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Genes leave some kids prone to weakness in wrist bones

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Pediatric researchers have discovered gene locations affecting bone strength in wrist bones, the most common site for fractures in children. Children who have those genetic variants may be at higher-than-average risk of wrist fractures, and could especially benefit from activities and diets that promote bone strength.

"Other genetic studies have analyzed bone strength in adults and over the whole skeleton, but this study focused on genetic influences specific to childhood, which is when future bone density is established," said co-study leader Struan F.A. Grant, Ph.D., a genomics expert at The Children's Hospital of Philadelphia (CHOP). "Furthermore, this research was the first genome-wide study in children to examine bone strength of the wrist, a particularly vulnerable site for fractures."

Grant and colleagues, including first author Alessandra Chesi, Ph.D., and co-study leader Babette S. Zemel, Ph.D., also from CHOP, published the study online June 3 in *Human Molecular Genetics*.

Zemel, the director of CHOP's Nutrition and Growth Laboratory, is an expert on childhood growth, body composition, energy expenditure and bone density. "Between 30 and 50 percent of children have at least one fracture by adolescence, so identifying and understanding genetic risk factors will help us design more effective preventive strategies."

The study team performed a genome-wide association study on a cohort of 1,399 healthy children drawn from a larger group, the Bone Mineral

Density in Childhood Study. The cohort was 53 percent Caucasian, 22 percent African American and 14 percent Hispanic, comprising 720 girls and 679 boys from four pediatric hospitals. The researchers also did a replication study in an independent cohort of 486 Caucasian children.

The study focused on genetic signals associated with bone strength. As indicators of bone strength, the team used dual energy X-ray tools (DXA scans) to measure areal bone mineral density and bone mineral content.

The team found two distinct but gender-specific gene signals. For girls, lower bone strength was associated with genetic variation within the CPED1 gene, a locus previously reported for other bone sites in both children and adults. In boys, the team found a novel signal on chromosome 9. In boys, this pattern held for both Caucasians and African American children. In the girls, the gene signal appeared only in Caucasians.

"Further studies are needed to determine the precise culprit mechanisms at these newly established genetic locations," said Grant. He added that later research should also reveal more about the functional roles of these and other bone-related genes not yet identified.

Zemel stressed that better understanding of the genetic landscape will help guide future recommendations for children carrying gene variants that raise their risk of bone injury. "We already know some of the modifiable, nongenetic factors that we can encourage to improve bone strength in children: a healthy diet, vitamin D and getting physical activity," she said. "These factors may be especially important in children who carry genetic risks for fractures."

More information: "A Trans-ethnic Genome-wide Association Study Identifies Gender-Specific Loci Influencing Pediatric aBMD and BMC at the Distal Radius," *Human Molecular Genetics*, published online June

3, 2015. doi.org/10.1093/hmg/ddv210