased the risk of first fracture by 75% for every 3 months of use
    • corticosteroid use, bisphosphonate use, and calcium/vitamin D use did not significantly affect risk in the final adjusted model.

Probability of **Not** Experiencing a fracture

Despite Glucocorticoids, there is an increased risk of experiencing a fracture in non ambulatory patients

While overall time to Vertebral Fracture is lower with Glucocorticoids, Vertebral Fracture do occur on Glucocorticoids.

A latency period of 40 months after commencement of steroids occurred before the first vertebral fracture appeared. However, by 100 months of treatment approximately 75% had sustained a vertebral fracture.

FX risk increases with Steroid use

FX risk increases with age ; > 10

Summary of Glucocorticoid Use & Outcomes

Glucocorticoids have a direct, inhibitory effect on the growth plate. Impairment affected by dose & longer duration of glucocorticoid use. Prednisone-equivalent dose was 0.5 ± 0.6 mg/kg per day. Most pronounced when glucocorticoids are administered daily. A larger number can have growth of less than 4 cm/year.
Steroid Induced Complications

- Weight gain
- Effect on bone mineral density
- Behavioral problems
- Growth failure
- Dyspepsia
- Cataracts
- Immune and adrenal suppression
- Hypertension
- Glucose intolerance

Glucocorticoids treatment
Usage of corticosteroids In DMD: In many patients but not all

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Screening of Bone Mineral Density and Fractures in Individuals with Duchenne Muscular Dystrophy

- PHYSICAL EXAM
- DXA (BONE DENSITY)
- LABS
- X-Rays
Monitoring and diagnosis
At each clinical visit
+ Presence of back pain or fractures

At baseline only (follow up as appropriate)
+ Serum calcium
+ Phosphate
+ Magnesium
+ Alkaline phosphatase
+ Parathyroid hormone

At baseline and annually
+ Calcium/vitamin D intake
+ Spine BMD by DXA
+ Serum 25-hydroxyvitamin D₃

At baseline and follow-up
+ Lateral thoracolumbar spine radiograph:
  • On steroids, every 1–2 years
  • Not on steroids, every 2–3 years

David J Birnkrant eal Diagnosis and management of Duchenne muscular dystrophy, part 2: respiratory, cardiac, bone health, and orthopaedic management Lancet Neurology 2018
Screening for Osteoporosis: DXA

**DEXA scan†**
- Obtain a baseline at:
  - Age 3+ years
  - Start of glucocorticoid therapy
- Repeat annually for those at risk:
  - History of fractures
  - On chronic glucocorticoid therapy
  - DEXA Z score ≤-2

**Spine radiograph‡**
- If kyphoscoliosis is noted on clinical examination therapy
- If back pain is present, to assess vertebral compression fracture
Bone Basics: Dual Energy X Ray Absorptiometry (DXA)

- The National Osteoporosis Foundation indications for DXA in children include: systemic long-term steroids, chronic inflammatory conditions, hypogonadism, prolonged immobilization, recurrent low trauma fractures, and apparent osteopenia on radiographs.

- Baseline DXA examination for patients for whom systemic corticosteroids will be used for more than 2 months or who are at significant risk of osteoporotic fracture.

- DXA of the lumbar spine and hip for pediatric patients with a significant risk factor for osteoporosis.
Bone Basics: Dual Energy X Ray Absorptiometry (DXA) – Measure Bone Mineral Density

DXA can report T score

\[
T_{score} = \frac{\text{Patient's BMD} - \text{population mean peak BMD, matched for sex and ethnic group}}{\text{Standard deviation of population peak BMD, matched for sex and ethnic group}}
\]

T-score- BMD in individuals who have achieved peak bone mass matched for sex and ethnicity (age ≥ 20) not used in children as BMD has yet to peak (T-scores which compare the patient's BMD with that of a healthy young adult should not be used before 20 years of age)

DXA can report Z score

\[
Z_{score} = \frac{\text{Patient's BMD} - \text{population age, ethnic group, and sex matched mean BMD}}{\text{Standard deviation of population age, ethnic group, and sex matched mean BMD}}
\]

Z-score- BMD in individuals age matched, sex matched, race matched; can be used in children < 20 yrs of age

Reduced BMD also is associated with increased fracture risk in children and teenagers, but the data are not sufficient to establish the diagnosis of osteoporosis on the basis of bone densitometry criteria alone

*Pediatrics.* 2016;138(4):e20162398
**Bone Basics: Dual Energy X Ray Absorptiometry (DXA) – Measure Bone Mineral Density**

### Z score

<table>
<thead>
<tr>
<th>Category</th>
<th>Z-score (children)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>0 and above</td>
</tr>
<tr>
<td>At risk for low bone mineral density or bone mineral content for chronologic age</td>
<td>-1.0 and -1.9</td>
</tr>
<tr>
<td>Low bone mineral density or bone mineral content for chronologic age</td>
<td>-2.0 and below</td>
</tr>
</tbody>
</table>

Can be used in children < 20 yrs of age

### T score

<table>
<thead>
<tr>
<th>Category</th>
<th>T-score (adults)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>-1.0 and above</td>
</tr>
<tr>
<td>Low bone mass (osteopenia)</td>
<td>Between -1.0 to -2.5</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>-2.5 and below</td>
</tr>
</tbody>
</table>

Can be used in ≥ 20 yrs of age

*Pediatrics. 2016;138(4):e20162398*
The diagnosis of osteoporosis in children and adolescents should not be made on the basis of densitometric (DXA) criteria alone.

In the absence of vertebral compression (crush) fractures, the diagnosis of osteoporosis is indicated by the presence of both:

- fracture history
- DXA BMD Z-score ≤ -2.0.

A BMC/BMD Z-score > -2.0 does not preclude the possibility of skeletal fragility and increased fracture risk.

Although BMD Z scores are no longer at the forefront of diagnosis, they remain useful to determine the overall trajectory of bone health in an individual child and thereby guide frequency of lateral spine radiographs during the monitoring phase.
Screening for Osteoporosis: X-RAYS

DXA scan
- Obtain a baseline at:
  - Age 3+ years
  - Start of glucocorticoid therapy
- Repeat annually for those at risk:
  - History of fractures
  - On chronic glucocorticoid therapy
  - DEXA Z score < -2

Spine radiograph
- If kyphoscoliosis is noted on clinical examination therapy
- If back pain is present, to assess vertebral compression fracture

David J Birnkrant et al Diagnosis and management of Duchenne muscular dystrophy, part 2: respiratory, cardiac, bone health, and orthopaedic management Lancet Neurology 2018
Screening for Osteoporosis: DMD Care Guidelines 2018: X-Rays

If back pain or ≥0.5 SD decline in spine BMD Z score on serial measurements over 12-month period
• Lateral thoracolumbar spine radiograph

Continue monitoring until signs of bone fragility

David J Birnkrant et al. Diagnosis and management of Duchenne muscular dystrophy, part 2: respiratory, cardiac, bone health, and orthopaedic management. Lancet Neurology 2018
Frequency and Location of Vertebral Fractures In Boys with DMD (Pre-bisphosphonate Treatment)

Wedge fractures are most common in Mid-thoracic region (T7–T9) with Anterior wedge (thoracic) more common. In Thoracolumbar junction, T12–L1 are more common with Crush/Symmetric compression (T-L junction) more common. In Lumbar region, Biconcave (upper lumbar) are more common.


Wong C, Girt M Vertebral compressions fractures: a review of current management and multimodal therapy Multidiscip Health 2013; 6:205-21
Vertebral Fractures In Boys with DMD

• Vertebral fractures can occur irrespective of Z score

  • Vertebral fractures can occur in children who have BMD Z scores \( \leq -2 \text{ SD} \)

  • Vertebral fractures can occur in children who have BMD Z scores \( > -2 \text{ SD} \)

• This observation prompted the International Society for Clinical Densitometry to revise the definition of osteoporosis in a child with a low-trauma vertebral fracture so that cutoff criteria based on BMD Z scores are no longer required to make the diagnosis of osteoporosis
Femur Fractures

• Femur fractures can occur in children who have BMD Z scores ≤ −2 SD

• 15% of children with neuromuscular disorders and extremity fractures will have BMD Z scores for the distal femur > −2 SD

• I.e. need X-rays
Screening for Osteoporosis: DMD Care Guidelines 2018 & X-Rays

• No published studies of DMD or any osteoporotic condition of childhood have assessed the safety and efficacy of medical therapy in preventing the first-ever fracture

• Untreated, vertebral fractures can lead to chronic back pain and spine deformity,

• Leg fractures can cause premature, permanent loss of ambulation

David J Birnkrant eal Diagnosis and management of Duchenne muscular dystrophy, part 2: respiratory, cardiac, bone health, and orthopaedic management Lancet Neurology 2018
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Intervention: Calcium & Vitamin D Treatment

- Adequate calcium and vitamin D intake is important for normal bone mineral deposition.
- Many boys with DMD are vitamin D insufficient or deficient.
- Adequate calcium and vitamin D intake is important for normal bone mineral deposition.
- With Calcium + vitamin D in boys with DMD, there were increases in BMD after 12 months.
Intervention: Calcium & Vitamin D Treatment

Table 2: Recommended daily allowance for calcium and vitamin D [67].

<table>
<thead>
<tr>
<th>Age</th>
<th>Calcium RDA* (mg/d)</th>
<th>Vitamin D RDA* (IU/D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–6 months old</td>
<td>200**</td>
<td>400**</td>
</tr>
<tr>
<td>6–12 months old</td>
<td>260**</td>
<td>400**</td>
</tr>
<tr>
<td>1–3 years old</td>
<td>700</td>
<td>600</td>
</tr>
<tr>
<td>4–8 years old</td>
<td>1000</td>
<td>600</td>
</tr>
<tr>
<td>9–13 years old</td>
<td>1300</td>
<td>600</td>
</tr>
<tr>
<td>14–18 years old</td>
<td>1300</td>
<td>600</td>
</tr>
</tbody>
</table>

*RDA = recommended daily allowance.
**RDAs not established, and thus values are adequate intake reference.

I use 1000 IU of vitamin D3

Treatment of Osteoporosis: DMD Care Guidelines 2018- Bisphosphonates

Bisphosphonates
- Intravenous bisphosphonates for vertebral fracture are indicated
- Oral bisphosphonates as treatment or as a prophylactic measure remain controversial

Treatment: stabilisation phase
Before initiating intravenous bisphosphonate therapy
• Treat calcium/vitamin D deficiency
• Verify normal renal function
When starting intravenous bisphosphonate therapy
• Follow published regimen
• Treat until clinically stable
For monitoring of safety and efficacy of treatment
• Obtain thoracolumbar spine radiograph annually and monitor the following every 6 months:
  • Spine BMD by DXA
  • Serum hydroxyvitamin D3
  • Patient-reported back pain
  • Calcium/vitamin D intake
  • Biochemical markers of bone and mineral ion metabolism

Clinically stable†

Treatment: maintenance phase
Once clinically stable
• Consider continuing intravenous bisphosphonate therapy with titration to a lower dose to preserve gains realised during stabilisation phase
• Vary duration of maintenance therapy depending on bone health status and whether steroid therapy is ongoing
Monitor safety and efficacy of maintenance therapy

No longer clinically stable†

Treatment of Osteoporosis: Bisphosphonates

Pamidronate or Zolendronate can be used

Treatment of Osteoporosis in DMD: DMD Care Guidelines 2018

• DMD and Osteoporosis –
  • No published studies of DMD have assessed the safety and efficacy of medical therapy in preventing the first-ever fracture.

• Current standard is to identify and treat early indications of bone fragility (eg, vertebral fractures) in individuals with chronic illnesses who have little possibility of recovery.

• Current standard is secondary prevention approach has the goal of mitigating osteoporosis progression and promoting recovery among patients presenting with early,

David J Birnkrant et al Diagnosis and management of Duchenne muscular dystrophy, part 2: respiratory, cardiac, bone health, and orthopaedic management Lancet Neurology 2018
Treatment of Osteoporosis: DMD Care Guidelines 2018

• Indications for treatment with intravenous bisphosphonate—
  • the presence of low-trauma vertebral fractures
    • Previously, only back pain or spine deformity prompted a radiograph to identify vertebral fractures necessitating bisphosphonate therapy.
    • Now asymptomatic but nevertheless advanced (ie, moderate and severe) vertebral fractures
      • reshaping of previously fractured vertebral bodies have been reported in boys with DMD
  
• the presence of low-trauma long-bone fractures

• We endorse the use of intravenous (and not oral) bisphosphonates as first-line therapy for the treatment of osteoporosis in patients with DMD
Extra Slides
Scoliosis in DMD: Impact of Glucocorticoids

• Patients not treated with glucocorticoids have a 90% chance of developing significant progressive scoliosis
  • In Non Steroid Tx: Scoliosis ≥ 10° occurred in 85 of 88 patients (97%), ≥ 20° in 78 of 88 (89%) and ≥ 30° in 66 of 88 patients (75%)  

• With Steroid Tx : Daily glucocorticoid treatment has been shown to reduce the risk of scoliosis;

Scoliosis in DMD: Monitoring

- Monitoring for scoliosis
  - Ambulatory phase, with spinal radiography warranted only if scoliosis is observed.
  - In the non-ambulatory phase, clinical assessment for scoliosis is essential at each visit.
    - Baseline Spinal radiography I for all patients around the time that wheelchair dependency begins with a sitting AP full-spine radiograph and LP film.
    - An AP spinal radiograph: annually for curves of less than 15–20°
    - An AP spinal radiograph every 6 months for curves of more than 20°, irrespective of glucocorticoid treatment, up to skeletal maturity

Spinal Alignment/Scoliosis Improves with Glucocorticoid Therapy


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**Table 1**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Treatment</th>
<th>Untreated group, n (%)</th>
<th>Treated group, n (%)</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>Prednisone/deflazacort</td>
<td>41/117 (37)</td>
<td>2/14 (14)</td>
<td>0.39 (0.11–1.44)</td>
</tr>
<tr>
<td>6</td>
<td>Deflazacort</td>
<td>22/24 (92)</td>
<td>6/30 (20)</td>
<td>0.22 (0.11–0.45)</td>
</tr>
<tr>
<td>19</td>
<td>Prednisone</td>
<td>10/19 (53)</td>
<td>2/18 (11)</td>
<td>0.21 (0.05–0.83)</td>
</tr>
<tr>
<td>18</td>
<td>Prednisone/deflazacort</td>
<td>13/45 (29)</td>
<td>11/75 (15)</td>
<td>0.51 (0.25–1.04)</td>
</tr>
<tr>
<td>13</td>
<td>Deflazacort</td>
<td>13/24 (54)</td>
<td>0/30 (0)</td>
<td>0.03 (0.00–0.48)</td>
</tr>
</tbody>
</table>

Abbreviations: CI = confidence interval; RR = relative rate.

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**Figure 1**

Scoliosis Surgeries with time. Scoliosis surgeries decrease with all glucocorticoid treatment.

---

**Figure 2**

Scoliosis Surgeries with time. Scoliosis surgeries decrease with time.
Scoliosis in DMD: Treatment

• Tx for scoliosis
  • Not on Glucocorticoids
    • Posterior spinal fusion is warranted only in non-ambulatory patients who have spinal curvature of more than 20°, and have yet to reach skeletal maturity
  • On Glucocorticoids
    • Posterior spinal fusion is warranted if curve progression continues and is associated with vertebral fractures and pain after optimization of medical therapy to strengthen the bones, irrespective of skeletal maturation.

## Trials with Bisphosphonate Therapy in DMD

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Study type</th>
<th>Patient number</th>
<th>Steroids</th>
<th>Bisphosphonate</th>
<th>Mean Age at Bisphosphonate Initiation</th>
<th>Results</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Houston et al.</td>
<td>2014</td>
<td>Retrospective cohort</td>
<td>39</td>
<td>29 were on prednisone or deflazacort</td>
<td>Alendronate PO</td>
<td>12 years old (no range given)</td>
<td>Z-score trended up at the hip with alendronate, but it is not statistically significant</td>
<td>10 did not receive alendronate, varying dosages of alendronate used</td>
</tr>
<tr>
<td>Sbrocchi et al.</td>
<td>2012</td>
<td>Retrospective observational</td>
<td>7</td>
<td>All but 1 were reported as prednisone equivalents</td>
<td>Pamidronate IV</td>
<td>11.6 years old (range: 8.5–14.3 years old)</td>
<td>Improved back pain and stabilization to improvement in vertebral height ratios for the previously fractured vertebrae</td>
<td>Only patients with vertebral fractures were included in the study</td>
</tr>
</tbody>
</table>
Trials with Bisphosphonate Therapy in DMD

Gordon et al. 2011 Retrospective observational 44 5 prednisone only; 13 changed from prednisone to deflazacort; 26 deflazacort only 11 used pamidronate only; 1 changed from pamidronate to alendronate; 3 alendronate only; 1 clodronate only 12.5 years old (range: 7–23 years old) Survival curve showed improvement in survival rate ($P = 0.005$, log-rank test); also, possible therapy duration effect could be present ($P = 0.007$, log-rank test) Pamidronate was IV; alendronate was PO; clodronate was PO

Atance et al. 2011 Case reports 3 2 on deflazacort Alendronate 10 mg daily PO 11.4 years old (range: 8.1–15.8 years old) Reduced back pain and improved BMD Only 3 patients were reported

Int J Endocrinol. 2015;2015
Trials with Bisphosphonate Therapy in DMD

Hawker et al. 2005 Before-after trial 23 All on deflazacort Alendronate 0.08 mg/kg/d old (range: 6.9–15.6 years old) 10.8 years old Positive effect on BMD and Z-scores, better BMD outcome when given early in the course of disease

Also received 750 mg daily calcium and 1000 IU vitamin D
Trials with Bisphosphonate Therapy in DMD

• randomized participants with a spine Z-score less than -1.0 to risedronate plus calcium and vitamin D → improved BMD in spine & Whole body

<table>
<thead>
<tr>
<th>Risedronate (plus calcium and vitamin D supplementation)</th>
<th>Control (calcium and vitamin D supplementation alone)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median spine Z-score (range)</td>
<td>Baseline</td>
</tr>
<tr>
<td>-1.75 (-1.2 to -3.5)</td>
<td>-1.75</td>
</tr>
<tr>
<td>Median whole-body Z-score (range)</td>
<td>Baseline</td>
</tr>
<tr>
<td>-1.95 (-0.5 to 2.7)*</td>
<td>1.3 (-1.0 to 2.5)</td>
</tr>
</tbody>
</table>