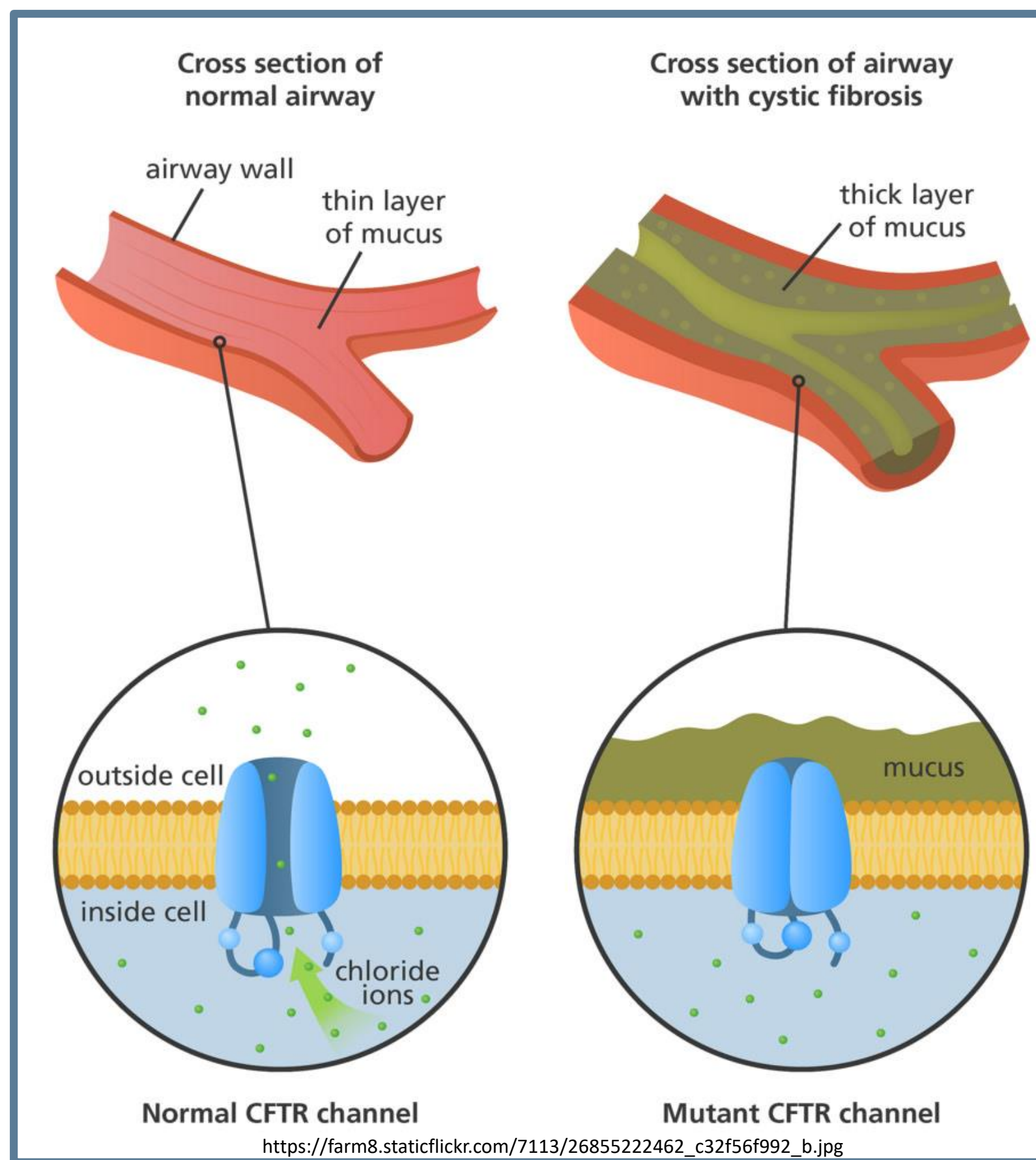


Identifying Cystic Fibrosis (CF) Skeletally: A Proposed Differential Diagnosis

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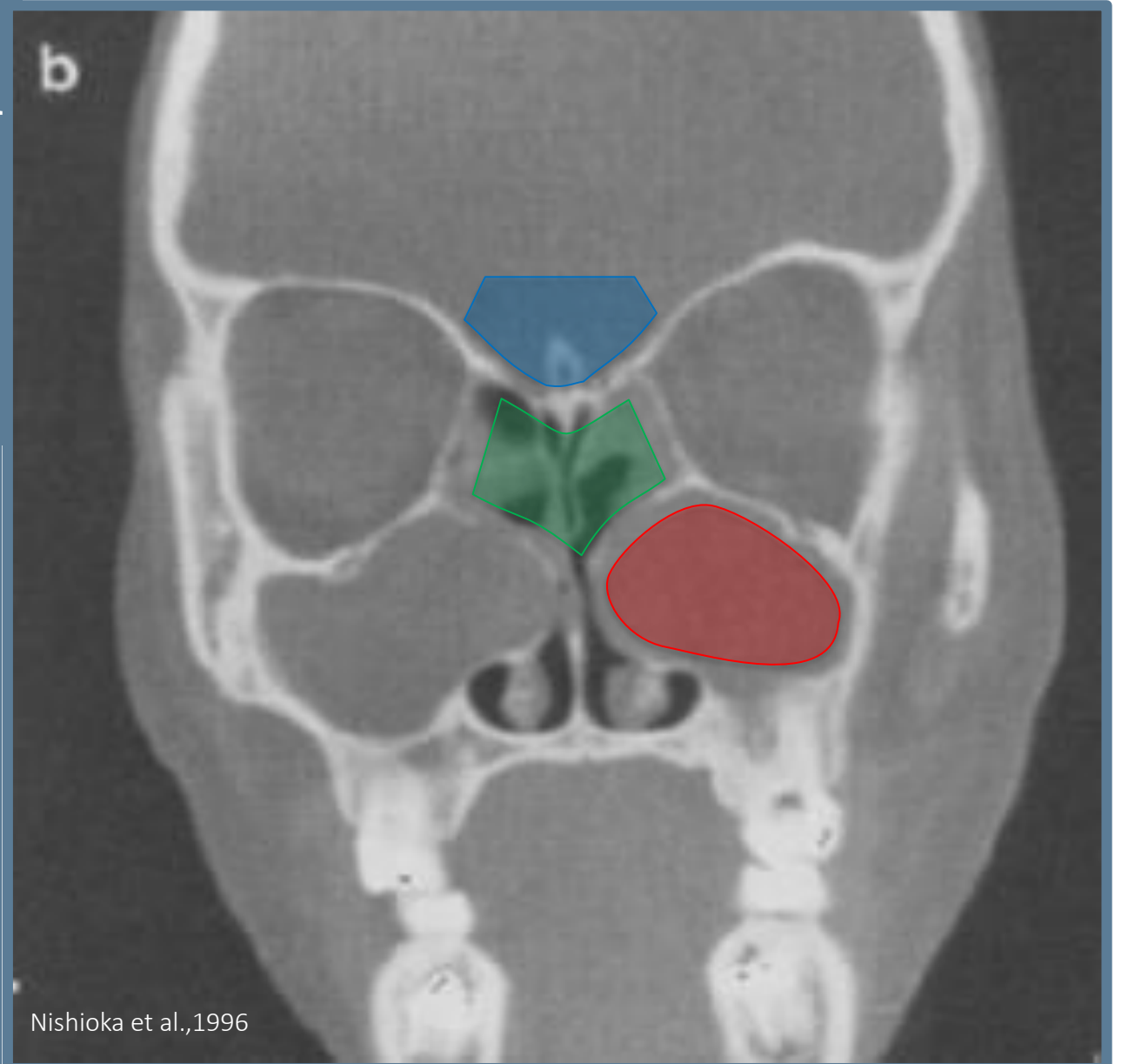


What is Cystic Fibrosis?

- A common genetic disorder in people of European descent
- Linked to over 2,000 different mutations
- Affects approximately **70,000 individuals**
- Mutant CFTR channel fails to regulate salt diffusion in and out cells (Farrell et al., 2017)
- Passageways of lungs and digestive tract blocked by mucus
- With treatment, CF patients can survive into their 50s

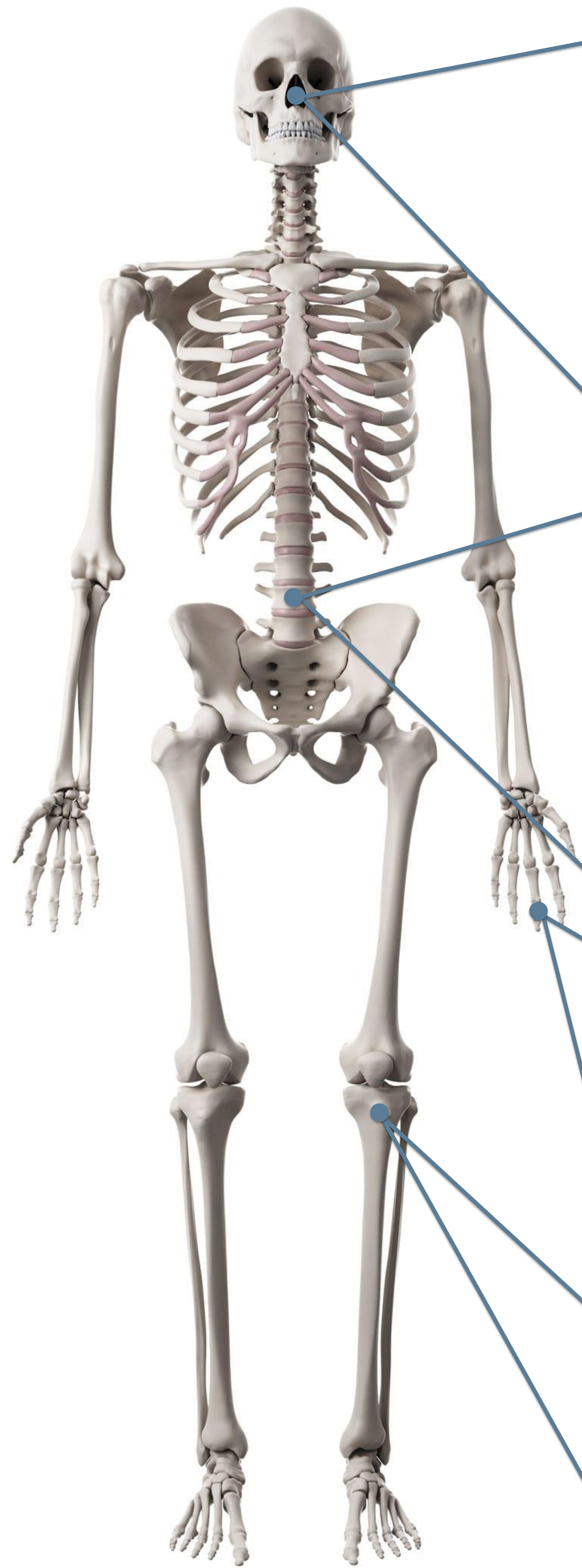
Chronic Sinus Inflammation (Sinusitis) Causes Unique Bony Pathologies in CF

- **Medial bulging of the lateral nasal wall and frontal sinus agenesis is unique to CF patients**
- **expansion of medial wall of maxillary sinus**
- **reduction or absence of ethmoid partitions**
- **abnormal pitting and spicules on sinus walls** (Nishioka et al., 1996; Cauwenberge and Watelet 2000; Ramsey and Richardson, 1992; Schraven et al., 2011; Wang et al., 2005; Gentile and Isaacson, 1996)



Why is Skeletal Diagnosis Important?

- **Forensics** – as life expectancy increases, CF may become more relevant in forensic casework for identification of unknown remains
- **Bioarchaeology** – in coastal populations of European ancestry, an individual with a less-severe gene mutation might have survived into early adulthood
- **Paleopathology** – to add to the field of understanding bone diseases



Kyphosis and Vertebral Compression are Common and Early Onset in CF Patients

- **Young CF patients have kyphotic angles higher than 60-year-old controls and decades earlier** (Aris et al., 1998)
- Spinal deterioration accelerated by three decades (Aris et al., 1998)
- **Atraumatic vertebral deformity present in 17-51% of CF patients**
- 12% prevalence in non-CF 50- to 79-year-old Europeans (Elkin et al., 2001; Garcia et al., 2011)



Digital Clubbing Is a Common Symptom of CF, but Its Skeletal Effects Have Not Been Studied

- **Clubbing presents in 15% of all CF patients, and is correlated with disease severity** (Cohen et al., 1986; Lemen et al., 1978; Pitts-Tucker et al., 1986)



Low Bone Density and Poor Nutrient Uptake Lead to Decreased Stature in CF Individuals

- **Shorter stature by about 6 cm** (Aris et al., 1998)
- **Early onset osteopenia and osteoporosis** (Henderson and Madsen, 1996)
- **40% of CF children below the fifth percentile in height** (Landon et al., 1984; Aris et al., 1998)

Signs and Symptoms	Skeletal Indicator	Prevalence CF (non-CF)
Chronic Sinusitis	Irregular bony growths	74-100% (14%)
Frontal Sinus	Agenesis	More research needed
Maxillary Sinus	Medial bulging of lateral nasal wall	More research needed
Digital Clubbing	Need skeletal quantification method	15% (1%)
Kyphosis	Vertebral fractures, compression and abnormal curvature	17-51% (12%)
Bone density loss	Early onset osteopenia/osteoporosis	50-70% (25%)
Stature	Shorter by ~6 cm	Need population specific data
Chest Diameter	Need skeletal quantification method	More research needed
Rib Fracture	Microcracking of ribs and delayed healing of fractures	More research needed

While low bone density, fractures, and short stature can co-occur due to other etiologies, we feel the combination of the above factors with evidence of chronic sinusitis and digital clubbing makes a strong case for the considering a skeletal diagnosis of CF. Future work is needed to quantify the certainty of diagnosis using these criteria.

Acknowledgments

Thanks to Justin Seleska for inspiring this project. I would like to thank Dr. Beasley for including me on this project, and Dr. Mundorff for advocating for my involvement. Thanks to all reviewers and editors for their contributions.

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