



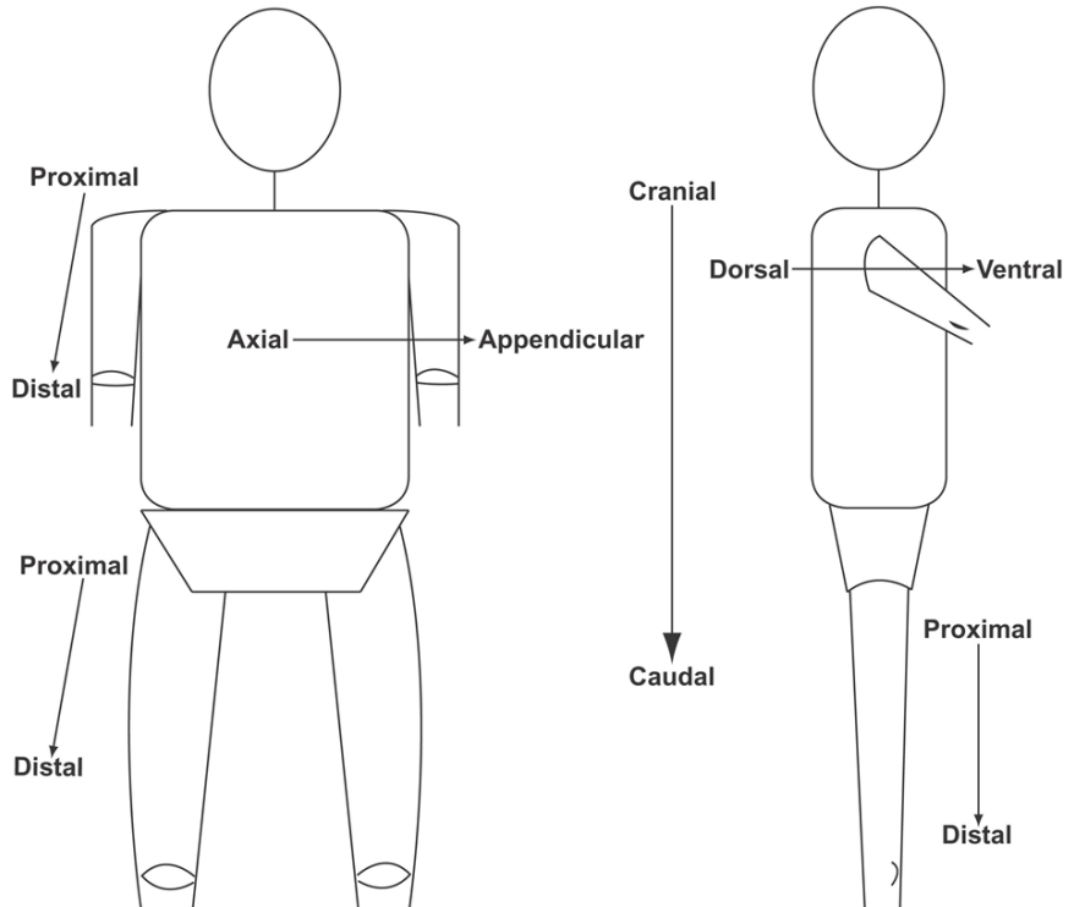
# What is FOP? The science for non-scientists

## Insights from natural history and clinical studies

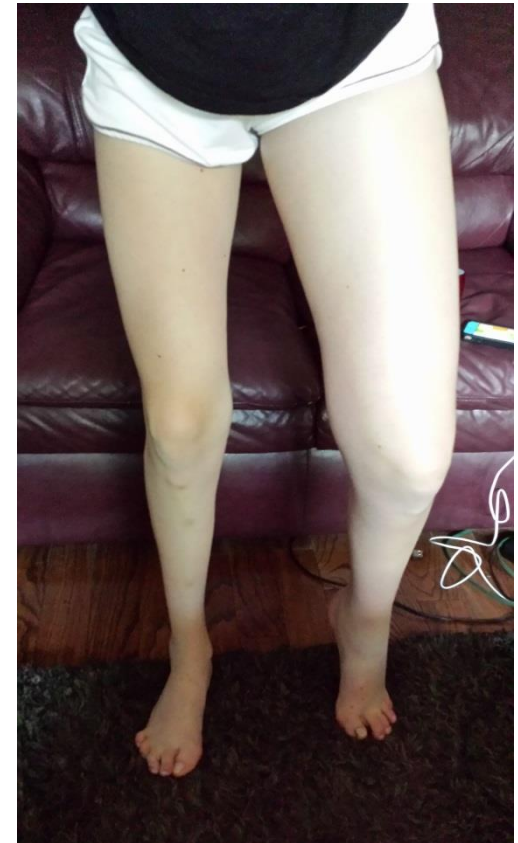
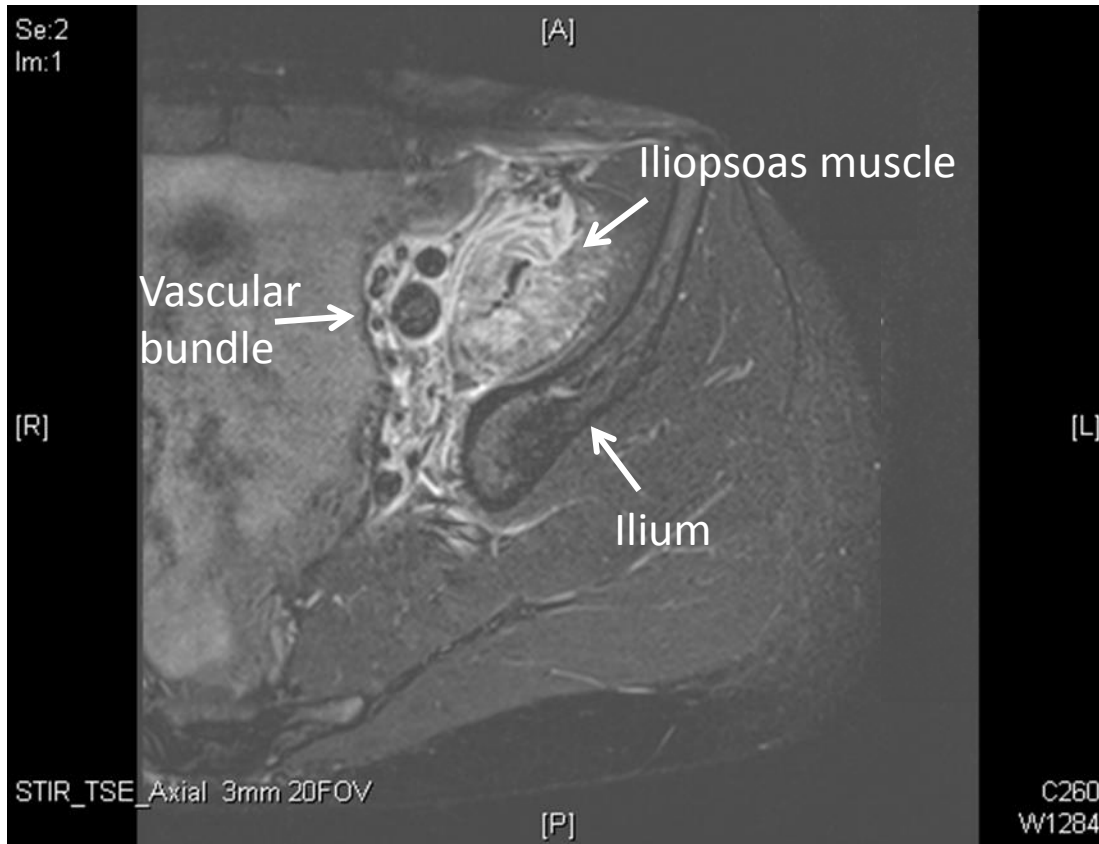
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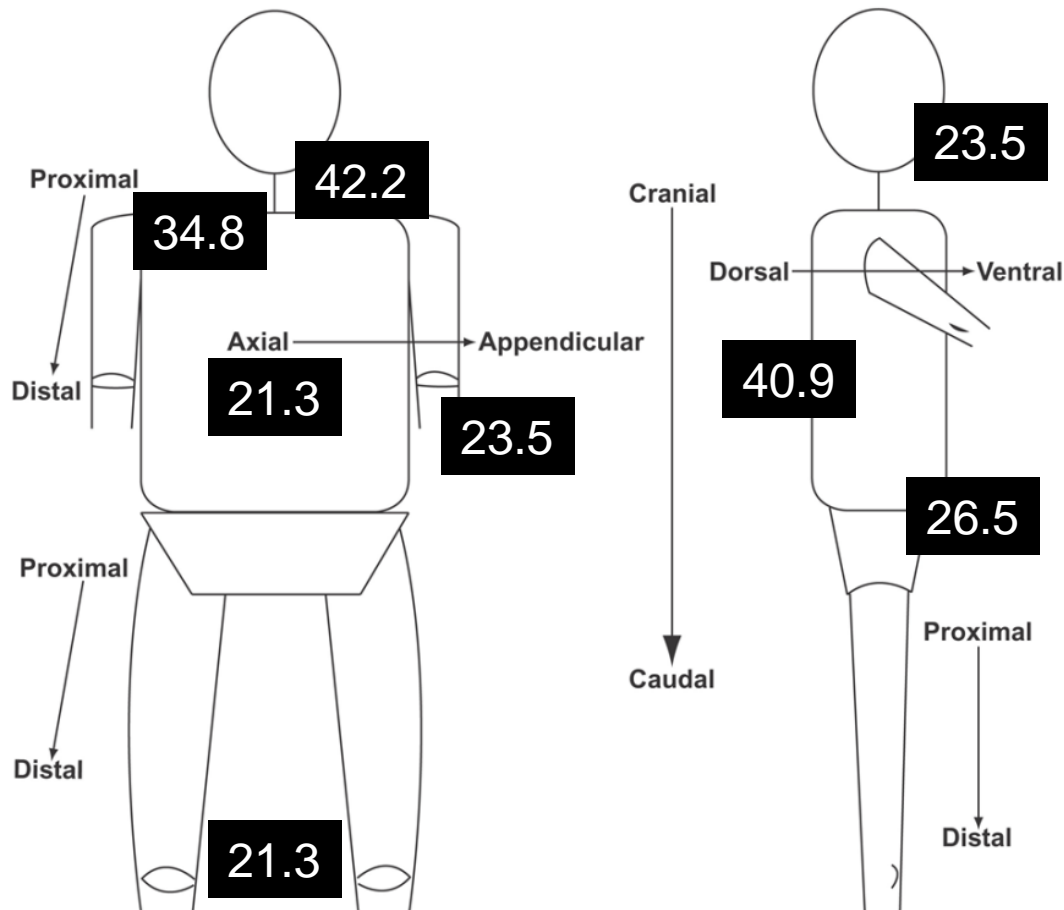
# Patterns of FOP progression



# FOP progression via flare-up



# FOP progression without flare-ups

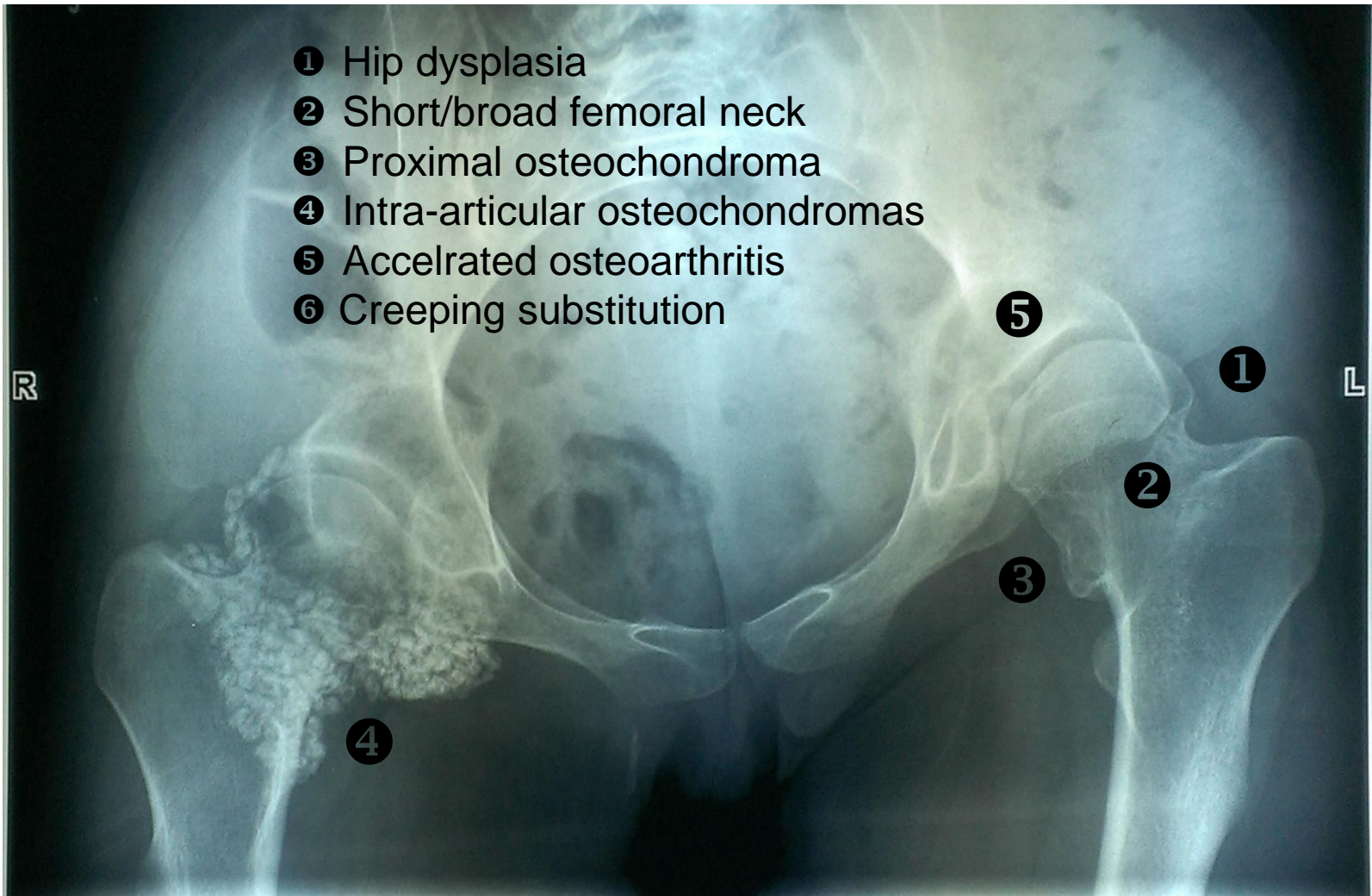


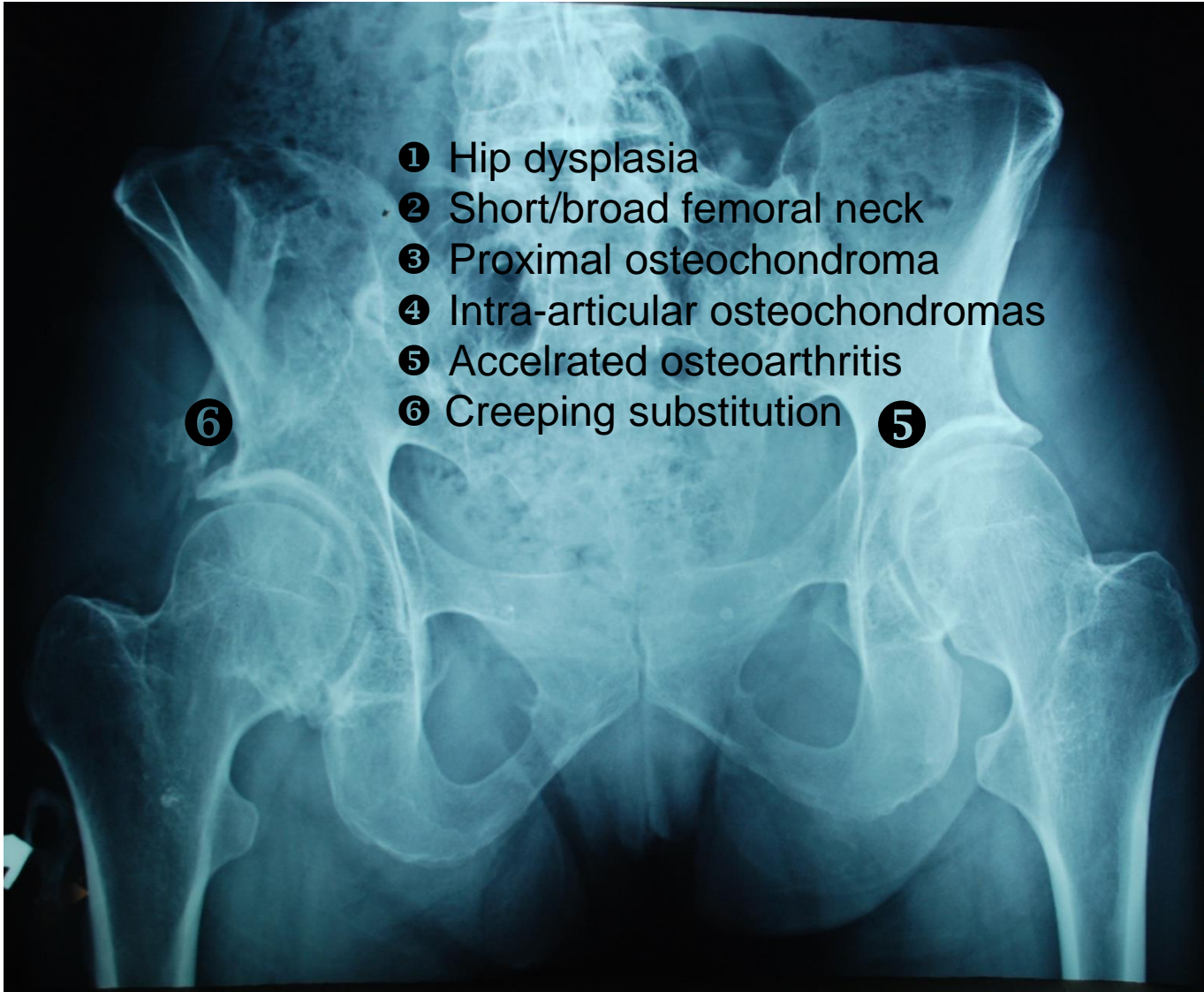
Almost half of all patients (46.9% [230/490]) reported disease progression without flare-up symptoms. Body regions where over 20% of patients who reported such progression are shown.

Why might FOP progress  
in the absence of flare-ups?

# Possible causes in the hip

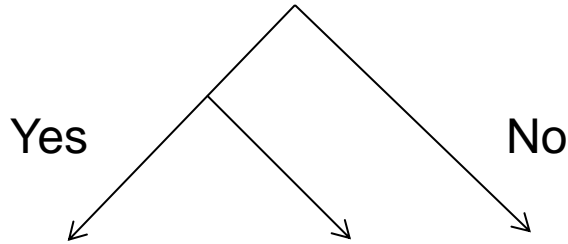
1. Hip dysplasia
  - Flattening of acetabula with failure to cover both femoral heads
  - Late discomfort and stiffness of one or both hips
2. Short/broad femoral necks
  - Possibly a source of impingement
3. Proximal femoral osteochondromas
  - Possibly a source of impingement and synovitis
4. Intra-articular synovial osteochondromas
  - Can be the source for very painful episodes
5. Accelerated osteoarthritis
  - Can cause progressive pain and loss of joint movement
6. Creeping substitution
  - Continued progression of fibroproliferative or cartilage stages to ossification after resolution of a clinical flare-up







# Flare-up symptoms



Soft tissue edema

None  
Minimal

Substantial

No HO

HO

- Joint dysplasia
- Accelerated arthritis
- Joint impingement syndromes
- Intra-articular synovial osteochondromas
- Worsening scoliosis
- Creeping substitution

Progression of FOP

# Implications for clinical trials

- Successful episodic treatment of flare-ups (or their prevention) may not be sufficient to completely prevent long term complications of the disease
  - E.g., embryonic effects on specifying the fate of articular cartilage may be fixed
- However, specific therapeutic down-regulation of BMP activity *may* be effective at preventing disability unrelated to heterotopic ossification if targeted early
- Markers of soft tissue inflammation, including edema, will be important to identify flare-ups that result in HO formation