

Concept Paper Template

Is repeated childhood fracture is related to poor bone or body composition in middle age?

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Please describe your proposal in 2-3 pages with sufficient detail for helpful review.

Objective of the study:

To determine the association between children (<18 years) who suffered multiple fractures (>1) compared to those who did not suffer from multiple fracture on abnormal bone and body composition at age 45y.

Data analysis methods:

The original dataset relating to childhood fracture history was developed by Jones et al. ¹ and methods used to determine the fracture history were as follows: At age 5 years (phase 5) the parents were asked to provide information on all injuries requiring medical attention suffered by their children during the first 5 years of the child's life. This covered inpatient, outpatient and general practitioner treatment. Thereafter injury information was collected at each phase and covered the period of time since the last assessment. Information was obtained regarding the nature of the injury and the age of the child when the injury occurred. All fractures were given a separate code and site of fracture was identified. No information concerning the severity of trauma associated with individual fractures was available and no attempt to evaluate the possible contribution of underlying medical conditions or medication use to fracture occurrence was made. Cases were censored on the first occasion they did not attend for assessment or failed to complete the questions about injuries. To be included they had to have completed the questions about injuries sustained since birth at age 5 years. This dataset was combined with data collected (n=904) on bone and body composition at Phase 45 and two fracture groups were created for the current analyses; children who suffered from more than 1 fracture (Repeat fracture, (n=896) and those who suffered from 1 or less (n=896). Regression was used to analyse the association between repeat fracture and body composition and bone density at age 45. Statistical analyses were performed with STATA (release 6, StataCorp, College Station, TX).

Variables needed at which ages:

- Fractures prior to age 18 (childhood): This dataset is already available within the Dunedin School of Medicine's Bone and Body Composition Unit as it was created for the publication titled "How Many Children Remain Fracture-Free During Growth? A Longitudinal Study of Children and Adolescents Participating in the Dunedin Multidisciplinary Health and Development Study. (2002). Jones I.E., Williams S.M., Goulding A.
- Age 45 DXA body composition variables (lean mass, fat mass, % body fat, appendicular lean muscle index) and DXA hip bone density variables (hip BMD, hip BMC, hip T-scores, hip z-scores).
- Other variables which are known to affect fracture history and bone health including birthweight, childhood and adult SES, impulsivity, sport involvement, adult self-report fracture history, abuse, maltreatment, Vit D, serum calcium.

Significance of the Study (for theory, research methods or clinical practice):

Personal fracture history is one of the strongest predictors of future fractures,² yet current practice guidelines, including commonly used osteoporosis risk scores, ignore fractures that occur during childhood.^{3, 4} Several years ago our lab investigated the incidence of childhood fractures in the Dunedin Study cohort and demonstrated that although about half of the sample remained fracture-free during childhood almost a quarter of boys and 15% of girls suffered from multiple fractures.¹ The reasons some children fracture repeatedly are unclear. These children may have especially fragile skeletons or they may be accident-prone or conversely these fractures may be the price of risk-taking behaviors that could optimize bone strength during growth.¹ While the majority of adult fracture research has focused on determinants of fractures with aging,^{5, 6} fracture risk has two peaks with an earlier peak during puberty.^{7, 8} Thus, it remains unclear whether childhood fractures are related, in part, to transient reductions in bone strength during rapid growth or to skeletal deficits that will track into adulthood. Because achieving optimal bone strength early in life likely predicts lower fracture risk later in life,⁹ it is critical to identify events during childhood that foreshadow suboptimal peak bone strength in adulthood.

If poor adult bone health has its antecedents in childhood so to could abnormal body composition such as low muscle mass and strength (sarcopenia) or low muscle and low bone (osteosarcopenia) and high fat mass. Recent research has demonstrated a close relationship between skeletal muscle mass and bone mass that exists throughout the lifecourse.¹⁰ Children who fracture have lower muscle mass and higher fat mass^{11, 12} and during growth bones mineralize in response to changes in lean mas.¹³ In adults, age-related loss of muscle mass (sarcopenia) is intricately linked with changes in bone mass.¹⁴ Osteoporotic fracture accelerates

the onset of sarcopenia in older adults and sarcopenia increases the risk of falls and fractures;¹⁵ thus, these two conditions feed perpetually into each other. Obesity, once believed to be protective of bone and muscle mass, is increasingly linked to deterioration in bone and muscle, especially with aging.¹⁶

Thus, identifying children who fracture repeatedly could have important clinical ramifications to identifying those at risk of future fracture and abnormal body composition if the skeletal deficits track into adulthood and predict changes in muscle and fat mass. Although some observational studies have demonstrated that bone size and shape tend to track throughout life^{17, 18} and cross-sectional studies have found that volumetric bone mineral density (vBMD) and bone structure are worse in young adults,^{19, 20} with prior fracture, no longitudinal study has tested whether individuals who repeatedly fracture in childhood have altered bone and/or body composition in adulthood. If skeletal deficits in children and adolescents with repeat fracture persist into adult life and predict abnormal body composition, then individuals with a history of such fractures may need to be more aggressively monitored for subsequent skeletal and body composition complications.

Therefore, we aim to examine whether study members who sustained more than one fracture during childhood (at age <18 years) have alterations in bone density, and/or body composition compared to those who did not repeatedly fracture during childhood. We also plan to conduct sensitivity analyses to determine whether there were any differences between those with no history of fracture, <2 fractures or 2 or more fractures, while controlling for other measures known to affect bone and body composition including demographics including birthweight, childhood and adult SES, sport involvement, impulsivity, adult fracture history, maltreatment and child abuse.

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